HOUSE OF LORDS

European Union Committee

22nd Report of Session 2008–09

The revision of the EU Directive on the protection of animals used for scientific purposes

Volume II: Evidence

Ordered to be printed 3 November 2009 and published 10 November 2009

Published by the Authority of the House of Lords

London : The Stationery Office Limited
£price

HL Paper 164–II

CONTENTS

Written Evidence

Supplementary Written Evidence was also received from:

Animal Defenders International (ADI)
British Union for the Abolition of Vivisection (BUAV)
Medical Research Council and the Wellcome Trust
Royal Society for the Prevention of Cruelty to Animals
UK Biosciences Federation

This has not been not been printed, but is available for inspection at the House of Lords Record Office (020 7219 5314).

We would like to take the opportunity to thank all our witnesses for their submissions to our inquiry.

NOTE:
The Report of the Committee is published in Volume I (HL Paper 164-I)

Minutes of Evidence

TAKEN BEFORE THE SELECT COMMITTEE ON THE EUROPEAN UNION (SUB-COMMITTEE D)

WEDNESDAY 3 JUNE 2009

Present	Brooke of Alverthorpe, L	Palmer, L
	Brookeborough, V	Sewel, L (Chairman)
	Caithness, E of	Sharp of Guildford, B
	Jones of Whitchurch, B	Ullswater, V
	Livsey of Talgarth, L	

Examination of Witness

Witness: Ms Susanna Louhimies, Policy Officer, Directorate-General Environment, European Commission, examined.

Q1 ***Chairman:*** Welcome. First of all, thanks very much for agreeing to come and talk to us and help us with our inquiry into this complex and potentially controversial subject. Can I start off by explaining a couple of things. This is a formal evidence-taking session of the Sub-Committee, which means that a full shorthand note will be taken. You will be sent a copy of that shortly and you will be able to revise it in terms of any sort of minor errors that have crept in. The other thing is that we are being broadcast. Do not be concerned by that because we have never actually had any evidence that anybody ever listens to it. So there we are. I wonder if I could start, first of all, by inviting you, if you want, to make any sort of general opening statement, or would you prefer to go into a question and answer routine? Over to you, frankly.
Ms Louhimies: Thank you, my Lord Chairman. First of all, good morning everybody. My name is Susanna Louhimies; I work for the European Commission in the DG Environment, in the Chemicals Unit, and I am the Policy Officer dealing with the protection and welfare of animals used for scientific purposes. The Commission is delighted to be here to be able to give evidence to you and give some clarity on questions that might need further explanation. We feel that our proposal is based on very strong scientific evidence and full stakeholder consultation. We also carried out an impact assessment which was then confirmed later on by the stakeholders. Finally, maybe, just one word about the process and where we are, at this moment in time. We have had the Parliamentary First Reading report adopted at the beginning of May and, a little bit exceptionally, the Council work is not as advanced as it normally is at this stage. Therefore, we are just finishing the first rounds of discussions at the Council. We do not have a lot of Member States' firm positions yet because lots of them are still in the middle of their internal consultation. The last point, maybe, is to say that the Swedish Presidency is putting this very high on their agenda and they would actually try to reach some kind of early Second Reading political agreement.

Q2 ***Chairman:*** What would that mean in terms of the calendar? When would you expect an early Second Reading to emerge?
Ms Louhimies: The way the Swedish have drafted the calendar, it looks like the December Agriculture Council is always reserved for the fishery matters, and therefore the work should really be carried out before the 19–20 November Agriculture Council. So it means work between September, when the Parliament is back and once they have decided on the rapporteur, until the end of October. So very hard work.

Q3 ***Chairman:*** Is the fact that you are going to have a new Parliament and new Commission likely to raise any problems?
Ms Louhimies: The new Parliament has the discretion that they can accept or they can refuse the result of the First Reading. It is quite uncommon, and because it got very high support at the First Reading it is unlikely to happen, but can happen.

Q4 ***Chairman:*** I wonder if I could ask some general questions to begin with. I suppose the first question is: why is there a need to go ahead with something like this? What is the general justification and reason for these proposals?
Ms Louhimies: Thank you, my Lord Chairman. It is a very good question and asked often. The reasons are three-fold: firstly, the current piece of legislation we have in place is old—quite out-dated; it is open to interpretation because it is based on a Council of Europe Convention text, and it is rather political than regulatory in nature; it lacks main elements like

ethical evaluation and authorisation of procedures using animals, and it does not even explicitly mention the 3Rs principle—replacement, reduction and refinement. So we need to get that to the level that we are at today. Secondly, because of that reason, a lot of the Member States have adopted national legislation which widens the gap of standards between the different Member States in the EU, and that is, of course, contrary to the harmonisation of the internal market, and we have some evidence later on about that. Finally, obviously, the legislation has to follow the evolvement of the understanding of the humane and ethical treatment of animals that we have today compared to what the situation was in the late-1970s.

Q5 ***Chairman:*** And the objectives?
Ms Louhimies: Again, three-fold: we have to make sure that we are harmonising the internal market; secondly, we want to strengthen the protection of those animals we still need to use, because we do need them still; and there are not enough scientific alternative replacement methods available. So to increase the animal welfare and then, through the ethical evaluation, specifically, to reduce the numbers that we use today to the minimum necessary.

Q6 ***Chairman:*** You have mentioned the famous 3Rs—replacement, reduction and refinement. What is your idea of full implementation of replacement, reduction and refinement?
Ms Louhimies: On the 3Rs, we have a little change in this Directive to the *aspiration* that the current Directive has. The new Directive makes sure that the 3Rs cover also the breeding and housing. Originally, it was limited to the use of animals and we looked at how we can replace, reduce or refine their use, but especially the refinement element is now making sure that it covers the areas of breeding and housing of animals. The 3Rs implementation is very much linked to the ethical evaluation. That is the moment when it will be scrutinised. By systematic implementation of the 3Rs we will increase animal welfare but we also probably will be able to increase the value of the scientific results of the procedures.

Q7 ***Chairman:*** What is your feeling on how far reduction, replacement and refinement has gone so far? Or is it patchy throughout the Member States?
Ms Louhimies: There are two aspects: what the Member States are doing and how far we have come. I think we are doing a lot in the EU today; I think Europe is seen as the leader in the area of alternatives and the implementation of the 3Rs. Different Member States put in different efforts. We have a very good example from the UK: lots of efforts put into the 3Rs—the NC3Rs centre, for example. I think we can harmonise and get more resources into it through this revision as well.

Q8 ***Lord Brooke of Alverthorpe:*** If I may just follow up on your comments about the 1986 Directive, you said that this led to individual country legislation which varied and, in fact, the gap between some widened. How can you ensure that the new legislation which will be put in place does not lead to a further widening in standards?
Ms Louhimies: The areas where we have differences today are to do with authorisation—authorisation of experiments—and the housing and care standards. These have been the two biggest areas where there has been a widening of gaps, and that has led to problems where, for example, the authorisation time, from the time of application to receiving the authorisation, can vary anywhere up to 100 days. Therefore, the different operators in the different Member States are on a different footing. If we were to adopt the proposal as it is, we are looking at putting authorisation throughout the 27 Member States; we are looking at the minimum requirements for housing and care standards throughout the 27 Member States, and within the authorisation we are looking at setting time limits. So there are several measures that would streamline the current situation where the biggest differences are.

Q9 ***Lord Brooke of Alverthorpe:*** How do you make sure it is implemented?
Ms Louhimies: Implementation, as always, is a matter for the Member States' national authorities. So we will produce and adopt with Member States a Directive and then it is transposed into the national legislation. National legislation is enforced by the national authorities. However, we have built a lot of provisions in this proposal to increase transparency and, also, we have some standards for inspections. With those two, and increased transparency, we now believe it will also increase self-compliance automatically, but there are limits also to the inspections.

Q10 ***Chairman:*** Inspection is the key thing, is it not? Having a sufficiently rigorous and robust inspection regime is critical in this area. Do you think it could deliver that?
Ms Louhimies: The Commission is ambitious but we have to say that we based our proposal exactly on the results of the Technical Expert Working Group, which was agreed with the Member States. The Technical Expert Working Group was one of the first consultation processes we started, and it consisted of representatives of all Member States and main stakeholders, and they were presented with different elements that we would like to look at during this revision, and one of the elements was the inspection. The recommendation from that working group was to have two-yearly inspections covering not only the user establishment but, also, breeding and supplying

establishments, and have one of those inspections unannounced. That, it was felt, would give enough security and assurance.

Q11 ***Viscount Brookeborough:*** What are the issues and problems with today's registration?
Ms Louhimies: Problems and issues. Please correct me if I have misunderstood the question. We felt that we needed to have a deadline there, and that is linked to the competitiveness of the EU research and EU industry vis-à-vis the outside world. When we look at other regions, regions where there is no authorisation or in regions where there are authorisations in place, we would want to make sure that our industry or research community is not disadvantaged by extremely long implementation of authorisation deadlines. However, the issue is with the Member State authorities because they are the ones who have to deliver, and obviously we may receive some resistance from some of the Member States who are to implement this.
Viscount Brookeborough: I am sorry; I used the wrong word; I meant "authorisation" not "registration". Thank you.

Q12 ***Earl of Caithness:*** Could you tell us something about the consultation process you entered into before you published your proposals?
Ms Louhimies: The consultation process has been very lengthy and very thorough. We started in 2002 already with this Technical Expert Working Group, and, as I have just mentioned, it consisted of representatives of Member States and all the key stakeholders. They worked for about six months to cover all the main elements we felt should be covered during this revision process. The results of that consultation process were then fed into the preliminary drafting, and the preliminary drafting was put under an impact assessment which was carried out by an expert outside contractor. That impact assessment study included yet another round of consultations—it included questionnaires to the national authorities; it included questionnaires to the stakeholders—and once the preliminary analyses were drafted or rather identified they were then put out in the open in a public internet consultation. Alongside with that, we had a public consultation with the general public on general issues, and then we had the expert consultation specifically on these elements. We had a huge number of responses. We had over 12,000 expert comments. What is important to underline here is that the expert comments were coming from the users, so it is really the users who use animals on a day-to-day basis; over 50 per cent were from animal users. From the 51 per cent, the majority was from the public institutes and the rest from the industry. Then there were breeders involved, other stakeholders and NGOs, etc. All those consultation results were then fed into the final drafting and, also, to redirect our impact assessment.

Q13 ***Earl of Caithness:*** Did you consult outside the EU? When you have got your consultations, how do you balance something in which there is huge public interest against the scientific community's interest?
Ms Louhimies: I will cover first the issue of consultation outside of the EU. We had consulted other regions like the USA, Canada, Australia and New Zealand (Japan is very limited in terms of the legislation they have in place currently)—so to obtain all the information that was available. Also, the impact assessment did a search on the situation with the different Member States, and that is made available in the annex of the study. So we have looked at the situation vis-à-vis the EU and the outside world. The second question was about how do we reconcile the animal welfare and the public wishes, and then the science. The public consultation we organised for the general public was, in fact, the third largest public consultation the Commission has ever carried out, which indeed indicates there is a huge public interest in this matter. NGOs represent the public and they have been active from the very start in this process, but equally we have the European Parliament representing the public and they have a number of concerns they have produced an own initiative report back in 2002 by MEP Jill Evans as the rapporteur. So, based on all this information we have gathered, the Commission started off with a very ambitious proposal and was looking at, also, answering the concerns of the public. Then that was put through this impact assessment, as I mentioned earlier, and this impact assessment then looked at the feasibility of these proposed provisions as well as the cost implications, as well as the benefits to the animal welfare where there are really some benefits to be harvested and, also, benefits to science because in some areas we are hoping to receive benefits for science. So that was the process that was balancing up these two parts. Then, as a result of this consultation, we have either abandoned some of the proposals we originally had or we have fine-tuned them or we have changed them, so it was taking this feedback from the consultation into account.

Q14 ***Earl of Caithness:*** Could you just send us a list of the people you have consulted in the UK, if that is at all possible?
Ms Louhimies: I will do my best. The issues for the public consultation and the expert consultation—some organisations, some respondents, preferred to remain anonymous. So we have a number of groups or respondents who have not given their names. I will try to collect a list as comprehensive as possible.

Q15 ***Baroness Jones of Whitchurch:*** I am not absolutely clear: when you say it was a public consultation did you do it with non-interested members of the public? Obviously, there are interest groups, but did you also do what we would call a Mori poll (I am sure there is an EU version of that)? Did you do a poll of that nature?
Ms Louhimies: The public consultation we did was based on the people's own interest, and therefore it is not comparable to an opinion poll that is getting an average number of people; this was based on people's interest in participating and coming up with their responses. However, for the expert consultation, we made sure that we advertised to all the stakeholders that we had consulted from the start and asked them to further advertise. So we tried to reach as wide as possible a base for the expert consultation, but it was based on the people's initiative to respond to this consultation.

Q16 ***Baroness Jones of Whitchurch:*** Can I just follow that up? Were there big disparities country-by-country within Europe? In other words, were there one or two countries that were vehemently in favour of all your proposals and then others which were: "Actually, we don't really care"? Is there a big disparity between different countries?
Ms Louhimies: It is a very good question. I think for the general public consultation we can see differences. For the expert consultation, which looked at the details of all the options that we were putting forward, we have not actually made the analysis. We had 12,000 comments to go through and we did not go to that kind of analysis at that moment in time because we wanted to capture first what is relevant to the impact assessment and finding that correctly, and, secondly, to make sure that if there are any ideas for drafting or changes to the drafting that we should take on board we would capture those. So time did not allow us to do a further analysis.

Q17 ***Baroness Jones of Whitchurch:*** Was the UK one of those that was the most vehemently in favour of better animal welfare? Or was it more widely spread than that?
Ms Louhimies: I would say the UK is traditionally, and has always been, a very strong speaker in favour of high standards of animal welfare. I think it is also reflected in the responses that we are getting from your business people; they are used to your environment and they feel comfortable with your standards. I have to say that a lot of what is in the proposal could be aspiration from what you have here—certain elements that you have here—in your legislation. So I would say the UK would be very much one in favour of high standards and good animal welfare.

Q18 ***Chairman:*** Can I go back to the inspection issue? I have in front of me the amendments from the Parliament. Although we start off with the draft saying "inspections carried out by the competent authorities at least twice a year" there is an amendment from the Parliament which says: "national inspections shall be carried out by the competent authority on average once a year, with the competent authority adapting the frequency of its inspection on the basis of the risk analysis of each establishment." If you are doing it "on average" once a year that means that some will be less than once a year. That does not seem to be particularly robust.
Ms Louhimies: My Lord Chairman, I would personally agree with that statement. The Commission position, at this state of play, because Member States' position is not really known, is not to move away from our current proposal, and we would be standing behind our "twice a year". In fact, in the provision it says it should be on a risk management basis, so that in cases where you have a huge establishment the frequency could be more often.
Chairman: Thank you for that clarification.

Q19 ***Lord Livsey of Talgarth:*** These questions are specific and refer to Chapter 2, the procedures and provisions for the use of certain animals. The proposal in Article 8 of that document limits the use of non-human primates to research related to life-threatening conditions. Can you comment on concerns that this would be too restrictive and might actually prevent research in the EU in other important areas of health, such as fertility? I notice in Article 8 it does actually refer to "debilitating clinical conditions in the human being". Is that a let-out clause?
Ms Louhimies: Thank you, my Lord. The Commission feels that we need to be strict on what we do with non-human primates, and we need to be more severe in our scrutiny of what we do with the non-human primates, being the species closest to humans and capable of building up social groups and living in partnerships throughout their lifetime. We also feel that the current provision—how we have worded it—should not pose undue difficulty in making that link between, for example, certain areas of research that is carried out today. We have a wealth of knowledge of the biology and anatomy of the human body today; we know what areas of the body are affected with different types of disease, and therefore the link should be able to be made between the non-human primate research and these areas. In addition to life-threatening we also talk about debilitating conditions in humans, and Recital 16 further clarifies and says that it has to be a condition that has an effect on the day-to-day functioning of the person. We feel that, for example, infertility could be considered in this category. We have references to it

being considered as a debilitating condition, and we know that infertility can result in depression and it can result in psychosomatic disorders. Therefore, we feel that link can be made.
Lord Livsey of Talgarth: Thank you for clarifying that.

Q20 ***Chairman:*** Would you specify that at all in the Directive? Would you make it absolutely clear?
Ms Louhimies: The current text is in the hands of the Parliament and the Council. The amendments will be fed through—if there are amendments to the text and further clarification—the national authorities or the Parliament.
Chairman: Under "debilitating", I take it, we would include diabetes and Parkinson's.

Q21 ***Lord Livsey of Talgarth:*** I have another part of my question. The proposal in Article 10 (Annex III) sets dates, which vary according to the species, from when researchers in the EU will be able to use only non-human primates which are the offspring of animals bred in captivity. How confident are you that there will be sufficient availability of such animals by these dates? That is one point. The second point is: have you information about the implications? After that I would like to ask a simple question.
Ms Louhimies: Thank you, my Lord. If I may I would like to be a little bit more generous with this response because it is a very complicated matter. We feel that the move over to the second or higher generation purpose-bred animals is needed for animal welfare, for scientific reasons and for biodiversity reasons. So we have several reasons for that. We have looked very carefully at the issue of cost and the demand and the supplies of the availability of these animals for EU use. The EU uses around 10,000 non-human primates a year, whereas the USA alone uses something like 50,000. So we are not the market leader in the demand. We are relying on our non-human primates to come from outside of the EU. The impact assessment study concluded that there are a number of uncertainties that are very difficult to predict because we are working in a global market. However, it concluded, also, that the price would not become the determining factor because the price of the animal out of the total cost of the project is marginal. The example the study was quoting was looking at a long-term average study using macaques; if the price of the macaques were to have doubled that would have had a 2.8 per cent increase in the total project cost. So the conclusion was that the price will not be the determining factor, but the determining factor will be the demand and supply. Will there be species available? Due to these uncertainties, the impact assessment concluded, also, that we should be flexible in what we can propose in the Directive. Often, certain parts of the proposal are looked at in isolation. In fact, what we have done here is that we have built a proposal which is composed of five different elements. First of all, we have these transitional periods which you mentioned in the Annex III. They are there based on the impact assessment study; they are there to give the push to that direction. We are not 100 per cent sure that these will be attained within the time limits that we have set. We have then an element which requires strategies to be put in place to provide an increasing number of second generation or higher generation purpose-bred animals. Furthermore, we have a requirement for the Member States to report specifically on the origins of the non-human primates, so that we can follow up where these animals are coming from; are they second generation; are we getting increasing numbers of them? Then there is a review requirement for the Commission to carry out a review to analyse the situation where we are. Finally, we have a comitology procedure foreseen for Annex III, which allows the Commission, where appropriate, to revise these deadlines that have been set. So we are following very much the conclusion of the impact assessment. We want to make a push; without putting anything in the Directive the status quo would be highly unlikely to change, so we need the push there, but we build it in a flexible manner, so that, in case we need to, we can go back and we can revise these deadlines. The final comment I would like to say is relating to the demand and supply, because that was considered one of the biggest unknowns in this whole scenario. Just recently, in March of this year, there was a meeting on a US initiative called International Primate Plan. It is grouping together all the big players in non-human primate production and the users. In that meeting they agreed or they came to the conclusion that the aspiration and the objective should be to move away from first to second-generation, purpose-bred animals, so we have now confirmation that our proposal, moving to this direction, is also now supported worldwide and that would then positively impact on this biggest unknown that we have.

Q22 ***Lord Livsey of Talgarth:*** Thank you. That is a very comprehensive answer. Just to add to that (you have more or less answered my question from what you have just said), finally: the enforcement of this agreement, you are confident, will secure the objective?
Ms Louhimies: At this stage I will not talk about agreement or enforcement. It is a consensus that was agreed that that should be the way forward. There has been no discussion yet on the timeline because it is a complex issue and it is involving breeders in countries like China, Cambodia and Mauritius. So we talk about worldwide development, and this will not happen overnight. We will still have the first

generation animals with us for quite some time, but what the Commission would like is to kick off this move and follow and try to achieve it and speed up the process.

Lord Livsey of Talgarth: Thank you.

Q23 ***Viscount Ullswater:*** Perhaps not quite such a headline as non-human primates, but I notice now that in Article 2.2(b) invertebrates are to be included. Could you tell us: is that the first time that invertebrates are to be included? Is it really necessary that invertebrates should be included in such an all-embracing Directive as this one? Although they are specified in Annex I, are they the only ones that are ever used in experimentation? Do you know anything about the intensity of research in these sorts of animals—invertebrates?

Ms Louhimies: Thank you, my Lord. It is the first time we are proposing it at the EU level—yes, that is correct. The basis on which we are proposing this is a scientific report we requested in support of this Directive from the European Food Safety Authority that hosts the Scientific Panel on Animal Health and Animal Welfare. They looked at a number of issues and one of the issues was to look at the sentience of invertebrate species, based on their biology but, also, their pain system development, their behaviour, cognitive ability and memory retention—so: if I am experiencing stimuli that are adversive do I want to go back to those stimuli again? Based on these different criteria the opinion concluded that the groups we have included in Annex I should be provided protection in case they are used in procedures that have a likelihood of causing pain or suffering. It is the first time, at the EU level, that we are doing this. The UK is looking at some. There are also other regions that are covering invertebrate species under their legislation, for example New Zealand. Are these the only ones and at what level of intensity they are used? Unfortunately, because they are not covered by legislation in larger scale, we do not have any reliable data on the extent of their use.

Q24 ***Viscount Ullswater:*** Do you feel this might have any repercussions for the fishing industry?

Ms Louhimies: I would not think so because fish have been protected already, since 1986. So the fishing industry, I would not see how that would be affected, but obviously if there is more information on what the link is we would be willing to examine that.

Q25 ***Chairman:*** Do you think it has any implications for the catering industry—food safety?

Ms Louhimies: We are talking here about only animals that are used or intended to be used for the purpose of experiments, and we know that, for example, the method of killing lobster in the food industry is not necessarily what the scientific community would consider the most humane, but it is not covered by this Directive.

Chairman: Let us go on to severity classifications.

Q26 ***Baroness Jones of Whitchurch:*** You will know what your own proposals are but, as I understand it, the European Parliament has come up with a different set of classifications. I wondered if you saw any merit in that. Could you see some arguments as to whether theirs should be adopted rather than the ones that the Commission have come up with? I suppose that is my first question: do the alternatives have merit?

Ms Louhimies: Thank you, my Lord. The European Parliament is actually filling in a part of the Directive a package that we wanted to fill in at the end of the adoption process. They are providing the detailed criteria which we left to be carried out and filled in later on, so they are proposing criteria which are mainly based on the Swiss criteria. When we the Member States and the Parliament, will determine the final criteria for the EU, I think all existing criteria and good practice should be looked at, and should be looked at in detail. We have a number of Member States who have severity classifications in place today and have lots of experience, and therefore we should look at all the available information also outside of the EU, like Switzerland and also other regions.

Q27 ***Baroness Jones of Whitchurch:*** I thought the Parliament was, also—without going into the detail of the criteria—to suggest different classifications then.

Ms Louhimies: Yes. However, at this moment in time the Commission would not like to move from its Proposal, as I said before. Also, in this particular case, because it is very much linked to the other provisions, we have based our proposal on having criteria for three levels of severity and non-recovery grouping, and therefore we would like to keep that grouping because it has a link with the other provisions in the Directive.

Q28 ***Baroness Jones of Whitchurch:*** It did seem rather odd that you are not going to explain the criteria until 18 months down the line. Can you give us some idea of why there is going to be that delay? What steps do you have to take, because this is a rather crucial issue about pain, to be frank. Why is it going to take so long? What steps do you have to go through to come up with a sensible proposal?

Ms Louhimies: Thank you, my Lord. That is a very valid question and it has been asked several times. At the time of drafting, the Commission was of the opinion that we have currently enough common knowledge and understanding of what the main categories of these criteria are because they are used

by scientists in a number of Member States today. Therefore we left only the fine-tuning, the limits between the different categories to be fine-tuned afterwards, together with providing examples of these different categories. We do understand the urgency of this matter and we realise that it has been picked out as one of the key issues. For that reason we have sent out recently invitations to Member States and to all main stakeholders to come together to an expert working group which will convene on 9 and 10 July. We hope that by the end of this expert working group looking at all the current evidence and current experience that we have that they will be able to agree what should be the criteria that we will be using in the EU. The results of that expert working group work will then be fed into the European Parliament and the Council for their discussion.

Q29 ***Baroness Jones of Whitchurch:*** Presumably one of the tasks of this group will be to pin down the scientific measurement of pain so that it is no longer subjective but becomes much more measurable? Presumably, in most cases, you can actually measure the level of distress, through increased hormones or whatever, that an animal is going through, so that will be one of the tasks to move away from it just being the operatives' best guess?
Ms Louhimies: Definitely and that is a very good comment. That is exactly what we are looking at. We are looking at clinical signs that are objective as a way of determining the animal stress and suffering and pain, so we are looking at clinical science that can be easily explained to the technicians dealing with the animals.
Chairman: We will move on to care and accommodation standards. Baroness Sharp?

Q30 ***Baroness Sharp of Guildford:*** Article 32 and Annex IV set out the minimum standards for care and accommodation of animals and we understand that these standards were originally aspirational standards but as they stand now they are being specified as norms. Could you explain to us what evidence led you to justify setting these standards in Annex IV as norms and what do you estimate to be the cost implications for Member States of adopting such standards?
Ms Louhimies: Thank you, my Lord. I probably will take a little bit longer with this one as well because it is a complicated issue again. As you rightly say, they were developed at the Council of Europe as guidance. They were developed with Member States, with full stakeholder involvement and with expert consultation that took over seven years. Furthermore, it was based on the animals' needs in terms of fulfilling their ethological and behavioural needs, and that was then backed up with scientific information and scientific evidence, and when the information was not available then we used common best practice as the basis. The outcome of that work was a balancing act between the economic needs and needs of animal welfare, supported by scientific information and best practice. Therefore, we feel that there is enough animal welfare, scientific and economic justification to use some of these elements in our Directive. The whole of the Council of Europe guidelines have been transposed into the EU legislative framework through a Commission decision as a Commission Recommendation, so we already apply as guidelines all of these that were agreed at the Council of Europe. What we are proposing here is going beyond that. We take in certain elements which can be applied 100 per cent of the time in 100 per cent of the cases and which can be legally held in front of the court, and those have been put into the Directive, provided it is reasonable to demand so. That has a very big impact on the harmonisation of the internal market. As I said a little bit earlier, one of the elements that has created the distortion of the current uneven playing-field for the operators is the level of standards that we have on housing and care, and therefore we feel that we need to address this issue because that is the way to level the playing-field considerably. I think those are the main points.

Q31 ***Chairman:*** It is where you level the playing-field, is it not, in this one, and what is the justification for a particular threshold?
Ms Louhimies: The justification for using these ones was that it was based on the latest science available then about animal welfare. There was an understanding of animals' needs, their level of suffering, et cetera, and that was already balanced against economic needs, and therefore we feel that it is justifiable. We have a situation where some Member States have already implemented them as the legal minimum and we also have Member States who want to go even further, so therefore we feel that this strikes a balance between the different ends of the scale.

Q32 ***Baroness Sharp of Guildford:*** I think there is a real fear amongst the pharmaceutical companies who are users of the research based on animals that the setting of these standards might lead to research going outside the EU to countries which do not adhere to these sorts of standards. Is there much worry that there might be a knock-on effect in that way?
Ms Louhimies: The Commission does not believe that that would be the case. We have no evidence of transfer of research in the pharmaceutical industry due to high standards of animal welfare or a strict regulatory environment. A good case example is the UK which has a very large and profitable industry

with research and you have one of the highest standards in the EU already. Another point of example is Switzerland, so we have examples that would contradict that statement. Relocation is a very complex issue. We feel that the drivers for the relocation are elsewhere, especially now with the economic recession going on. We look at where the construction is cheap, we look at whether the infrastructure is sufficient to support it, and we look at perks that different host governments provide. For example, China today is very much pushing to have non-human primate research over there. They are wanting to limit the exports of non-human primates. They want to attract foreign companies to come in. We feel that there are other drivers. One specific driver in this area is the existing expertise. We have examples of that both inside and outside the EU. The EU has expertise in vaccine production. 80 per cent of vaccines are produced in the EU, and we are collecting more and more research in this area and we are getting more companies establishing here because the expertise and scientific infrastructure is here. Therefore we feel those are not reasons why it would take place. In the proposal itself we have specific provisions to try to make the administrative burden as minimal as possible. We have foreseen a number of measures there. We have foreseen, for example, group authorisation for regulatory testing to reduce the administration around it. We have foreseen a lighter authorisation structure for projects that consist only of "mild" procedures and do not use non-human primates. Also those ones would be exempted from non-technical summaries and retrospective assessment. Finally, if there is no response given by the authorities in 30 days for this last group, the project can start. We have filled in a number of elements in the proposal that would make sure that the competitiveness remains here. One element is important. We have drafted the Directive in a way that it will look at objectives that have to be met, but it does not necessarily state how they should be achieved, and therefore the Member States have a main role to play in how they implement these requirements, these objectives. It also gives, we feel, an opportunity to some Member States to look critically at the internal structure and how we have managed today. We need to achieve these objectives: is this the optimum and least bureaucratic way of achieving it? We feel that we have built the elements that would keep the competitiveness of our industry and research over here.

Chairman: Having opened the issue of international competitiveness a little earlier than I anticipated, can I invite Lord Brooke to develop it.

Q33 ***Lord Brooke of Alverthorpe:*** If I may come back to the comments which you made about the standards practised in the UK and the British Government's position. Nonetheless there is concern that whilst broadly our Government, I understand, is in support of the objectives which you are seeking, they feel that you have taken some of the practices here, adopted the objectives, but in fact have devised inefficient and clumsy methods and bureaucratic approaches which will be more costly than the present practices and will add to problems over international competitiveness. What would you say to those accusations?

Ms Louhimies: Thank you, my Lord. I would say that we would need to look at the individual items that would be presented. We do not feel that the way that we have worded it increases bureaucracy unnecessarily. We have been very flexible in terms of saying that we would require authorisation and we would require ethical evaluation. We do not determine what is the best body to do those tasks, so in one Member State it could be one single central body doing both tasks and another Member State could implement it by having a regional ethical evaluation body and having central authorisation, so all these different possibilities of implementation are there to make sure that the current infrastructure is being used to the optimum and we do not need to reinvent the wheel when it is functioning well.

Q34 ***Lord Brooke of Alverthorpe:*** Is there not a shift from the requirement for self-policing and notification to actually having central authorisation?

Ms Louhimies: The Directive does not say that. The Directive requires authorisation and it is for the Member States to decide who is the competent authority to carry out that task. It may well be that a Member State can decide that a regional ethical evaluation committee will be also assigned the competent authority hat to authorise and that could be done in a single process. It really does not require specific ways of implementing it. It describes the objectives to be met and it is for the Member States to decide how they are going to achieve that.

Q35 ***Lord Brooke of Alverthorpe:*** So you would argue then that the British Government's claim that this is a substantial additional bureaucratic charge which is going on operations is invalid?

Ms Louhimies: I would not go that far. I would like to discuss the details with the British Government. I think that would be the best way to say it!

Q36 ***Chairman:*** Have you got any evidence, in the area of academic research, of academics who use animals in their research, and they may be employed by universities in the EU but they also make sure that they have appointments or interests in the Far or Middle East and so they do their animal experiments there?

Ms Louhimies: When we did our consultation the biggest respondent group was from academic research. 33 per cent of the comments came from academic research. We do identify in the impact assessment that academic research will have more costs or rather that they would require longer transitional periods for certain elements than the private sector. For example, the current level of housing and care and the upgrading of it, in 2006, 35 per cent of the private sector had already updated to these new standards but in the Economic Area that was 20 per cent, so we see a difference there because they are also competing on funding money. I am not quite sure if I answered your question on the interaction.

Q37 ***Chairman:*** I was just wondering whether you had any evidence that, because of even the present level of the regulatory burden, academics are making sure that their animal research is being carried out in the Middle and Far East rather than the EU?
Ms Louhimies: I would in fact argue the opposite. Industry has a better chance of relocating but academic research is very much in the host country. They do do combined studies and they do international co-operation in an increasing manner, but I would say that industry is the first one to move if there were to be relocation due to that. As I said earlier, we do not really have evidence that high regulation and good animal welfare would actually translate to transportation of the research.
Chairman: Data-sharing, Lord Palmer?

Q38 ***Lord Palmer:*** We were on a site visit two weeks ago and I was intrigued by the amount of data-sharing that obviously goes on, particularly within the Union, but the proposal under Article 44 requires Member States to share research data (subject obviously to safeguarding confidential information) in the interests of avoiding unnecessary duplication of procedures. What evidence do you think there is that procedures are currently being duplicated unnecessarily? Perhaps if I then could go on to a supplementary: does the proposal require more data-sharing than already happens, for example through scientific publication of research? What assessment have you carried out of the impact of extending data-sharing?
Ms Louhimies: Thank you, my Lord. Data-sharing is an important question because there we can cut testing if there is unjustified use of animals. We looked during the impact assessment for evidence of unnecessary duplication. We have to differentiate between two types of testing on animals: those that are required by regulation and by legislation e.g. for chemical safety or pharmaceutical safety, and then we look at the basic research and applied research. The situation is very different in these two areas. In the regulatory testing area there is duplication. It is duplication that is derived from legislation that requires retesting of pharmaceutical ingredients when they come in from outside of the EU. In terms of vaccines there is an option for Member States to retest but not an obligation. Nevertheless, ten to 15 Member States use that option to retest when the vaccine arrives here when it has been tested previously outside of the EU. Based on these calculations, it was estimated that there are about 160,000 animals used for retesting for regulatory purposes.

Q39 ***Lord Palmer:*** 160,000?
Ms Louhimies: 160,000 on a yearly basis.

Q40 ***Baroness Sharp of Guildford:*** They will be rats and mice.
Ms Louhimies: Yes. We feel that the regulatory testing is best addressed by vertical legislation because we have legislation requiring this so we have to address these areas. We have already ensured that the chemicals legislation addresses data-sharing very strongly to make sure that we do not have unjustified retesting. Pesticides is following the same line. We have cosmetics legislation with very specific provisions actually prohibiting animal testing, so the Commission feels that regulatory testing should be addressed within the sectors. It is very unlikely that you would have duplication between sectors because you are using your substances for very different purposes, so the likelihood of the testing requirements being the same is very limited. When we move over to the basic research and applied research, applied research is a very problematic area because we talk about innovation proprietary data and that is a very difficult area to tackle. When we talk about basic research the only evidence we could find of unjustified duplication would be in the areas where research results are "negative", meaning that I have a hypothesis at the start of my project but my hypothesis has not proven to be correct. That kind of result is not very interesting on a newsflash basis. Scientific journals are not interested in having that. Therefore you will have difficulties in getting it peer-reviewed and you will have difficulties getting these results published. We have in bilateral consultation and discussion with professors heard comments saying that, "Yes, I have experienced myself that an experiment that I was carrying out was a little bit along the same hypothesis that somebody had already done but I only found out about that after the event." We have some evidence but it is an area again which is very, very difficult to tackle. How do you tackle that? In our proposal we have addressed it and we have foreseen a provision that says that Member States should step up efforts to share data which is generated by the use of animals, so we have made a

provision there, but how that will be implemented in practice will be discussed with the Member States.

Q41 ***Lord Palmer:*** Would registration help, do you think?
Ms Louhimies: We looked at a databank at an EU level as one of the options to start off with, and that was when we started off identifying the different areas, and we said that an overall data-sharing by registering all the projects into one big databank was not feasible. That was also confirmed by the impact assessment. The work required to be put into it with very questionable benefits, especially if it is cross-sectoral, was too much to merit the building up of such a databank.

Q42 ***Chairman:*** The reality in basic research is that you will get a number of teams that are doing broadly the same sort of thing and working up and they will be very possessive of their data until it is finally submitted for peer review.
Ms Louhimies: That is exactly correct. The problems with data come in the area of applied research but also very much in the area of fundamental research. That also is linked to the funding because universities are competing on funding not only in the EU but internationally. Therefore it is a very, very problematic area to tackle.

Q43 ***Chairman:*** Do you want to tackle that area because it seems to me that you would destroy the whole basis of how basic research is conducted if you do?
Ms Louhimies: We wanted to tackle it at least in terms of seeing what could be done, especially when I refer back to the negative results, because that is an area that people are not generally keen on publishing. That is the only area where we heard that there was evidence that there was unjustified duplication and therefore that is the area that we wanted to tackle.
Chairman: Negative results? OK.

Q44 ***Baroness Jones of Whitchurch:*** Surely in the pharmaceutical sector, for example, it would be fantastically secretive and fantastically competitive and the last thing they would want to do is share it? Is there any way that you think that you can break down some of that innate secretiveness?
Ms Louhimies: We have good evidence of the pharmaceutical industry especially stepping up their efforts in terms of voluntary agreements. I think this is an area where we have to tackle it with the tools that we have. In one part we can try regulation but especially in the development phase, at the very early stage of the development phase, it is almost impossible to tackle it because it is their income and bread and butter at the end of the day. When it comes to the later testing when the ingredients are already analysed, the pharmaceutical industry is today setting up certain specific areas of testing where they are trying to share the data to see what can be achieved in terms of a reduction in numbers.

Q45 ***Lord Brooke of Alverthorpe:*** If I may stay on the same theme. The Germans did not accept that the 1986 Directive applied to academia in Germany. That is still the position, as I understand it; yes or no?
Ms Louhimies: I would need to double-check and confirm the current situation in Germany but my understanding is that it is not covered by this Directive. However, our proposal—

Q46 ***Lord Brooke of Alverthorpe:*** —That was going to be my second question.
Ms Louhimies: —is to cover basic research.
Earl of Caithness: On your first point on regulatory research, what work are you doing to minimise the chances of retesting in the EU by getting agreements with other countries to meet certain standards? As I understood it, quite a lot stuff was being retested in the EU which was coming from outside the EU. Surely it would be much better to get them to agree a standard so that it does not have to be retested here?

Q47 ***Chairman:*** That raises some issues!
Ms Louhimies: My Lord Chairman, I think if you want me to be brief, it is a very, very complex area. We have different areas the pharmaceutical area: we can talk about the chemicals legislation. The Commission is taking the initiative at an international level, both for chemicals and for pharmaceuticals. There is international classification and harmonisation of pharmaceuticals in the human medicine area and the veterinary medicine area which is looking at accepting and providing similar test requirements globally. We are working on the same thing under the OECD to make sure that we have test methods, so that when a chemical substance is tested here the results would be accepted elsewhere. We are very much in favour of international harmonisation in all fields of testing. There are similar activities going on in the pesticides area as well. In fact, there are good results especially deriving from the pesticides side where they have identified areas where there is still redundant testing taking place, so we are working at an international level to get harmonisation at the international level.
Chairman: Let us move on to the illusive level playing-field.

Q48 ***Viscount Brookeborough:*** I think you have answered quite a lot of how you wish to achieve it. When the document *Questions and answers on revising the Directive for the protection of animals* states that the proposal "strikes a balance between promoting research and competitiveness", one thing

I do not fully understand is if the data is largely shared and the universities know what is happening, at what stage does it become the property of the pharmaceutical business, because they are the competitive side and once they get the data they might produce a drug that other pharmaceutical businesses have not yet produced?
Ms Louhimies: I am not a specialist in the proprietary data area. I will probably be able to get some information for you afterwards but I will not be able to answer that question unfortunately.
Viscount Brookeborough: Thank you. It is just that there obviously is competition but the more you try to go for shared data, what I am not quite clear on is exactly when the serious competition gets it. Even looking at share prices and the price of a drug related, it has been a lot of interest.
Chairman: There are real difficulties about sharing data and how you try and offload cost.

Q49 ***Viscount Brookeborough:*** Connected with that a little bit, and I hope you might be able to say something, the type of research done, whether it is with F1 or F2 mammals of any kind, the argument that we were given when we went to a research place the other day was that it compromises the scientific results, because they will not be pure results because if they are not F2 and they have not been bred primarily for experimentation, ie if you capture from the wild, they are contaminated by all the things that they come on in the wild. The pharmaceutical industry is a very large industry and it relies on pure research. How come they are even prepared to contemplate research from anything other than F2 or animals that have been bred purely in an isolated society? Surely, it almost ought to be self-regulating because it is such big business? I understand that there are all sorts of other issues like counterfeit or less well-regulated areas, and I am not talking about that, I am talking about the major issue.
Ms Louhimies: Thank you, my Lord. That is a very good question. Why is the pharmaceutical industry ready to compromise? I think we have to look at the species' appropriateness to mimic conditions in humans. In the pharmaceutical area of testing often the last testing phase before the clinical trials going into humans is done on non-human primates because they are the closest to us. The next factor that is in the picture is the availability of the animals. Non-human primates are not available to supply the demand that is there today. There are other elements—

Q50 ***Viscount Brookeborough:*** Why not, because they have had so many years in order to do it?
Ms Louhimies: The big difference with non-human primates for example, compared to rats and mice, is first of all their reproductive cycle. If we talk about macaques, and I will have to double-check, they only reach sexual maturity at the age of five years and their offspring consist of 1 progeny so we are talking about a very different type of animal compared to rats or mice or rabbits. The availability of those animals is not there. There are also claims about their breeding in captivity. There are claims by breeders in Mauritius who say that when they get the F1 generation and compare them as breeding parents to the ones that they are picking up from the wild, they are not as good breeders as the ones taken from the wild. There is more obesity and there are other factors that come into play, so it is not necessarily the case that they are easier to breed. On the other hand, we know that for example with marmosets, which are also used in regulatory testing in the EU, we are using second or much higher generation purpose-bred animals for years but they are easier to breed in captivity. So I think it is a question of what you can do with the animals that you have available. One last comment I would like to mention is the herpes virus. In Mauritius we have a colony of macaques which is completely herpes-free and that is having implications for the workers working with these animals because herpes, as everyone knows, can be passed from the animals to the workers, and sometimes the herpes virus may interfere with the results of the testing that you are doing. The macaques that we are getting from China, Cambodia and Vietnam, for example, can be tested for herpes at the time when they are sold but we cannot say that they come from a herpes-free colony and the herpes can still become active later on. There are several issues in relation to what can be used in which kind of testing environment and that affects their availability.

Q51 ***Viscount Brookeborough:*** On the question itself, have you have got anything else to say about level playing fields? You have already addressed it largely in Europe. Do you have anything else to say about world opinion or international opinion as to the documents that you are bringing forward?
Ms Louhimies: We have not received too much feedback from other regions. One thing maybe that I would like to mention is that a lot of the elements that we have in our proposal are also mimicked in the other regions.

Q52 ***Viscount Brookeborough:*** Providing they are policed properly?
Ms Louhimies: Yes, I wanted to come back to in which way because in some cases they are embedded in the legislation and in some regions they are in the guidance. If we take the US, for example, their legislation is not providing protection for certain species but those certain species are still covered by the requirements from the funding bodies, and when the funding bodies are then giving money away they require the same standards to apply to all species. In

Australia and New Zealand, they have very similar requirements of ethical evaluation and authorisation, so we have a lot of the elements that we have built in mimicked in other areas, but not necessarily in the hard-core legislation; they can be guidance and they can be codes of practice as well.

Q53 ***Chairman:*** We are nearly there, I think. Can I just go back really to the beginning almost and where we are with the process. At the First Reading on 5 May the Parliament agreed a number of amendments to the proposal. The Commission, as I understand it, explained in the debate that you could accept in full or in part 83 of the 200-odd amendments that have been proposed. Can you tell us the main impact on the proposal of the amendments that you are accepting and where you still disagree with the Parliament?
Ms Louhimies: Thank you, my Lord Chairman. I have a slight problem with a very concrete answer in this area because the Commission's final response to the Parliament vote is not yet adopted by the College and therefore I cannot go into the details. However, as I mentioned earlier, we do not know the situation with the Member States and we do not know which direction they are heading. At this moment in time it would be very unwise for the Commission to move. Any proposal that would touch on the significant structure or the main elements of our proposal we would not be likely to move towards, at this moment in time. I am talking about issues like authorisation, loosening of reuse requirements, loosening of the requirements for non-human primates, the independence of the ethical evaluation, and the principle of authorisation, and those are core key elements of our proposal, cornerstones of our proposal, and we would not like to move on any of those areas. The likely areas that we would be moving on would be insignificant in terms of the main core issues.

Q54 ***Chairman:*** Could you help us with identifying the more insignificant ones?
Ms Louhimies: Unfortunately I would need to wait for the College to get there, my Lord Chairman.

Q55 ***Chairman:*** When will you be able to do that?
Ms Louhimies: I would not like to commit the College. Hopefully in the coming weeks.

Q56 ***Chairman:*** Could we be in touch with you or would you be in touch with us on that?
Ms Louhimies: Gladly.
Chairman: Thank you very much. OK, I think that is it, thank you very much indeed. That was really very, very helpful in helping us to understand the thinking of the Commission and the arguments, so thank you very much indeed.

WEDNESDAY 10 JUNE 2009

Present	Arran, E	Jones of Whitchurch, B
	Brooke of Alverthorpe, L	Livsey of Talgarth, L
	Brookeborough, V	Palmer, L
	Caithness, E	Sewel, L (Chairman)
	Cameron of Dillington, L	Sharp of Guildford, B
	Dundee, E	Ullswater, V

Memorandum by the Bioscience Sector

1. This document has been prepared as a response to the call for evidence from the Housse of Lords European Union Committee, Sub-Committee D (Environment and Agriculture). It encompasses the views of a number of organizations, including umbrella organizations, that represent academia, industry, SMEs, charities and other research funders in the United Kingdom, all of which will be directly affected by the revision of the Directive.

Organisations Supporting this Submission

Association of Medical Research Charities

BioIndustry Association

Biotechnology and Biological Sciences Research Council

Institute of Animal Technology

Laboratory Animals Breeders Association

Medical Research Council

Society of Biology (Biosciences Federation and Institute of Biology until 1 September 2009)

The Academy of Medical Sciences

The Association of the British Pharmaceutical Industry

Understanding Animal Research

Wellcome Trust

Context of this Submission

2. The House of Lords Committee will be well aware of the publication of the original Commission proposal in November 2008, and of the plenary vote which finalised the first reading in the European Parliament in May 2009.

3. For the purposes of this submission, we refer to a large extent to the original Commission proposal. Our sector had many serious concerns about that proposal, which are given detailed consideration here. Our organisations published a "Declaration of Concern" in March 2009 about the Commission proposal.[1] As well as problems with the content, the wording throughout the Directive requires significant review for scientific accuracy and internal consistency.

4. However, we also refer at times to the outcome of the European Parliament's first reading. Our sector engaged in some depth with the debate in the Parliament. We published a "Declaration of Support" for the report of the Agriculture Committee which was put to the plenary for a vote. Despite significant reservations, we supported many of the amendments which were passed by Parliament. However, we pointed out that we retained "strong reservations about some amendments in the Parish Report, which would impact negatively on scientific research that utilizes animals. In addition, some of the problems with the original Commission proposal remain. These outstanding issues will need to be addressed in future stages of the revision of this Directive".[2]

[1] www.understandinganimalresearch.org.uk/policy_issues/european_regulation/uk_bioscience_sector_declaration
[2] www.understandinganimalresearch.org.uk/policy_issues/european_regulation/declaration_of_support_for_the_parish_report_

5. We understand that the Commission has so far accepted only a minority of the Parliament's amendments. It has apparently not supported many of the amendments which would be of most importance to continued biomedical research using animals in Europe.

6. For this reason, the position of the UK Government as it engages in the first reading with the Council of the European Union is of considerable significance.

Executive Summary

1. *Objectives of the Directive*

7. The bioscience sector recognises the need for Europe-wide legislation concerning the use of animals in research, and we agree that it is timely to update the 1986 Directive. We support the high-level policy objectives outlined in the Home Office consultation on this Directive (of May 2009). These include (in our own wording):

- Harmonisation of EU regulatory requirements.
- Promotion of high-quality science and patient benefits.
- Promotion of public confidence in humane animal research.
- Ensuring high animal welfare standards and the application of the 3Rs (reduction, refinement and replacement).

8. We consider that harmonisation, as well as having potential benefits to animal welfare, is in the UK's economic and scientific interests, in particular in those areas concerning the mobility of personnel, the sharing of projects, and the cost drivers affecting animal supplies. However, we do not believe the draft Directive will adequately fulfill the aim of harmonisation of the market. Indeed some provisions could create greater disparity both within the single market and the global market.

Further information is provided on page 9.

2. *International competition*

9. We have serious concerns that the draft Directive would undermine UK and European competitiveness. In particular, it would create in many areas a disproportionate workload, excessive cost-burden, and unnecessary restrictions to research, without proportionate benefit to animal welfare. It will make it increasingly difficult for international scientific collaborations with countries outside of the EU.

10. The Commission has stated its intention to reduce the burden and costs of legislation for SMEs and larger companies in order to improve competitiveness, and to continue to strive for the goals laid out in the Lisbon and Gothenburg agendas. In this draft Directive it has failed to carry through that intention.

Further information is provided on page 13.

3. *Non-human primates (NHPs)*

11. We agree that, as with all animal research, careful ethical evaluation and harm-benefit assessment is required before primate use is authorised. In most EU countries this type of assessment already exists. We disagree with attempts to impose sweeping restrictions or ban NHP use. This could have seriously negative impacts upon the ability of fundamental and applied science to bring much needed medical advances to UK and EU citizens and patients across the world.

12. A blanket requirement for the use of second generation (F2) NHPs (ie offspring of animals that have been bred in captivity) would be problematic. Before time lines can be established this would require a feasibility study to assess the impact of such a policy both on animal welfare and on the availability of NHPs to EU researchers.

13. We support the amendments made in Parliament to improve the ability to conduct vital research using NHPs.

Further information is provided on page 16.

4. *Extension of the scope*

14. A number of the proposed extensions to the scope of the directive are not justified, would significantly increase costs, and present an unworkable administrative burden with no benefit to the welfare of animals. These include the full regulation of all vertebrates humanely killed for their tissues, and the extension of species covered by the Directive to include all embryonic and foetal forms of vertebrates, as well as certain additional

classes of invertebrate, including their larval forms. Reliable evidence of sentience has not been scientifically established for most of the animals covered by these extensions.

15. We support those amendments made in the European Parliament to restrict the scope of invertebrate cover, but believe that the scope is still too wide, and not scientifically robust. Other amendments would still represent a major increase in the range of vertebrate studies included under regulation from the existing Directive.

Further information is provided on page 21.

5/6. *Authorisations*

16. The administrative implementation of the Directive must be clear and well-defined. It is currently confusing and unnecessarily bureaucratic, with potential for unnecessary delays and restrictions to research that would not promote animal welfare or the 3Rs. The Directive does not apply proportionality, in that the degree of control is not adjusted in relation to the potential harm to the animals. The controls need further consideration and amendment.

Further information is provided on page 26.

7. *Care and accommodation*

17. We support the principle of minimum standards of care and accommodation across Europe (with derogations where necessary, eg for farm animal research). The Directive, as currently proposed, is overly prescriptive around cage sizing and environmental requirements. As well as greatly increasing costs for research, some proposals would be actively deleterious to welfare and may compromise the ability of the UK to maintain its animal breeding capabilities.

Further information is provided on page 33.

8. *Alternative methods*

18. The 3Rs are an intrinsic part of scientific research, not a separate activity. Much of the evidence contributing to the 3Rs has come from research that had other primary aims. "Validation" of the 3Rs is best undertaken through normal scientific processes and not through separate national reference laboratories in every individual Member State. It is unlikely that these could ever contain all the necessary expertise and facilities, and they would be expensive and duplicative.

Further information is provided on page 38.

9. *Subsidiarity and legal base*

19. The Directive should seek harmonisation across Member States over the principles and outcomes of regulation affecting animal welfare, while permitting flexibility in methods of implementation.

20. The Directive currently lacks proportionality and gives excessive weight to restrictions which would impede research yet have minimal welfare benefit.

Further information is provided on page 41.

Additional Areas of Concern

Sharing and disclosing data

21. We emphasise the need to adequately balance public interest with the protection of intellectual property rights.

22. Mandatory data-sharing proposals fail to recognise existing initiatives to avoid unnecessary duplication of animal research, the degree of success already achieved, and the technical and legal difficulties involved. They are impractical to implement and would have a detrimental impact on the competitiveness of both industrial and academic research in a globally competitive marketplace, even though there is no evidence that significant welfare benefit would result. The Commission belief that duplication is widespread is not reflected in evidence or in the bioscience sector experience.

Further information is provided on page 44.

Re-use

23. The excessive restrictions imposed by the Commission on the re-use of animals would make it extremely difficult to maintain many research programmes in the EU and, by hindering the application of the 3Rs, would have adverse effects on animal welfare.

24. These concerns were addressed in amendments from the European Parliament.

Classification of severity levels

25. It is very important that severity levels of procedures are properly and precisely defined within the Directive, not least since this is relevant to important judgements elsewhere in the Directive. Clear bands must appropriately encompass all levels of regulated use, so as to encourage refinement from one band to a lower one.

26. We support the approach taken by the Parliament to initiate the establishment of severity classifications, and welcome the proposal for a Council Working Group to move this forward.

Concluding remarks

27. In summary, health, wealth and social benefits, EU scientific and industrial competitiveness and, importantly, animal welfare, all need to be balanced to ensure the EU adopts a proportionate approach to regulating animal research. The bioscience sector is committed to providing the necessary evidence as well as to working with the UK Government and European institutions to ensure that the revised Directive achieves this balance. The rest of this submission provides a more detailed assessment that we hope will help guide discussion within Government.

Background

28. The UK bioscience sector welcomes this inquiry. We supported the conclusions of an earlier committee—the House of Lords Select Committee on animals in scientific procedures—whose report was published in July 2002. In particular, we agreed with the findings that (i) there is a continued need for animal experiments in applied research, toxicological testing, and in research aimed purely at extending knowledge, (ii) that the UK should strive not for the tightest regulation, but for the best regulation, and (iii) that more consideration could be given to the pursuit of the 3Rs.

29. Both the UK bioscience sector and the Government have responded positively in many ways to the recommendations made by that House of Lords inquiry. We consider the revision of European Directive 86/609 to be an opportunity to further implement and build on those concepts.

30. Research in academia and industry is essential for the acquisition of knowledge and the development of new medicines for medical and veterinary purposes. The use of animals is a small but vital part of that research. Animals are used only when necessary and unavoidable, and where appropriate non-animal methods are unavailable. Both academia and industry have active 3Rs programmes focused on the replacement, refinement, and reduction of the use of animals, and both sectors support and actively collaborate with the UK National Centre for the 3Rs.[3]

31. We have responded in detail below to the issues raised in the call for evidence, as well as raising some other issues over which we have concerns, or which have arisen in the European Parliament. Whilst we have addressed the issues in much the same order as the call for evidence, we wish to highlight the following as having the most impact on bioscience research in the UK, so that we consider them to be priorities:

- Competitiveness of the EU.
- Restrictions on the use and supply of non-human primates.
- Restrictions on the re-use of animals.
- Sharing of data.
- Authorisation of decisions.
- Scope of the directive.
- Care and accommodation.
- Classification of severity levels.

[3] www.nc3rs.org.uk

Terminology and references

32. We have occasionally used different terminology in different parts of our submission. The Committee can assume that, unless otherwise stated, any reference to:

- The "Committee" refers to the House of Lords Committee.
- The "Directive" or the "proposal" refers to the draft Directive published by the European Commission in November 2008 as a Proposal for a Directive of the European Parliament and of the Council on the protection of animals used for scientific purposes.
- The "Parliament" refers to the European Parliament.
- "Parliamentary Amendments" referred to the European Parliament Legislative Resolution of 5 May 2009, first reading.[4]
- The "Commission" refers to the European Commission.
- The "Impact Assessment" refers to the Commission Staff Working Paper titled Impact Assessment.[5]
- The "Prognos Study" refers to the "Study on the impacts of different options for the Revision of the Directive 86/609/EEC on the Protection of Laboratory Animals, Draft summary, Prognos AG".[6]
- The "Technical Expert Working Group" or "TEWG" refers to the group(s) organised by the Commission to collect scientific and technical background information for the revision.[7]
- The "Expert Internet Consultation" refers to both the process and the results of the Commission "expert questionnaire on the revision of Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes, 16 June–18 August 2006".[8]

Additional information

33. Throughout this submission, we have tried to avoid excessive detail. This has sometimes been at the expense of omitting fully referenced background evidence. We are very willing to provide the Committee with additional scientific or policy information on any aspect of this submission, or the draft Directive, on request.

1. Objectives

34. A degree of harmonisation of the rules governing the protection of animals in research is required to avoid distortion of the single market and to harmonise animal welfare standards. Some Member States, such as the UK, have particularly high regulatory requirements for using animals in research. We do not wish to compromise the principles operating in the UK, but to point out the potential or actual economic disadvantages created by regulation that would significantly expand that currently in place in the UK.

35. We do not believe the draft Directive is a proportionate response to the problems caused by the current differences in regulatory regimes. Although it might harmonise some aspects, in others it would further exacerbate the internal market distortions. Importantly it further distorts the global market and would therefore render the EU globally uncompetitive.

36. As the "call for evidence" points out, the Commission has stated two aims for its proposed revision of the 1986 Directive, namely:

- Harmonisation of rules to create a level playing field.
- Strengthening the protection of animals used in scientific procedures.

37. In its consultation document of 11 May 2009, the Home Office has broken down these two aims into five high-level policy objectives (p39).[9] The UK bioscience sector supports these objectives.

38. There is no question that the original 1986 Directive contains ambiguous rules and that it is not uniformly implemented in all Member States. We agree with the Home Office statement that "this has left those with higher standards (such as UK) at a competitive disadvantage".[10] However added regulation does not of itself necessarily result in more uniform implementation.

[4] http://www.europarl.europa.eu/sides/getDoc.do?type=TA&reference=P6-TA-2009-0343&language=EN
[5] http://ec.europa.eu/environment/chemicals/lab_animals/ia_en.htm
[6] http://ec.europa.eu/environment/chemicals/lab_animals/ia_en.htm
[7] http://ec.europa.eu/environment/chemicals/lab_animals/scientific_en.htm
[8] http://ec.europa.eu/environment/chemicals/lab_animals/questionnaire2.htm
[9] www.homeoffice.gov.uk/documents/cons-2009-animals-research/cons-2009-animals-research?view=Binary
[10] 11 May 2009. UK Home Office. Consultation on EU proposals for a new directive on the protection of animals used for scientific purposes.

Current market distortions

Currently, the most significant variations between Member States which impact adversely on competition (or could do so) are in the following policy areas:

— animal accommodation requirements;

— the rigour of authorisation of procedures;

— training and licensing; and

— the development, validation and acceptance of alternative methods.

39. Together, these preclude ready mobility of staff and projects between Member States, and/or cause substantial distortions in the cost base of animal research for different countries.

40. In practice this is a much greater problem for EU members visiting the UK than vice versa. For instance an advanced training course was cancelled in 2008 because EU registrants could not be permitted to undertake the course without advance full training and licensing to UK standards. Despite recent adjustments by the Home Office, it is still much more difficult to have senior colleagues from overseas (including the EU) contribute to studies within the UK than vice versa. This results in a steady drain of certain types of experiments abroad in order to facilitate collaboration at minimum bureaucratic cost.

41. Regulations that apply and/or are applied in the UK but not in other Member States have major financial implications. The combination of higher accommodation requirements in the UK and the drive to "full economic costing" of animal pricing in academia are ever increasing deterrents to research using animals.

Requirements of a revised Directive

42. Greater harmonisation is therefore in the UK's economic and scientific interests in those areas concerning the mobility of personnel, the sharing of projects, and the cost drivers affecting animal supplies.

43. In any revised Directive it would be in the interests of animal welfare to ensure that the minimum acceptable standards are raised above those currently operating in some Member States, and that they are applied uniformly. This encompasses both animal accommodation and the application of ethical evaluation and harm-benefit analysis to the authorisation of projects.

44. The draft Directive covers the issues that require harmonisation but:

— goes well beyond what is necessary in many areas (eg scope and controls over authorisation of procedures); and

— encourages Member States to adopt procedures that would in fact hinder harmonisation (eg by determining that training requirements be established by Members States).

45. In general there should be subsidiarity over how the harmonised standards are implemented.

46. Specific problems associated with the draft Commission Proposal, and Amendments from the European Parliament, are illustrated in subsequent sections.

Proportionality

47. We do not accept that the proposed Directive meets the criteria for proportionality which is fundamental to EU law. According to this principle, any action by the Community shall go only as far as is necessary to achieve the objectives of a Treaty, and no further.

48. To justify the proposed Directive, the Commission describes a bleak and negative picture of European bioscience. For example, the Commission Impact Assessment describes numerous economic, animal welfare, scientific and social problems (page 4). We neither recognise nor accept this description. Whilst improvements can always be made, Europe still has a successful and competitive bioscience sector, with higher animal welfare standards than most of the globe, good scientific outcomes, and a high level of public support for well-conducted animal research. A major risk to this sector, in fact, would be the excessive regulation proposed by the Commission. Such regulation would run counter to the EU "Better Regulation" agenda.[11]

49. The explanatory memorandum claims that the Commission Proposal "complies with the proportionality principle" (page 13) on the basis that : (i) it harmonises practices whilst leaving scope to Member States to identify the most suitable measures for implementation, and (ii) the benefits of the proposed measures to the internal market as well as to animal welfare outweigh the costs.

[11] http://ec.europa.eu/enterprise/regulation/better_regulation/index_en.htm

50. In our view neither of the above requirements is met because: (i) the Directive is too prescriptive in how practices such as authorisations and care and accommodation requirements are implemented, and (ii) some provisions have very few benefits to the internal market, instead significantly distorting the global market whilst bringing very few animal welfare benefits.

51. Proportionality should also involve an assessment of whether the effects of the measure are disproportionate or excessive in relation to the intended benefits, or whether alternative measures exist which are less restrictive. A careful assessment of the costs and benefits should take place, taking into account the spectrum of potential stakeholders. An example of where the proposal has lacked proportionality is the application of highly bureaucratic administrative measures to regulate microscopic non-sentient invertebrate animals. It has estimated a small financial cost to public bodies, but has considered neither the practicability nor the significant cost to industry, academia, and therefore, the EU market place of such a provision.

52. Specific areas where the requirements could be simplified with little/no impact on animal welfare include:

- Restricting the Scope of the Directive to those areas where there is scientific evidence that it would benefit animal welfare;
- Within the Scope, tailoring the extent of control to be proportionate to the potential harm (welfare deficit) caused by procedures;
- Removal of multiple levels of authorisation;
- Harmonisation of training and mobility of staff between Member States;
- Collection of statistical information.

Impact assessments

53. We would have appreciated the opportunity to consider the full independent impact assessment carried out by Prognos (of which only a draft summary was published).[12] Furthermore, the Commission Impact Assessment does not accord with our own experience and views on the impact or cost of the proposal.

54. The Commission has acknowledged the need to improve its impact assessments, and claims that "in the new impact assessment system, continued attention is given to the analysis of impacts on businesses, in order to ensure a regulatory environment that is conducive to their competitiveness, innovation and growth".[13] We do not consider that this has been fulfilled in the Impact Assessment for the proposed Directive. Indeed, the issue of competitiveness detailed on page 62 of the Impact Assessment only considers the current issue of outsourcing of animal procedures from EU countries. It does not consider the impact that the proposed Directive itself would have.

55. The Prognos study appears to be based on little more evidence than that of the information in the 66 questionnaires which it states were returned and analysed, and which by its own admission were "not as complete, detailed and fact-based as expected". There are over 200 certified establishments in the UK alone. Greater effort should have been made to gather evidence, and only then to identify ways to streamline existing regulatory burdens in Member States which the Commission had identified, as well as minimise any additional administrative burden and costs that would result from the Directive. This would be more compatible with the EU better regulation agenda which claims that in "reducing red tape and overbearing bureaucracy, the Commission helps business people and entrepreneurs improve competitiveness."[14]

2. International Competition

56. High animal welfare standards are welcomed by the bioscience community, in part because good animal welfare and good science go hand in hand. We believe the EU should be at the forefront of promoting best practice in animal welfare where there is sound scientific evidence of benefit, and would hope this encourages other countries to raise their standards.

57. Our concern is that many of the provisions which purport to increase animal welfare standards merely increase bureaucracy with little or no animal welfare improvement. Such bureaucracy increases costs, thus diminishing international competitiveness. We are already seeing commercial investment increasing faster in countries outside the EU, such as the USA, China and India. Increased costs and bureaucracy are inevitably likely to be contributing factors, even if they are not the only reasons. In UK academia, displacement of animal research even takes place to other Member States where the regulation is less onerous than in the UK.

[12] http://ec.europa.eu/environment/chemicals/lab_animals/ia_en.htm
[13] http://ec.europa.eu/enterprise/regulation/better_regulation/impact_assessment_en.htm
[14] http://ec.europa.eu/enterprise/regulation/better_regulation/index_en.htm

58. The position of the proposal on this issue is not sufficiently explained. On the one hand, the Impact Assessment identifies that there is a "competitive disadvantage for countries with high animal welfare standards resulting from price differences" (page 4). But at the same time, the Impact Assessment suggests that "outsourcing from the European Community" is not likely to be "due to the stringency of animal welfare legislation" (page 62).

59. While international competitiveness is most obvious in a commercial context, the UK's (and EU's) leading academic role in fundamental and applied bioscience research depends critically on controlling costs and reducing bureaucratic delays. The cutting-edge of bioscience research can move very quickly, and bureaucratic delays can kill the lead held by a research group. This is a significant driver to the export of projects to less regulated countries, whether in the EU or elsewhere.

60. UK academic groups undertaking work requiring non-human primates often collaborate with researchers in other countries where the cost of undertaking such research is less (though there is a requirement for all work supported by the BBSRC, MRC, Wellcome Trust, NC3Rs and Defra that "when collaborating with other laboratories, or where animal facilities are provided by third parties, researchers and the local ethics committee in the UK should satisfy themselves that welfare standards are consistent with the principles of UK legislation (eg. the ASPA) and set out in this guidance are applied and maintained").[15] Pushing all such research outside the UK, and indeed outside the EU, would seriously deplete the EU R & D skills base and productivity.

61. Unless adequate harmonisation (of regulations and, more particularly, their implementation) is achieved by the new Directive, this will remain a significant issue. Indeed, it may become worse if more stringent minimum requirements are implemented by some Member States but not others. It is therefore vital that the revised Directive does not exceed levels at which it can and will be implemented uniformly.

62. The primary issues affecting competitiveness in the proposed revised Directive are:

- the increased costs of the regulatory burden (in bureaucracy and animal costs);
- regulatory restrictions limiting research that may be undertaken;
- regulatory delays to approvals; and
- disincentive to staff and institutions of investment in animal-based research in the EU.

63. The first three are addressed more specifically in subsequent sections. The last is more generic, but encompasses all three. Animal-based research is extremely expensive to set up—the facilities are costly and the significant scientific and technical staff involved all need extensive training. Animal costs are high and the rate of generating results usually very low (most obviously compared with many of the robotic systems that are increasingly used in biomedical research). Unless the first three factors are implemented satisfactorily, institutions will not invest in the facilities and staff required. And even if they do, the most able staff will not engage in research that is subject to undue restrictions; they will either stop doing animal-based research, or will do it elsewhere.

64. We consider that there would be a major welfare cost if research is relocated outside the EU. Because UK regulations are both tighter and more rigorously implemented than in most other Member States, the drive to export research has to date been greater in the UK than elsewhere in the EU (indeed, some of that export is to other Member States). If EU-wide regulation is stricter and fully implemented then the likelihood is that research relocates entirely outside the EU. If standards slip even only somewhat following displacement, those EU countries with the lowest current standards that the Directive is designed to enhance would fall yet further behind the new Directive standards.

65. Particularly strong drivers of displacement are the requirements and associated costs of animal accommodation, which is often of a lower standard outside the EU. Even when EU scientists apply best practice to the procedures they themselves undertake outside the EU, they have little or no control over the accommodation standards in which animals are bred or kept. Displacement is therefore almost bound to have adverse welfare impact on the animals used, and is to be avoided.

66. While the major international pharmaceutical companies are likely to maintain sound standards in their in-house research, wherever undertaken, they are increasingly subcontracting animal work to contract organisations. This is particularly true of biotechnology SMEs which would be unable to undertake much of their research without such organisations. If contract organisations, which operate in a highly competitive global market place, are subjected to uncompetitive costs, they will be forced move from their concentrated base in the UK to more accommodating regimes. This could result in a serious debasement of welfare standards most particularly for the more advanced species (dogs, non-human primates) that are used in much contract research. It would also cause serious economic loss to the UK.

[15] www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d = MRC001897

67. There is substantial competition from countries such as China, India and Singapore in developing infrastructure to undertake animal research, which includes not just routine toxicity tests but also R & D. To maintain their competitive edge, the UK and other EU countries need to ensure their brightest and best scientists and industries have sufficient incentive to remain within the EU.

68. Of particular concern in terms of international competitiveness are the amendments passed by the European Parliament on data sharing (Amendments 132, 180, 134, 135, 136, 137). Our sector considers these to be ill-informed, ill-thought out, impossible to implement rigorously, and to have the potential to drive out of the EU most research with any potential intellectual property value.

69. The explanatory memorandum of the Commission proposal claims that "optimum implementation at the national level through the use of identified best practices will provide ample opportunity to reduce unnecessary red-tape and administrative costs". Unfortunately, in many cases the provisions proposed will do exactly the opposite. For example, making mandatory methods of appropriate (humane) killing and cage sizes will increase the cost of research, and hinder the application of best practice without proportionate animal welfare benefits. For example, it does not allow yet-to-be-developed refinements or superior methods of humane killing and housing regimes to be incorporated into the respective Annex or introduced into practice. By creating rigid and complex systems of authorisations and other permissions, the draft Directive fails to reflect the good practice that exists currently in many member states (such as the use of notifications where harms to animals are minimal).

70. These examples illustrate the disincentives which would be created by the proposed Directive to retaining animal based research within the EU.

3. Restrictions to Research on Non-human Primates

(Article 8, Article 10, Article 50 and Amendments No 56, 57, 58, 59, 60, and 61)

71. Around 12 million animals are used each year in scientific procedures in the EU. Of these, around 10,000 (less than 0.1%) are non-human primates (NHPs). By comparison, the US uses three times the number of NHPs in relation to total animal procedures.

72. "NHPs"[16] include:

- Great Apes, such as chimpanzees and gorillas; (Great Apes have not been used for medical research in any EU country since 2000).
- New world monkeys such as marmosets and squirrel monkeys; and
- Old world monkeys such as macaques.

Impact of limitation of NHP use

73. We agree with the statement in the draft Directive that use of non-human primates is of highest concern to the public. Although there is evidence of this from surveys, the public remains supportive of research including the use of NHPs when appropriate and proportionate controls are in place. The proposed restrictions to the use of NHPs on the basis of their phylogenetic relation to humans are disproportionate and potentially detrimental. The revised Directive should recognise the positive contribution that the use of NHP has made to the fundamental knowledge which has led to treatments for humans and animals.

74. Limiting the use of NHPs to "life threatening or debilitating clinical conditions" as per Article 8 (1) (a) would have the effect of:

- Restricting fundamental research into structure, function and malfunction of humans and other animals, including studies in immunology, anatomy, physiology (including reproductive health), microbiology and neuroscience. Such research is crucial to further development of therapeutics for human and animal health.
- Limiting R & D investment in health related-sectors;[17] and thereby impairing EU competitiveness.
- Slowing innovation and impeding vaccine and drug development and commercial collaboration.

75. We are concerned that this proposed restriction has never appeared in the documents or deliberations of the Technical Expert Working Groups, the Internet Consultation or the impact assessments for the Directive.

[16] Reference in this document to NHPs refers to new and old world monkeys only.

[17] Olsen J., Baker M., Freund T., di Luca M., Mendlewicz J., Ragen I., Westphal M., "Consensus document on European brain research" Journal of Neurology, Neurosurgery and Psychiatry (2006) 77 (supplement 1) notes that Europe's young neuroscientists are taking up posts in the USA and staying there.

76. The Commission Impact Assessment claims, in relation to the use of NHPs in scientific procedures, that it is "controversial whether their high sensitivity and awareness makes them a good scientific model under the current breeding, housing and care conditions" (page 50).

77. We are concerned that there is no evidence to support this claim that current care and accommodation requirements adversely affect their efficacy as a scientific model. It is contrary to the views of leading researchers and institutions across the world. The reports of the Weatherall Committee[18] and the Scientific Steering Committee (SSC),[19] were already in the public domain at that time, but were not cited by the Commission.

78. Furthermore, the Commission made their proposals for restricting the use of NHPs after requesting an assessment from the Scientific Committee on Health and Environmental Risks (SCHER), but before the report was published. This report[20] found that at present there are no valid alternatives which would allow for a discontinuation in the use of NHPs. Both the SCHER Report and the UK Weatherall Report clearly detail the disease areas in which the use of NHPs have made a major contribution to therapeutic outputs and where continued use is deemed to be necessary. Neither suggests that current accommodation and care standards impede this vital contribution.

79. We believe the amendments introduced by the European Parliament report (Amendments 56 and 57) adequately addresses our concerns regarding use by lifting the restrictions on the use of NHPs. It should therefore be supported.

Areas of research which may be curtailed due to the proposed restrictions

80. The provisions in Article 8(1) (a) have the potential to prohibit certain lines of research which are essential in developing fundamental areas of knowledge into human and animal health. The inability to undertake such fundamental research in the EU will erode the scientific knowledge-base and drive R & D investment out of the EU.

81. Some examples of fundamental research which may be curtailed by the current draft of the Directive include research on:

— memory systems in the primate brain (to potentially assist memory disorders);

— decision-making and social valuation (to be applied to neurological illnesses such as autism, depression and obsessive compulsive disorder);

— attention (to help understand disorders such as Alzheimer's disease or attention deficit hyperactivity);

— neurostimulation (to help develop techniques to improve the recovery of limb function following injury to the brain or spinal cord);

— vision (to help understand and treat visual disorders); and

— reproduction (to help understand and treat early miscarriage, endometriosis, polycystic ovary syndrome and problems with menstrual cycles).

82. Limiting the use of NHPs in the EU will certainly drive researchers to non-EU countries such as the USA and Asia. We have already seen trends within industry to move research using NHPs out of the UK due to the high costs of supply, transportation and previously to gain protection from animal extremism as well as to limit bureaucracy. We would not wish to see a further erosion of the research-base due to restrictions in NHP use. In the public sector, academics are noting that young researchers in neuroscience are "taking up posts in the USA and staying there".[21] Movement of young researchers out of the UK and out of the EU will have a significant impact on the UK's research base.

Ban on use of great apes (Article 8 (2) and Safeguard Clause (Article 50)

83. Article 8(2) bans the use of great apes in procedures, subject to the safeguard clause in Article 50. Great apes have not been used in research in Europe since 2000 or in the UK since 1998. This is not cause however for an outright legislative ban, and therefore we strongly argue that the safeguard clause be retained. An outright ban should logically and ethically mean that any vaccines developed using great apes should also be banned in Europe. For example, vaccines for Hepatitis C are being developed in chimpanzees, as that is the

[18] www.acmedsci.ac.uk/images/project/nhpdownl.pdf
[19] "The need for non-human primates in biomedical research" by The Scientific Steering Committee (SSC), April 2002
[20] http://ec.europa.eu/environment/chemicals/lab_animals/pdf/scher_o_110.pdf
[21] Olsen J., Baker M., Freund T., di Luca M., Mendlewicz J., Ragen I., Westphal M., "Consensus document on European brain research" Journal of Neurology, Neurosurgery and Psychiatry (2006) 77 (supplement 1)

only other species, aside from humans, which develops a Hepatitis C infection. It is essential that we keep our options open to use great apes if the need arises, especially as we see the development of new variants of disease and new global pandemic threats.

Animals bred for use in procedures (Article 10)

84. The draft Directive requires that non-human primates must be second generation bred in captivity (F2) to be able to be used in research and in Annex III sets out a timetable for breeding up of F2 animals for use in research. The rationale for this provision is to end the use of wild-caught primates for breeding purposes.

85. No research has been carried out, however, as to:

- whether this proposal will have any real impact in reducing the taking of animals in the wild;
- the achievability of the proposal within the designated timeframe;
- the animal welfare impact for the F1 animals that would need to be culled, and the impact of increased breeding pressure on stock females;
- the impact of significant in-breeding to achieve the targets; and
- whether there would in practice be the real welfare gains that appear to be assumed.

86. The Commission's Impact Assessment casts considerable doubt on its own proposal. The Impact Assessment points out that "for macaques, the shortest possible transitional period would be about seven years from now but it is very unclear when breeding colonies could achieve self-sustainability in practice" (page 50).

87. The assessment continues to point out numerous problems and uncertainties with the proposal. For example, it acknowledges that "a particular problem arises from the fact that it has turned out to be difficult for several species to establish self-sustaining breeding colonies" (page 22). In addition, the Commission acknowledges that "breeders would in the short run easily be able to sell the same amount of F1 animals to countries outside the European Community than they currently export to the European Community. Such a supply shift could only be prevented by a global move to use only F2+ animals". The Commission recognises that "the impacts on science and competitiveness would be highly negative".

88. Contrary to the above position, the Commission goes on to propose in the Impact Assessment that "a reasonable transitional period of seven years for the transition to F2+" for macaques (page 52).

89. This provision will have an immediate short-term impact on the availability of such animals for academic, government, EU and industrial research programmes in Europe—albeit with some exceptions, since F2+ macaques are available for academic research in the UK (at some considerable cost). Owing to the limited number of breeders and the significant demand from countries such as the USA which do not have such restrictions, it is likely that breeders will favour other countries first. This will consequently compromise supplies to the EU and hence the competitiveness of European-based research.

90. The requirement to use F2 animals will necessitate a greater than 100% increase in the number of animals kept in captivity for breeding purposes. Again, this appears to have animal welfare implications which are contradictory to the intended aim.

91. The availability of first and second generation purpose-bred macaques is already such that breeders and suppliers can currently only just cope with the demand from the global scientific community. Macaques (cynomolgus and rhesus) are the more frequently used species of NHPs in toxicology tests to assess the safety of new drugs in neurological disease models such as Parkinson's, and in infectious disease, malaria and the production of vaccines.

92. There are a number of ongoing pilot projects evaluating the impact of self-sustaining colonies and inbreeding. Some of these pilots show significant impact on fertility rates and other physiological parameters. These need to be properly completed to better assess the impact of an F2 requirement both on animal welfare and on research.

93. We therefore support the amendment (Amendment 60) from the European Parliament which provides that an animal welfare assessment and feasibility evaluation of implementation of the F2 requirements should take place five years after entry into force of the Directive.

Release of NHPs from controls

94. Parliamentary amendment (80) would preclude release of NHPs. Such a blanket ban would, for instance, prevent the disbanding of healthy animals in a breeding colony to zoos or other non-research institutions, outcomes which are contrary to 3Rs policies. Decisions on release should be based on individual assessment, with veterinary input, not on such sweeping rules.

NHPs as endangered species

95. Whilst this has not been a prominent part of the debate since the publication of the draft Directive, it is worth mentioning that antivivisection groups frequently imply that the use of NHPs in research is contributing to potential extinction.

96. This is not the case. None of the species of monkey commonly used in research is endangered. Indeed, in some countries these monkeys are considered as pests and are routinely shot or captured due to the damage caused by excessive numbers.

97. The issue of endangered species was properly addressed in the Commission Impact Assessment, which stated that there is "no indication that this is really a problem for those species used in large numbers for research." More generically it states that "Research plays an insignificant role for biodiversity in comparison to the destruction of habitats, eg of tropical forests, that should be urgently addressed via conservation policies" (page 39).

4. Extension of the Scope

(Article 2, Annex I, Amendments No.28, 30, 31, 34, 150, 151, 152)

Overview

98. The extension of the scope of the proposed Directive is not justified. It would bring large areas of research that were previously not regulated under bureaucratic control without any tangible animal welfare benefits. This would impede scientific research and markedly restrict our ability to compete internationally in areas of considerable commercial and scientific importance.

99. Whilst it is acknowledged that there is currently a significant disparity between Member States as to the extent of protection by regulation, the sweeping extension of scope of the draft Directive is likely to exacerbate the disparities between the internal EU market and the global market.

100. We believe that the economic burden on national authorising establishments, research institutes, and the commercial sector, estimated conservatively by the Commission in five Member States to cost between €6.6 million and €10 million per year, far outweigh any animal welfare benefit this provision might bring.

101. The provisions would impact negatively on UK scientific research, education, the development of aquaculture-related or other biotechnologies and environmental studies.

Pain, suffering distress or lasting harm

102. In addition to the general provisions on scope in Article 2, the draft Directive defines a "procedure" as any use of an animal for experimental or other scientific purposes, with known or unknown outcome, which "may" cause the animal pain, suffering distress or lasting harm.

103. Our organisations consider that use of the word "may" in the definition of a procedure is seriously problematic, because there is always a remote possibility that anything done to an animal "may" cause pain, suffering, distress and lasting harm even when it is neither likely nor intended to do so. This has caused difficulties for the interpretation of the A(SP)A in the UK. We support those amendments passed by the Parliament which substitute "is likely to" or "is expected to" for "may" (Amendments 28 and 42). However, Amendment 34 (definition of procedure) is problematic (i) because it uses "may" rather than "expected" or "likely", and (ii) because it uses "may or may not". This Amendment would therefore bring within the scope the use of any animal used for any scientific study, even when there is no harm inflicted and even when the animal is not sentient. This would cover animals humanely killed for their tissue, all animals used in observational studies and all immature invertebrates. In practice this would not be possible to manage, and is clearly inconsistent with Amendment 33 which excludes practices that do not cause pain, suffering, distress or lasting harm.

Vertebrates bred for organs and tissue

104. The Directive and Parliamentary amendments are inconsistent as to the inclusion of animals killed humanely for their tissues. The claim by the Commission in the Expert Internet Consultation that "the extension of the scope to cover animals bred for the primary purpose of their tissues and organs would significantly improve the welfare of the animals involved" is not supported by evidence, and was not supported by the Technical Expert Working Group.

105. Extension of the scope to all such animals would cause a major increase in regulatory burden with no animal welfare benefit. Indeed it may adversely affect welfare in that raising the level of bureaucracy and cost around using isolated organs and tissue removes an incentive to use them instead of using living animals. It therefore runs counter to the entire 3Rs agenda. The assumption from the Commission that "only a small number of companies will specialise in providing these services thus keeping additional administrative costs low" does not appear to have supporting evidence.

106. The Technical Expert Working Group for Scope agreed that the primary concern with such animals should be their welfare, and that this could in practice be promoted by ensuring that the authorisation of premises automatically meant that all animals of protected species contained therein were covered by the scope of the Directive with regard to housing and husbandry conditions, education and training of staff etc. Moreover allowable means for humane killing are also covered by the Directive.

107. The implication of this is consistent with our view, namely that animals bred for organs and tissues should fall under the general provisions of the Directive, but should not be classified as procedures or require specific authorisation for humane killing. We consider the situation to be improved by the Parliamentary Amendment 28, but this will require confirmation from the Council.

Routine procedures

108. The Technical Expert Working Group for Scope agreed that routine procedures, such as marking and any management or clinical veterinary duties carried out for the day-to-day well-being of the animals should be excluded. We support this conclusion. It would be particularly helpful if in Article 2.4 (b) the identification of the genetic status of animals was recognised as the routine husbandry procedure that it is.

Immature forms of vertebrates

109. Including all embryonic and foetal forms as from the last third of their development is arbitrary, since sentience has not been established for all of them. For example, the Technical Expert Working Group for Scope considered that they "were not in a position to form a scientific opinion as to when a rodent fetus or new-born may be capable of suffering, although suggested the final 20% of pregnancy may be appropriate for rodent and poultry species".

110. A particular issue would be the cover of embryonated hens' eggs for vaccine production and quality assessment (for some production processes), where more than a million eggs a day are used to fulfil the demand for flu vaccine supply and flu pandemic preparedness.

111. An amendment from the European Parliament (Amendment 30) has restricted the "independently feeding larval forms and embryonic or foetal forms" to species of mammal as from the last third of their normal development. This is helpful, although the wording will need further clarification, since mammals do not have independently feeding larval forms.

112. The European Parliament amendment would now exclude fish embryos, which are used as alternatives to higher animal species. We support this, since including them in the scope would subject them to administrative procedures listed in the Directive, and discourage further research on alternative methods using these immature non-sentient forms. Our view is consistent with that of the Technical Expert Working Group for Scope, which noted "significant difficulties with including these forms in such a way that all provisions of the Directive apply, in particular the impracticality of making an accurate count".

113. The issue of the development stage at which there is sufficient anatomical development to permit sentience, and therefore to warrant inclusion in the controls, requires a better scientific analysis.

Invertebrates

114. There is no clear scientific rationale as to why the scope should be extended to selected invertebrates (cyclostomes, cephalopods and decapods). The report of the Scientific Committee of the European Food Standards Agency (EFSA) does not provide robust scientific evidence to support such an extension. Extensive studies have not produced scientific evidence that decapods perceive pain and might "suffer" during scientific procedures.

115. There may be a tentative case for extending EU regulation to certain adult cephalopods, such as octopus (Superorder Octopodiformes), squid and cuttlefish (Superorder Decapodiformes). There is some evidence these animals may experience pain and suffering resulting from having well developed senses and complex nervous systems. The only invertebrate covered by the UK legislation is Octopus vulgaris. This conclusion would be consistent with the findings of the Technical Expert Working Group which found that "insufficient evidence is available at the present time to consider the inclusion of any invertebrate species other than of cephalopods".

116. Including other invertebrates, together with immature forms, has no scientific basis and would result in regulation covering potentially enormous numbers, given the density of immature planktonic forms in every sample of seawater. Certainly the Commission has provided little robust scientific evidence as to why such a provision is proportionate or necessary.

117. We consider that European Parliament amendments 151 and 152 (which remove cyclostomes and reduce the species of decapod crustaceans to infraorders Brachuyra and Astacidea) to be an improvement. However, the decapods Brachuyra and Astacidea, which cover lobsters, crabs and crayfish, constitute the majority of decapods used in academic research and research into aquaculture. In addition, immature forms are still covered. As a result, the regulatory burdens would in practice be little altered by the European Parliament amendment.

118. Extending the scope of the Directive to cover whole classes of invertebrates may also have the unintended consequence of undermining the incentive to use them as animal models in place of vertebrates; decapods are increasingly used as replacements for higher order animals as part of the 3Rs agenda.

119. Crustacea are common, cheap, abundant, the adults are relatively large, and they are easy to keep and handle. Their physiology makes them ideal for educational studies in behaviour and physiology. There is no justification, but much disadvantage, to banning such use for secondary education. It will also have an impact on in-vivo skills training at undergraduate and postgraduate levels. Decapods are regularly used in such training; imposing a regulatory cost for using such animals is likely to lead to the EU being a less attractive place to undertake such training. The ABPI has recently reported on the shortage of in-vivo skills in the UK and the need to ensure that live animal work is supported.[22] The Bioscience Innovation Growth Team Review and Refresh of Bioscience 2015 also proposes that in-vivo skills be included in the Strategically Important and Vulnerable Subjects list.

120. Decapods are ecologically sensitive and their biology therefore of great scientific interest in addressing environmental concerns (pollution and effects of climate change).

121. Decapods are commercially very important. Studies of decapod crustacea for the aquaculture industry could disappear very quickly to countries in the Far East where the UK faces intense commercial competition. The increased cost and bureaucracy in research would diminish the UK's competitive edge in industries such as the bio-discovery of useful biotechnologies and natural products.

122. Taking the above into account, we believe that decapods, cyclostomes and immature forms of all invertebrates should be removed completely from the scope of the Directive. The impact of including them in the legislation would be grossly disproportionate to any tangible welfare benefit achieved.

Problems of implementing the proposed legislation on invertebrates

123. It would be very difficult to apply the requirements of the Directive to invertebrates in the following areas:

- Assessment of "severity" level, since this is based on experience of pain for which there is very little scientific evidence in such species.
- Methods of humane killing, since there are no known methods of rapid, pharmacologically-validated euthanasia that could be specified for decapods. It is unclear if any of the reagents currently used to "anaesthetise" invertebrates have any analgesic benefit.
- Inclusion of larval (but nonetheless "free-feeding" stages) would pose questions over legal controls over sampling seawater, assessing plankton distribution, and even whether feeding plankton to experimental fish would be a regulated procedure.
- Only specialists could identify the species of immature forms, which can be microscopic. Even without species identification, counting the huge numbers would be an insurmountable obstacle.

[22] www.abpi.org.uk/Details.asp?ProductID = 325

— Supply and breeding, since decapods are obtained from fishing by-catches, collected directly from the wild or purchased from commercial growers. There are no dedicated breeding establishments and none are likely to be set up as viable businesses.

— The sheer diversity of species and lifestyles within the invertebrate orders would require regulations to be drawn up almost on a species by species basis.

— Few staff currently have the required knowledge of crustacean biology to enable them to assess potential welfare issues (even if they exist) or implement the legislation. Training would be costly and time-consuming. The only people available to provide any training would be the scientists proposing to do the work.

Death as a lasting harm

124. An amendment was tabled in the European Parliament to include death as falling within the definition of lasting harm. It was not passed, but could reappear at second reading.

125. Our organisations oppose the inclusion of death as falling within the scope of a "procedure" (under the term "lasting harm"). This could result in numerous appeals of decisions which apply a severity classification and conduct a harm-benefit assessment. In particular it would prove exceptionally difficult to determine what degree of harm should be given to death itself, given the fact that the overwhelming majority of animals used in scientific research are bred for the purpose, and are humanely killed at the end of the procedure in any case (in order to analyse their tissues).

126. We note that our view is consistent with a High Court ruling in 2008 in the UK which rejected the inclusion of death as a lasting harm under the UK A(SP)A.[23] We can provide a more detailed note to the Committee on our rationale if requested. The lesson from the High Court experience is that it would be much more satisfactory for the Directive to be explicit in excluding humane killing from being a regulated procedure.

5/6. Authorisation of Decisions

(Articles 20–43)

Principle

127. In accordance with general regulatory principles, the extent of control should be proportional to the potential harm caused by the procedures and therefore the potential welfare gains of regulation. The level of bureaucracy and burden of costs should be minimised when the harms to animals are least. This would allow the competent authority to concentrate efforts on maximising application of the 3Rs, and improving animal welfare for project licences that involve moderate or substantial pain, suffering, distress or lasting harm. The role of the competent authority should not detract from the importance of other safeguards elsewhere in the system, including ethical review, harm/benefit assessment, application of the 3Rs, humane endpoints etc.

Commission proposal

128. The Commission proposal is one of comprehensive mandatory authorisations. There are some benefits to authorisation, namely that it gives a centralised process which facilitates a consistent application of control procedures. It may reassure the public in that a further level of control is applied, and be more appropriate for smaller establishments that do not possess the ability to conduct robust processes because of limited internal expertise. It passes the final accountability to the competent authority in cases of dispute.

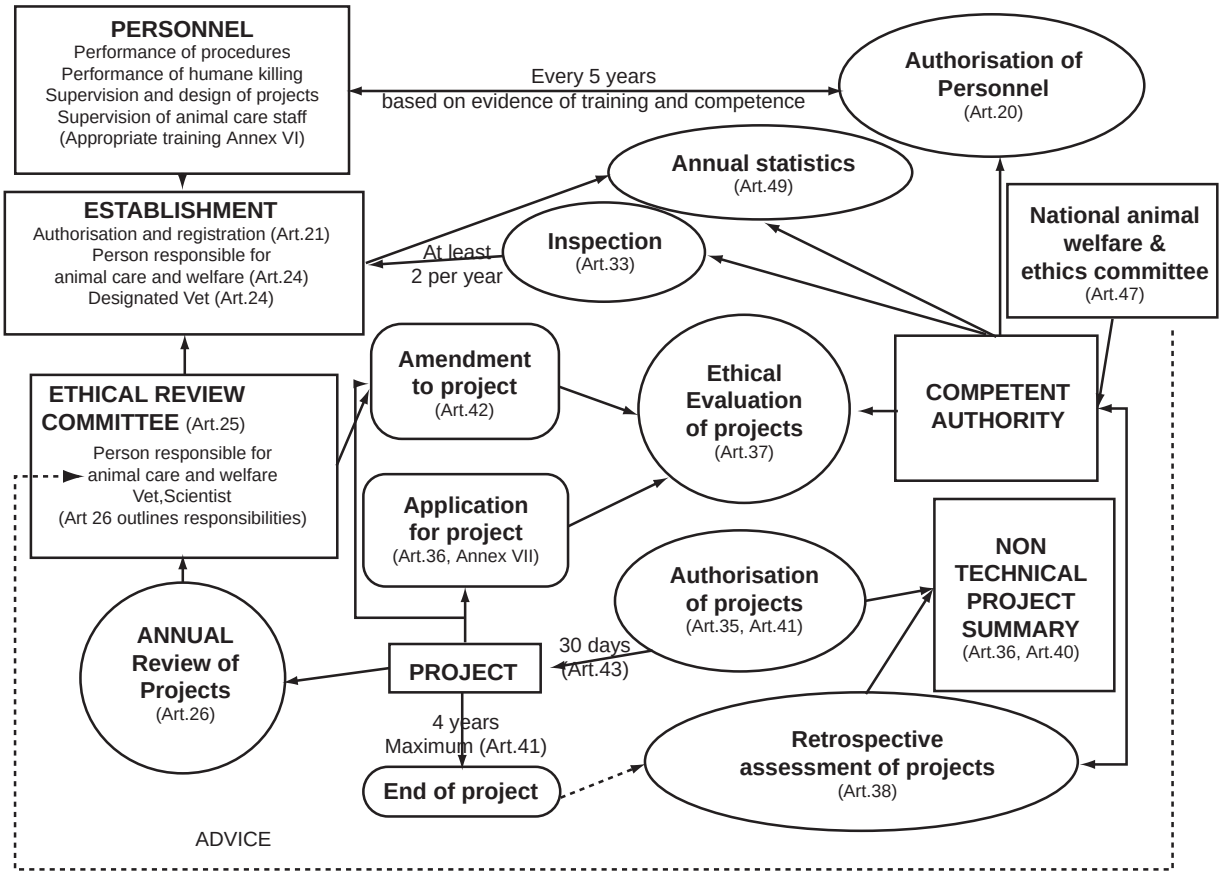
129. The explanatory memorandum in the Commission proposal points out that *"stakeholders supported the approach to ensure a flexible mechanism that allows implementation to be determined at a national level"*.

130. The reality is that the Commission has proposed complex and multiple levels of authorisation and review prior to and during the conduct of research. This will not automatically improve the implementation of the 3Rs; indeed it may have a negative welfare impact by hindering the flexibility to rapidly adopt new techniques which would advance animal welfare.

[23] http://scienceandresearch.homeoffice.gov.uk/animal-research/publications-and-reference/publications/09pcd-holders-circulars-2008/06june2008/PCD_Circular_June_2008.pdf?view=Binary. The BUAV argued that the death of an animal ie simply that it is no longer living, as distinct from any suffering preceding death should be considered in the cost benefit assessment of a project licence application as an adverse effect, but the court ruled against the BUAV.

Complexity of authorisation process

131. The complexity of the levels of authorisation and review currently proposed illustrated in the diagram below.



132. Before commencement of a project, six levels of authorisation must be obtained from the competent authority (authorisation of the establishment; personnel performing procedures; humane killing; supervising and designing projects; supervising animal care staff; authorisation of project (Articles 20, 21, 35 & 41)). The project is then potentially subject to a further five reviews during or at the end of its four-year lifespan (three annual reviews by the local ethical review committee, Article 26 plus retrospective assessment of project by the competent authority, Article 38; plus reporting of actual severity of procedures, Article 49). All this is carried out on a background of biannual inspection of the establishment to ensure compliance with the Directive (Article 33).

133. It is inappropriate that these multiple tiers of regulation apply comprehensively to procedures where there is no or minimal welfare impact (eg humane killing) as to those where the impact is severe. Parliamentary amendments would, for many projects, ameliorate some of the steps (eg annual review), but still leave much of the bureaucracy, for instance with all remaining categories of authorisation still required for humane killing.

134. The Commission claims that *"positive impacts would occur at the level of authorisation bodies in the member states due to more flexible and efficient handling of the procedures. Industry and academia would benefit from deadlines for authorisation decisions."*[24] Our conclusion is quite the opposite.

135. An example of how the proposed authorisation process might work is given here:

1. The applicant must submit details to a competent authority for ethical evaluation, on which apparently no time limit is placed. The ethical evaluation must involve extremely detailed assessment as set out in Article 37, with no less than 15 areas of information to submit. The results of the ethical evaluation are presumably returned to the applicant for revision.

2. The establishment must keep records of the ethical evaluation (from the competent authority), to submit back to the competent authority on request.

[24] Commission draft proposal (page 9)

3. The user establishment must then submit the modified application to a (probably different) competent authority for project authorisation, together with the project proposal and details of the 10 further areas of information required as set out in Annex VII.
4. The establishment must keep records (from the competent authority), in order to submit back to that competent authority upon request.
5. There are additional requirements for retrospective assessment to be determined during the ethical evaluation. The non-technical project summary must then be updated with the results of the retrospective assessment.

Timing of decision-making

136. The Commission Impact Assessment highlights that "member state authorities seem to have relatively unclear standards for the timing of these procedures and often also the criteria for decision-making seem from the applicant's point of view open to interpretation" (page 16).

137. We welcome, in principle, deadlines for authorisations. However, we believe such deadlines should also cover the ethical evaluation, which could be open-ended (depending on how the competent authorities are designated) and could cause substantial delays.

138. It is unclear why the proposal has separated these two processes, since it stated in its Expert Internet Consultation that "it is important to note that terms authorisation and ethical evaluation are interlinked. This is especially important when discussing delays due to authorisation… It is not possible to separate the two in a meaningful manner and in a way that would be applicable throughout the EU. Therefore the stated delays due to authorisation are considered to cover also delays due to ethical evaluation". We would support this analysis.

139. Although the proposal has reduced the problem of different interpretations of what is required for decision-making, this is at the cost of a system which is overly prescriptive, complex, and at times self-contradictory and confusing.

The possibility of notifications

140. The proposal is for a rigid system of authorisations of all projects, together with an ethical evaluation process to which it is not clear that time limits apply. The proposal does not take into consideration sufficiently the additional financial costs of such a highly controlled system, and has not adequately assessed the potential delays to research which could result. The Commission appears not to have assessed whether notifications could have been applied in some cases, even though they are occasionally used in some Member States where animal welfare standards are high.[25]

141. A notification process allows rapid progression of projects or amendments where harms to the animals are minimal and ethical evaluation at a local level has been favourable. The competent authority still has the opportunity to intervene and/or conduct retrospective audit if any issues deemed to be of concern arise. It also allows prompt implementation of refinements to procedures which can be identified during studies. It allows both the competent authority and the establishment to focus effort on those projects and procedures involving greater pain, suffering, distress or lasting harm.

An alternative approach

142. The Commission has consistently emphasised the need for flexible implementation of the Directive at the level of the Member State. In our view, this should include the ability for countries to use notifications where appropriate, and also to allow ethical evaluation at the institutional level in certain cases. Hence different mechanisms can apply in different Member States, as long as there are safeguards to ensure projects have been properly justified, ethically evaluated and all safeguards applied.

143. One possible approach would be for the internal permanent ethical review body (PERB) of an institution (which is capable of being designated as a competent authority for ethical evaluation under the Commission proposal) to conduct an initial ethical review in order to assign a severity classification to the proposed procedures. If these are only classified as mild, the PERB could continue to conduct a full ethical evaluation including harm/benefit assessment.

[25] For example the German Animal Welfare Act allows notifications for the use of invertebrates. Article 8a (1) states that "Any person intending to conduct experiments on cephalopods or decapods shall notify the planned experiment to the competent authority at least two weeks before the experiment begins".

144. Projects containing only mild procedures where the ethical evaluation was favourable could then be notified in advance to the competent authority for authorisations, together with details of the ethical evaluation and notice of the intended start date. There must be sufficient time for the competent authority to intervene, and a mechanism to flag up issues which might be of concern (for example, use of an unusually large number of a species of high sensitivity). Authorisation by the competent authority could be given retrospectively, or could be deemed to be given after a certain time period allowed ("Tell & Do after a preset interval").

145. This approach would be consistent with the findings of the Technical Expert Working Group. They noted that "in some countries the green light of the registered ethical review committee is at the same time the authorisation of the project", and considered that "without the green light of the ethical review committee no authorisation will be granted".

146. Projects containing moderate or substantial procedures and all those involving NHPs must be submitted to the competent authority for authorisation. The competent authority could conduct a full ethical evaluation and confirm whether a "favourable" assessment was correct. Applying a principle of proportionality, a decision of the competent authority should be available within 30 days for moderate procedures or 60 days for severe procedures or those using NHPs. A longer period may be appropriate for exceptionally complex projects ("Submit & Wait for authorisation").

Amendments to Projects

147. Amendments to mild or moderate project licences that do not increase the severity limit should be notified in advance to the competent authority with no time limit before implementation ("Tell & Do"). Amendments that involve an increase in severity limit, substantial procedures or those in NHPs should be submitted, together with the outcome of the PERB's ethical assessment, to the competent authority for authorisation. This is consistent with the Technical Expert Working Group's proposal that "a local ethics committee could approve minor changes on a fast-track basis and refer major changes to the national competent authority".

Additional parts of the authorisation process

148. The Prognos study states that "retrospective analysis has the potential to verify which types of animal tests have really been useful for the progress of science and which have been rather unreliable" (page 17). This is only of limited truth:

- Looking at single projects in isolation shortly after completion can have benefits for the 3Rs, but will not be particularly useful in determining scientific value given that the benefits of fundamental research can take a decade or more to become apparent.
- Systematic reviews may be of value but depend on a substantial body of research, not single studies.
- The assessment of the value of scientific research is, and should always be, an intrinsic part of the scientific process. It should come about through publication of results and subsequent assessment of a body of properly peer-reviewed scientific papers.
- For regulatory studies the majority of work is conducted to meet internationally agreed requirements. It will not be reasonable or appropriate to interpret the outcome of a single project and its impact on the overall scientific approach.

149. The Commission has itself acknowledged the potential problems with retrospective analysis which it identified in its preliminary analysis. The expert Internet consultation states that "preliminary results indicate that introduction of retrospective analysis of all projects would however lead to a high increase in costs in the short and medium term while it is yet uncertain if the objectives of learning from mistakes and achieving more accurate data collection on severity and benefits are met" (page 26).

150. Annual review of projects (Article 26) should be restricted to projects that are classified as "severe", as should retrospective review, as now proposed by the European Parliament.

Harmonisation of training

151. The Commission draft proposes that Member States be left to determine training requirements (Article 20). However, there are already clear differences in training and licensing requirements between Member States. This hinders ready mobility of staff and projects between Member States, and thereby incurs significant bureaucratic costs. Unless the new Directive specifically ensures that training requirements are unified and uniformly recognised across the EU, unnecessary bureaucratic obstacles will remain.

Collection of statistical information

152. Retrospective reporting of severity is agreed to be desirable but (as several groups internationally have found) surprisingly difficult to achieve in a manner that is meaningful, efficient and consistent. Making it mandatory, while leaving it to Member States to decide how it will operate, will result in further major disparities between Member States in terms of both the bureaucratic load and the comparability of data. If such a requirement is to be introduced, it needs to be designed to be effective and efficient and be operated consistently across Member States.

153. The enhanced scope of the Directive will greatly increase recording and reporting requirements, as described elsewhere.

Restrictions on procedures

154. The draft Directive and/or Parliament's amendments impose a series of restrictions on the research that may be undertaken within the EU. Several would have a serious impact on the ability of the EU to maintain its world-leading science base.

155. We do not consider these restrictions to be well justified. They are an example of how the Directive is in general overly-prescriptive, excessively detailed, and too complex.

156. Examples include:

— Restricting or preventing use of non-human primates (NHPs) in fundamental research. See section 3 on NHPs on page 16.

— Preventing procedures classified as "severe" if more than "transient". Neither word is currently defined adequately. This restriction could preclude research into the most debilitating or serious human and animal diseases, such as arthritis or toxaemias. Rather than an outright ban, the approach should be to ensure a rigorous ethical review incorporating a harm:benefit analysis that ensures that serious adverse impact is only authorised when the likely benefit warrants it. A reference point in human medicine would be appropriate here: the procedures to be undertaken would be no worse than those suffered by human patients and would almost always be far shorter lasting (eg about two weeks for arthritis studies in rodents compared to decades for the disease in humans).

— Prevention of some types of "reuse" (Article 16). If taken according to the wording of the Commission draft, this would prevent procedures such as the implantation of telemetry devices followed by recording data from them. Just such techniques foster the 3Rs by generating more and better data from fewer animals, and therefore should be encouraged rather than restricted. The Parliament amendments (Nos 72, 73, 74, 75) adequately address this problem, and should therefore be supported.

— Restrictions on research undertaken outside research institutions (Article 21). The draft is inconsistent but there is a strong potential for there to be serious restrictions on the use of animals that are not purpose bred (which would for instance restrict environmental studies) or the use of non-approved accommodation (which would prevent research on farm animal welfare under commercial conditions). The wording would appear to derive from a blinkered view that all animal research is for medical research, which is to ignore research for veterinary, farm animal or environmental studies.

— Restrictions on release from the controls. Article 19 includes "animals used or intended to be used in procedures", and Amendment 80 excludes NHPs from release. It is entirely right that such release should be controlled, and be subject to veterinary approval. But it is important to avoid wording that has unintended consequences. For instance, it would be absurd to prevent release back to the wild of wild animals caught in environmental studies. It would be similarly foolish to block the release of a monkey colony that was no longer required for research. Both these instances would currently require culling of the animals or the entire colony if no longer needed for research.

7. Care and Accommodation

(Article 32 and Annex IV)

157. The principle of minimum standards of care and accommodation for laboratory animals across Europe is desirable.

158. The draft Directive sets out mandatory standards for care and accommodation in Annex IV. This incorporates elements of the guidelines from Council of Europe ETS 123 Appendix A. The dates given when the guidelines would become mandatory are January 2012 or January 2017 depending on species. These are fixed dates, regardless of when the Directive is actually passed and then implemented in member states.

159. It is of note that the Commission has already approved ETS 123 as a recommendation "on guidelines for the accommodation and care of animals used for experimental and other scientific purposes (2007/526/EC—18 June 2007)" and states that "Member States should pay regard to the guidelines set out in the Annex to this Recommendation".

160. There is no consistent approach to the status of these guideline. They are referred to originally in the Impact Assessment as "standards" (page 11), but subsequently as "guidelines" (page 18).

161. Considerable expertise was involved from both scientific and animal welfare organisations over a number of years to develop the "good practice guidelines" for ETS 123. The expert groups submitted background information to support their proposals, based on scientific evidence and practical experience, and these are particularly valuable in the general sections which sets out the performance standards required for animal welfare. However, specifications for cage sizes are engineering standards, for which specific scientific evidence does not exist.

162. There are significant concerns in many sectors across the EU that this proposal is overly prescriptive and lacks proportionality, given the significant costs and uncertain welfare benefits, particularly for rodent species. The Commission has estimated that only about 20% of establishments in Europe have implemented ETS 123. Those complying could be smaller establishments where the standards were easiest to implement, and/or those with the greatest capital expenditure programmes, such as in the commercial sector.

163. A similar figure for compliance is specified by the Commission in its analysis of the data from the Prognos study in 2006 (page 48) as a "preliminary finding" and therefore cannot be relied upon, given the diversity of respondents and non-respondents to the survey. In fact, the sampling through the survey was likely to be biased towards those users who were more likely to be in full compliance, and did not take account of the fact that, where animals are not bred in-house, a small number of breeders supply the overwhelming majority of animals to user establishments.

164. It is a credible proposition that large laboratory animal species such as dogs and non-human primates need better housing and husbandry practices than they currently have in many EU member states. However, for rodents, a greater degree of flexibility in space allowances is adequate for stock animals, especially given the long-standing experience with current UK provisions. Good animal welfare can often be achieved by means other than increasing cage size, such as by environmental enrichment.

165. The standards now proposed in Annex IV for space allocation for stock rodents significantly exceed the enforced UK standards set out in the UK Codes of Practice. These provide animal welfare to the high standards demanded by the Home Office, even though they do not meet the exact specifications of ETS 123.

166. Several Articles (especially 32), probably unintentionally, would restrict the ability to undertake research on farm animals and on wildlife. It is essential that scientific research for the welfare of farm animals, and for ecological protection and wildlife or conservation purposes, can be carried out under conditions representative of those on the farm or in the wild or elsewhere. For example, the space allowance under which broiler chickens are kept on a farm is far less than that detailed in the draft Directive.

The situation in the UK

167. A strict and detailed Code of Practice has existed in the UK from 1986 with stocking density requirements less than those proposed in the revised Appendix A of ETS 123. The UK stock holding floor space allowances have never been cited as being inadequate or directly leading to compromises in animal welfare.

168. The UK's strict regulatory inspection regime to date has included the breeding facilities for all species within its scope, and the UK has been continuously self-sufficient in breeding and supplying standard stock animals. This significant experience of the use of research animals, combined with a strict inspection and monitoring regime, has not been considered in the Commission Impact Assessment despite providing significant practical evidence supporting appropriate standards in animal welfare.

169. Currently, as ETS 123 is guidance, the Home Office is able to provide derogation for research that involves animals covered by the legislation but where the ETS standards are either not necessary for welfare or where they are not appropriate for scientific reasons.

Alternative solutions

170. A preferable solution would be for the recitals to refer to Appendix A as preferred guidelines. Minimum standards in Annex IV could then be based on established criteria to strike a balance between animal welfare and cost.

171. An alternative proposal is that Appendix A should be neither a minimum requirement, nor a non-mandatory guideline. Rather, it should be the formal basis on which national authorities inspect and implement, with the ability to apply discretion and derogations, as well as scientific judgement.

172. In view of the issue concerning agricultural research, we therefore propose that the requirement that "all animals should be provided with accommodation, an environment, at least some freedom of movement, food, water and care which are appropriate to their health and well-being" (Article 32) should apply only to animals held within licensed establishments. For studies of commercial husbandry or management, animals should, where there is scientific justification, be allowed to be kept at the space allowance typical of standard husbandry. Equivalent derogations need to apply to environmental studies.

Background

173. Appendix A of ETS 123 was developed as a guideline, probably aspirational, not to be mandated as a minimum standard. It was always recognized that if it was to be transposed into a new Directive, it would remain guidance, in a similar manner to the status of Annex II in the current Directive. This reflects in part that there were aspects of ETS123 (eg the very expensive relative humidity requirements) that did not gain universal acceptance across the expert group.

174. It was always intended that the UK Home Office would ratify ETS 123 and this it did within one year, but derogating the space allowances for stock animals specified in Appendix A to those currently used and defined in existing Codes of Practice. ETS 123 was to be appended to A(SP)A as a Code of Practice, not as law.

175. If Annexes in a Directive cannot be guidelines, then more appropriate, realistic and considered minimum standards need to be adopted.

176. We have concerns over the Commission process for developing these provisions. The Commission relied upon its expert Internet consultation, but this involved only a single option being put forward——that elements of the revised Appendix A become minimum standards. No other options were suggested for the consultation, and no review of the suitability of ETS 123 as mandatory standards was carried out. This approach contravenes the Commission's own guidelines on impact assessments and consultations, which states that they should identify "alternative policy options and their likely positive and negative impacts".[26]

177. The overwhelming majority of respondents who gave comments to the Commission Expert Internet Consultation were opposed to Appendix A becoming minimum standards.

178. The Commission suggested that the adaptation of the revised guidelines would permanently increase daily housing costs for rodents by approximately €0.02 per animal. No evidence was given to support this. Comments from the consultation overwhelmingly assessed this to be a very large underestimate.

179. The Commission Impact Assessment suggests that currently "3% of the animal studies performed in all 25 Member States yield unreliable results due to inconsistent or unsuitable housing and care conditions" and that this would not happen if the revised ETS 123 standards had been mandatory. It then assumes the annual benefits in all (the then 25) Member States would be in the range of €90 million.

180. There was no evidence presented that 3% of animal studies yield unreliable results, nor that this is in some way linked to a failure to abide by ETS 123 standards. This appears to be based on an assumption that welfare standards are poor just because the ETS 123 has not been applied, although no evidence is supplied to support the assumption.

Flawed transposition

181. The statement by the Commission that the proposal to make elements of Appendix A mandatory would *"bring the Directive in line with current scientific and technical knowledge"* cannot be substantiated. The expert working group report from the ETS 123 states *"exact numeric values for minimum cage sizes and heights as well as for maximum stocking densities can never be scientifically evaluated and proved"* (Process of determining recommendations by the "expert group", Section II.1.1, rabbit and rodent report).

182. Much of the advice in Appendix A is aimed at encouraging good practice, with advisory qualifications. It is therefore regrettable that the Commission proposal has omitted much of the text of Appendix A, which contains the principles to be applied and the performance standards to be implemented. In fact, omission of

[26] http://ec.europa.eu/enterprise/regulation/better_regulation/impact_assessment_en.htm

such text could result in poor animal welfare. For example, requiring social housing without qualifications could result in injuries to male rabbits, some male strains of mice and male hamsters through their natural competitive behaviours. There is no provision for exemptions to group housing for scientific reasons eg for metabolism studies or for surgically prepared animals that need to recuperate in isolation.

183. The Commission acknowledges in its Impact Assessment that "many of the general provisions and recommendations of the revised guidelines for health, transport, quarantine, acclimatisation, isolation, watering, feeding, cleaning, records and identification are already in place in many establishments, as these are integral parts of good scientific/laboratory practice to obtain reliable and reproducible scientific results".

184. Annex IV in the Commission proposal incorporated much of the Revised Appendix A, but with some significant and concerning changes. The basis of reasoning for these changes has not been made clear. In some cases they would undermine animal welfare, in others they would interfere unnecessarily with legitimate research. Furthermore, the provisions do not cover breeding/weaning practices, nutritional and health issues, as well as environmental conditions and some relevant species-specific information.

185. For example, there has been an inadvertent transcription of text from the existing Directive which could lead to a 50% reduction in space allowances for laboratory dogs during procedures, and the temperatures specified for some amphibian and reptile species could result in their death. This serves to emphasize the potential dangers to welfare of the Directive incorporating legally-binding details of a technical nature.

Impact of the Commission proposal

186. The Commission appears not to have considered the economic and indirect welfare consequences of the proposed requirements.

187. Transition to the stocking densities in Annex IV, mandated by Article 32, would require massive capital investment in some establishments and sectors. It is not simply a matter of buying new cages and equipment. In some cases, lower stocking densities would reduce the capacity of existing space, and require new buildings to be constructed. This transition has to be carried out without jeopardising the research activity.

188. The total investment required for commercial laboratory animal breeders of common specifications of rodent species and rabbits in the UK could be substantial—equivalent to the total capital spend of the relevant businesses in Europe for several years (according to the calculations of the largest animal breeders in Europe[27]) meaning there would be enormous pressure on budgets at a time when there are already global constraints on access to capital. The total capital investment across Europe for additional space and replacement equipment could exceed €100 million which is very large in comparison with the size of the businesses that must support it.

189. Capital costs to the much larger number of universities and public research institutions would likewise be substantial.

190. Much of the pharmaceutical and contract research sector has anticipated the need to move to Appendix A standards already. However, within the public and academic sector, capital planning cycles can be prolonged. The time lag between planning, building and commissioning new facilities is very significant. A transitional time period of at least five years, and preferably 10, would be necessary to comply with the new annex.

191. All these factors could put great strain on capital budgets and substantially increase the cost of breeding many of the species and strains of animals used in biomedical research. This would be likely to lead to:

- — disruption to animal supplies and research activities during the required building programmes;
- — the significant additional costs of production being at some point passed on to users.
- — increased animal costs adding to regulatory costs in harming EU competitiveness;
- — research operations involving large numbers of animals moving out of the EU;
- — animal breeding being moved to areas either within or outside the EU with lower labour costs and/or capital requirements;
- — adverse welfare implications from the resulting increased transport distances and housing under conditions not controlled by the EU; and
- — undermining the security of supply because of limited portals of entry.

192. It is therefore far from clear that the proposed housing standards would result in the welfare gains envisaged, yet the direct and indirect economic costs would be great.

[27] As referred to in the submission to this inquiry from the Laboratory Animal Breeders Association

8. Alternative Methods (and the 3Rs)

(Article 46)

193. The "3Rs"

- Replace the use of animals wherever possible;
- Reduce the number of animals needed to achieve the objectives;
- Refine methods to cause animals the least possible distress.

194. Statistics collected by the Home Office show that the number of scientific procedures involving animals in 2007 in the UK was just over three million. This is significantly less than 25 years ago, although the numbers fluctuate from year to year. Yet, over the same period, the number of new medicines under development in the UK increased substantially, and remains high.

195. This reflects the fact that significant parts of the research process, which in the past required the use of many animals, now need comparatively few. This is in turn thanks to advances in science that have progressively yielded "alternatives" that, once validated scientifically, can replace the use of animals. From a political and welfare perspective it is important to appreciate that such improvements arise from a larger body of R&D and have to date resulted primarily as spin-offs from research that was not directed prima facie at the 3Rs—eg computer modelling, in silico assays, magnetic resonance imaging.

196. Scientists in academia and industry communicate extensively and collaborate to improve research methods and share best scientific practice. All researchers use alternative methods wherever possible—to do otherwise is not only illegal (in the UK) and unethical, but also far too expensive. While alternatives should be used where available and appropriate, they should not be mandated where there is no international acceptance, since animal studies would still be required outside the EU.

197. In the UK, the requirement to consider alternatives is assessed formally in the ethical review and harm: benefit analyses that are legally required before a licence to proceed is granted. The UK Home Office states that "use of animals in scientific procedures will not be licensed if alternative non-animal techniques are available".[28] We support moves in the draft Directive that would introduce EU-wide ethical review, provided that it is undertaken as efficiently as possible.

198. It remains the case, however, that some use of animals is essential in the development of clinical therapies. Where farm animal welfare, veterinary or environmental research is concerned, animal-free research would be impossible, as the final stage of such research inevitably requires animal trials of the species in question. Total replacement of animals in research is therefore not a feasible prospect.

199. Where animal use remains essential to scientific and clinical progress, the 3Rs are accepted as the basic principles for working towards minimising the adverse impact of those procedures that need to be undertaken. In that regard it is notable that good scientists are committed to good animal welfare since they recognise that good welfare is essential for good science.

200. The UK bioscience sector funds and works closely with the National Centre for the 3Rs on active programmes to support the 3Rs in research and embed them in daily practice. The NC3Rs in turn funds 3Rs research in the best research laboratories. This is a highly effective and efficient model that should be adopted across the EU.

201. However, developing alternatives to the use of animals in medicines research is a long and difficult process. At the moment, there is often a point in the process where there are barriers that computers and in vitro methods cannot yet help to cross. As our biological, medical and technological knowledge grows, we look forward to a time when animal research will become progressively less central to the development of human therapies. As this is not imminent, the priority remains to develop safe and effective medicines and other therapies involving considered and compassionate use of animals.

202. Recent examples of advances in 3Rs made by UK scientists in academia and industry, and relevant to medicines development, were showcased to members of the European Parliament in February 2009, and include:

- Developing gene expression analysis techniques for screening compounds;
- Adopting a "weight of evidence" approach—uses fewer animals per dose-tolerance study;
- Use of radio-telemetry devices (remote sensor implants)—95% reduction in number of dogs in 2005 in research to develop a bronchodilator agent for asthma;

[28] http://scienceandresearch.homeoffice.gov.uk/animal-research/animal-testing-faqs/

— Review of information required by regulators in conventional acute toxicology testing. Potential to reduce use by several thousands per year (cross-industry collaboration), currently in consideration by regulators.

203. Importantly, the most productive environment for generating 3R improvements and new alternatives is in active research laboratories, not in some standalone 3Rs laboratory centre, which was proposed in the draft Directive. While an EU-wide organisation could certainly help validate newly developed alternatives/ improvements, and push for acceptance by regulatory authorities, it does not make sense to duplicate this in each member state.

204. The proposals for National Reference Laboratories are unnecessary and infeasible and of would not be effective at developing alternative methods. They would divert research funding away from research which might not only develop alternatives, but further benefit biomedical discoveries.

205. Once validated, implementation is brought about by a combination of reduced costs (a strong incentive in both industry and academia), a flexible regulatory framework (which is difficult to implement given the global nature of medicine development, registration and use) and a 3Rs culture embedded in the day-to-day work of scientists, who in general would prefer not to use animals in studies targeted at human benefit. Across the EU this culture should be supported by effective but efficient ethical review and regulation over the use of animals in research.

206. The Commission claims in its Impact Assessment that "increased uptake of alternative methods will boost EU industry". There is no evidence to support this claim, which is frequently made by antivivisection groups. Researchers will wish to use the best method available in every case. As outlined above, there is already every incentive for industry to both develop and use alternative methods.

9. Subsidiarity and Legal Base

207. The UK bioscience sector does not claim to be in a specialist position to comment on the legalities of introducing EU legislation.

208. The Commission explains that the following broad options have been considered (explanatory memorandum page 8):

— Deregulation;

— Maintaining status quo;

— Strengthening the current legislation;

— Voluntary agreements as an alternative to legislation.

209. The UK bioscience sector accepts that strengthening the current EU legislation is a valid choice for some aspects of the Directive, such as minimum standards of animal welfare, which should apply uniformly across Europe. However, the approach of the proposed Directive appears to have been to collate all existing regulation and apply the most stringent level of regulation in each case. A more balanced approach would have been to identify and strengthen appropriate parts of the regulatory framework, whilst not adding legislation to cover aspects where animal welfare benefits would be virtually non-existent (such as designating as protected potentially billions of non-sentient microscopic crustacea).

210. Other examples where there is no welfare cost include humane killing of animals and non-recovery experiments performed entirely under anaesthesia. It is entirely unnecessary to incur the full weight of the proposed controls in these areas.

211. The Commission has acknowledged the possibility that Member States could "streamline" regulatory controls and so "contribute to simplification" (Impact Assessment page 11). But the complexity of the proposals allows virtually no opportunity for this to happen.

212. As a result, we are concerned that the Commission approach is excessively stringent. The Commission does not appear to have taken into account the risks of excessive regulation to the competitive position of Europe in the long-term.

Subsidiarity

213. If the advantages of harmonisation are accepted, as proposed in Section 1 ("Objectives"), then subsidiarity must be seen in relation to harmonisation.

214. We understand that EU law (as well as an amendment passed by the Parliament) permits Member States to implement more stringent conditions than those laid down in a Directive. We see the merits of this, but are also mindful of the ease with which the important benefits of harmonisation may be eroded.

215. In that light, the UK bioscience sector advocates harmonisation of those outcomes that (i) support the single market, and (ii) benefit animal welfare (assuming always that the benefits are based on scientific evidence). However, we would wish to see subsidiarity over the procedures by which those outcomes are achieved.

216. Importantly, one of the outcomes of the single market should be mobility of staff and projects. This is not incorporated into the draft articles, although stated in the preamble.

217. In particular, our sector feels it is not appropriate for the EU to determine:

— the structure of national committees responsible for the various authorisations;

— the structure and operation of pan-EU bodies to which Member States would be subservient; and

— the controls over data-sharing.

Legal Base

218. We are of the opinion that Article 95 of the Treaty of Rome is not properly fulfilled by the draft Directive. The Directive does not adequately guarantee harmonisation across the internal market for breeding, supplying and use of animals.

219. For the provisions in the draft Directive relating to animal welfare, the Commission is relying on the principles set out by the protocol on protection and welfare of animals annexed to the Amsterdam Treaty. This proposal recognises that animals (vertebrates in this context) are sentient beings, and requires that "in formulating and implementing the Community's agriculture, transport, internal market and research policies, the Community and the Member States shall pay full regard to the welfare requirements of animals…".

220. A number of measures proposed by the Commission involve restrictions such that certain types of research cannot be carried out at all. For example, the Commission proposes a ban on the use of non-human primates unless linked to life-threatening or debilitating disorders. In such cases where research is disallowed, the Commission appears to be arguing that animal welfare considerations override research policies. It is not clear that this is the intention of the protocol on protection and welfare of animals.

Legal status of annexes

221. One legal issue that is of significant concern is the status of annexes to the Directive. We understand from the Commission that, unlike the previous Directive, annexes to the new Directive will necessarily be mandatory and may not act as guidance. Absolute clarification of this issue is vital before the wording of the various annexes is discussed further and approved.

222. This is of greatest significance to Annex IV on accommodation standards. The content of this annex is based on, but does not accurately reflect, the Council of Europe Convention ETS123 for the protection of vertebrate animals used for experimental and other purposes.[29] This document was agreed by its expert committee subject to it being advisory only and not mandatory.

223. Moreover, the evidence on which ET123 was based is already at least five years old. It is essential that the wording of any mandatory annex is such as to permit new scientific evidence to be incorporated.

Sharing of Data

(Article 44, Amendment No.132, 134, 135, 136, 137, 180)

224. The UK bioscience sector strongly supports the overall concept of sharing non-confidential data to avoid duplication of procedures. Data should be (and are) reviewed, and new studies planned, on the basis of what is already known. Facilitating access to publicly-available data is a key priority.

225. Additional regulation on data-sharing could be used to generate some valuable additional exchanges of information with benefit to animal welfare, and to research progress. However, the proposals for mandatory data sharing as proposed by Parliamentary amendments are likely to disproportionately increase costs with little animal welfare benefit, and have a major adverse impact on the protection of intellectual property rights. This could threaten both the viability of pharmaceutical research in the EU and the competitiveness of academic institutions.

226. Regulation must be based on an understanding that there are many different types of animal research. A legal requirement for the same type of data sharing across all sectors is simply impracticable, and the cost of ensuring that all relevant data are easily accessible (as well as the difficulty in defining what is relevant) would be a significant burden on research institutions, funders of research and for administrative agencies

[29] http://conventions.coe.int/Treaty/en/Treaties/Html/123.htm

required to oversee that the required process had been followed. The Commission proposal, amended by the Parliament, intends to reflect legislation applied to the chemical industry (under REACH) across all sectors. This proposal has severe limitations:

— REACH is applied to chemicals which will have common usage but not to those covered by intellectual property protection;

— Academic research depends upon publications but the timing of disclosure is critical for correct interpretation and application, as well as for the protection of intellectual property;

— There appears to be confusion as to the amount of duplication involving animal work that actually occurs.

227. Our concerns are consistent with those of the Technical Expert Working Group, which noted that "any system for sharing data that required assessing the 'value' of studies, particularly those early in the R&D process, would be highly problematic and effectively make a system unworkable. It is unclear also how any requirement could extend to studies carried out in non-EU countries, thus placing EU industry in an uncompetitive situation" (page 14)

Duplication and validation

228. It is important to distinguish between the undesirable duplication of animal experiments and the validation of data from animal studies. Reproducibility of results is a necessary part of the scientific process as published data may later be found to be inaccurate or irreproducible. Blocking the ability to replicate critical observations would seriously restrict scientific progress. It is however right to prevent or limit duplication unless there is a scientific justification for doing so.

229. There is however no evidence of widespread unnecessary duplication. "Avoidance of unnecessary duplication of procedures" is already part of Annex VII (list of information requirements for applications for the project authorisation in Article 36) which implies the need to check for existing data. Agencies that fund research always expect to be assured that the proposal is new and does not simply repeat previous studies unless there are particularly good scientific reasons to do so.

230. Similar compounds are sometimes studied in the development of new medicines, but this should not be confused with duplication. Even slight modifications and variations to chemical structure can have huge impacts on safety and efficacy for patients, and can result in a product with a different mode of action or safety profile and therefore new or better treatment for a disease. For example, subtly different chemical changes to the dopamine structure can lead to the compound either being a useful drug to treat Parkinson's disease, or causing serious side-effects. Similarly, ketamine isomers can be either an anaesthetic or hallucinogen. In another example, the histamine H2-receptor antagonists, cimetidine and ranitidine, act in the same way and seem quite similar. Yet cimetidine is sometimes unusable because of adverse side-effects, and hence the development and animal testing of ranitidine represented a significant advance for some patients.

Transparency

231. We support the proposal for the provision of a lay summary of work outlined in the project licence (generated by the applicant) to be made publicly available. A similar scheme already operates in the UK with the disclosure of abstracts on the Home Office website for most project licences.

232. The benefits of public disclosure of animal research data must however be balanced against researchers' rights to privacy and the protection of personal data. It is paramount to ensure both the safety of staff and premises, and the integrity of intellectual property.

Proposals in the Directive

233. Under Article 44 of the original Commission proposal, Member States are required to ensure the sharing of data generated by procedures. Regulatory testing was excluded, and the proposal was subject to the safeguarding of confidential information.

234. Under the revisions from the European Parliament, the exclusion for regulatory testing and the safeguard for confidential information were removed. The new text included sharing of data generated by procedures which took place in the European Union prior to the Directive coming into force. An additional obligation is for anyone seeking to rely on data owned by another to contribute, where appropriate, towards the cost of producing such data.

235. These amendments from the European Parliament appear to be based on data-sharing requirements applied to chemical and pesticide legislation. However, in that case, data are from very standardised toxicology studies of off-patent chemicals. Pesticides are often re-formulations or combinations of older chemicals, and if new chemical entities were developed, these would not be subject to the requirement for toxicology data sharing. It is also key to understand that the purpose of toxicity testing in the pesticides sector is mainly to generate data for hazard assessment, deriving permitted daily exposures to control occupational hazard.

236. The situation for pharmaceutical/biotechnology research is significantly different. Pharmaceutical research is rarely duplicated, with much R&D effort focused on developing new molecular entities. Where different companies may be working on the same established entity, well-developed processes for the registration of generics avoid the recreation of existing data. In the pharmaceutical sector, toxicity testing is undertaken to assess risk prior to administration in humans. This is a different purpose from the pesticides sector, and data-sharing measures appropriate for pesticides are not directly applicable to the pharmaceutical sector. Furthermore the majority of animals used in the pharmaceutical sector are not involved in toxicity testing but in discovery and developing new areas of biology that may allow pharmaceutical intervention leading to disease benefit.

The commercial perspective

237. Bringing a new medicine to market is the result of usually over 10 years developmental work, at an average cost of €800 million per medicine. The cost and risk are borne by the pharmaceutical industry. This leaves limited years to recoup the cost of development before the expiry of patent terms.

238. Protecting intellectual property (IP) is critical to ensure that a company does not lose the product of its original research and development. For this reason, IP-sensitive or commercial information must be carefully excluded from disclosure. In addition, there are legal restrictions on publishing data on a patented molecule. To require such confidential research data to be shared would seriously compromise the commercial viability of the pharmaceutical industry in Europe.

239. Academic institutions will similarly need to protect IP prior to publication, and such data include those submitted in grant applications. Maintaining confidentiality in this area is essential in maintaining Europe's scientific and commercial competitiveness.

Regulatory research

240. Toxicity testing is required by law as part of the licensing process of a new medicine. It is carried out on novel, patented compounds, which by definition ensures there is no duplication. This type of research follows strict and uniform protocols. Any Member State should accept the validity of regulatory toxicity testing carried out in another. A well-developed generic medicines procedure ensures that data do not need to be recreated for existing molecular entities.

241. Industry and the regulatory agencies worldwide are already actively engaged in data-sharing initiatives, one of whose intentions is to reduce, refine and replace the use of animal toxicity tests. These initiatives include those intended to qualify novel biomarkers for disease, to better understand toxicological assessment and data interpretation, and to develop novel computer based processes. Among the many shared efforts are:

- ILSI HESI—Health and Environmental Sciences Institute.
- Critical Path Institute—Predictive Safety Testing Consortium.
- Innovative Medicines Initiative (Europe).
- ECVAM Consortium on In Vitro Models for Drug Induced Liver Injury.
- Registry of Industrial Toxicology Animal Data (RITA).
- Extractables and Leachables Safety Information Exchange (ELSIE) consortium.
- EFPIA[30]/RSPCA/FRAME,[31] Excipients[32] Database Consortium.

242. An example of these is the EFPIA/RSPCA/FRAME Excipients Database Consortium. This is a cross-pharmaceutical industry consortium formed under the auspices of the EFPIA Safety Working Group in collaboration with the RSPCA and FRAME. It contains 10 member companies and database host (LHASA) and its purpose is to build a common database of toxicity information on commonly used excipients with the

[30] EFPIA: European Federation of Pharmaceutical Industries and Associations. See Lhasa Ltd: A not-for-profit company specialising in toxicology, metabolism and data-sharing software. See wwww.lhasalimited.org
[31] FRAME: Fund for the Replacement of Animals in Medical Experiments
[32] Excipient: an inactive compound used to bulk out or support the active medicine

overall aim of decreasing the potential for new or additional toxicology testing, thereby reducing or eliminating animal use and refining future studies.

243. This will enable pharmaceutical companies to use new excipients with minimal needs for toxicity testing versus needing full toxicology programmes.

Basic and applied research

244. The very nature of basic and much applied research means that almost all projects and protocols are different. The desire to share data is very strong—all scientists want to see their work published, and they also exchange information at conferences. Indeed the UK Research Councils all have policies on data-sharing;[33] it is strongly encouraged, unless there are overriding IP considerations. However, it may be difficult to know at what stage data are to be published in a scientific journal, and their prior release in any form can jeopardise both scientific publication in high-level journals and the retention of intellectual property rights. The relevance of data from long-term programmes of research can take years to ascertain.

245. Fortunately there are already initiatives of networks and collaborations to encourage and facilitate sharing of data, and reduce any unnecessary duplication of animal procedures.

246. A pan-European database called ELIXIR[34] has recently been established to improve the sharing of biological data. Other initiatives such as EUCOM, NORCOM and KOMP are international collaborations that share knock-out mouse lines, reducing the number of genetically-modified animals produced internationally. Sharing the details of the mouse genome has resulted in far less duplication than might have happened otherwise.

247. These examples might suggest that this approach should be expanded across many areas of research, but the practicalities mean that this is not immediately feasible. In general, progress has been fastest and most successful for large, consistent and well-defined areas of research, such as genetics research in rodents. Many other areas of research are too diverse or fragmented to permit such gains, even with the high level of collaboration that is required.

248. Funders already require that applicants proposing to use animals will have undertaken due diligence in reviewing the existing literature in the field, and demonstrating that their proposed research does not repeat previous studies. There is no reason why funders would support studies that have already been undertaken and published. Each application must scientifically and ethically justify the use of animals, including why the procedure is necessary to further a certain field of knowledge.

249. In the UK, researchers must also address how they have considered refinement, replacement and reduction in their study design. Such information is reviewed by peer reviewers, funding committees, ethical review panels and the Home Office.

250. Forcing research institutions to share provisional data is not a proven methodology for advances in animal welfare or science. Instead, it would increase bureaucracy and divert time and resources away from the important quest to understand human and animal diseases.

Databases

251. Databases are often put forward as a way to collect and disseminate information on animal experiments, including information on procedures and welfare issues. The intention is to avoid duplication or repetition of research, and generate information to assist in progressing the 3Rs. However, the extraordinary complexity of such a venture means there is a long way to go before any meaningful attempt can be made on a European central data repository. A central database was rejected for possible inclusion in the Commission proposal.

252. There are some examples in biomedical science of centralised informatics activities that have been successful, for example ENSEMBL, which provides a central portal for a variety of annotations of genome sequences.

253. But these existing databases draw together datasets that are relatively well-defined and consistent in their format. By comparison, data on the outcomes of animal experimentation in insitutions across Europe will be highly diverse, primarily because the scientific questions being addressed, and therefore the protocols followed, are also highly diverse. We know, for example, that the outcome of a procedure on a genetically-modified mouse will depend upon a number of factors including:

— the precise procedure that is used (the standard operating procedure, SOP) which may vary across institutes;

[33] See eg: www.mrc.ac.uk/Ourresearch/Ethicsresearchguidance/Datasharinginitiative/index.htm
[34] http://www.elixir-europe.org/page.php?page = home

— the precise mutant allele generated in the genetically-modified mice; and

— the environmental conditions in the animal house, including the type of environmental enrichment in the cage, the diet and the bedding materials used.

254. All these factors will impinge upon the phenotype measured and the welfare outcomes. In essence, describing phenotype and welfare in an animal is complex , and must include genotype, phenotype, SOP and animal house environment. Whilst this can at times result in confusing variation, it can also throw up important differences that illuminate the underlying questions. For this reason it would be scientifically highly retrograde to attempt to standardise protocols in an attempt to get data to fit into any such database.

255. Standardised descriptions or vocabularies for phenotyping procedures and environmental conditions would have to be implemented across Europe if we are to have meaningful database entries in any central data repository. We would need to agree on the parameters and language to apply to the complex data sets, and on the standards that would need to be adopted.

256. There may appear merit in making available "negative" or "null" results. However, a mandatory data-sharing scheme, for example requiring researchers to publish negative data on a website, is unlikely to be successful. Even if it could be made to work, the data would not be accessible to researchers unless they already knew about them. One possible avenue to tackle this problem is a move to open-source publishing, with funding agencies insisting on research results being put into the public domain, when there is no risk to IP. This area is currently developing rapidly. However, there remains the essential problem with negative data of knowing whether it represents a true biological result or a technical failure to carry out the experiments in the manner that would have generated a positive result instead. The implication is that the database would need to include all technical details as well as the result—a daunting and impracticable task.

257. At the present time, developing the procedures for documentation and data acquisition would be an enormous task. Just to run a centralised database would require a huge institute with a vast budget. Experience from similarly complex ventures in other fields suggests it might well not succeed.

Conclusion

258. In summary, we strongly support the principle of sharing of data, where the data structure is appropriate, where the access to data is appropriately controlled, and where doing so is clearly linked to animal welfare benefits and/or good science. There are many successful initiatives already in operation, and we welcome more such plans where they are rationally conceived. We believe, however, that the Directive should encourage progress in this area, rather than mandate it—because of the immense difficulties outlined above of applying this practice across all areas.

May 2009

Examination of Witnesses

Witnesses: Professor Tim Hammond, Vice-President, Safety Assessment UK, AstraZeneca, Dr Paul Brooker, Director, UK Operations, Huntingdon Life Sciences, and Dr Colin Dunn, Country Manager Charles River UK and Executive Director European Veterinary & Professional Services, representatives of the Association of the British Pharmaceutical Industry, examined.

Q57 ***Chairman:*** Good morning. Thank you very much indeed for helping us with this inquiry on the use of animals in research. This is a formal evidence-taking session of the Sub-Committee of the House of Lords Select Committee on the European Union. A transcript will be taken; you will get a copy of that within a few days and be able to correct any minor slips and errors that have crept in. The session is webcast, so there is a possibility that someone somewhere may be listening, but I always have to say to everybody who gives evidence that we have never received any evidence that that is the case, so we will see. I would like to give you the opportunity, if you wish, to make any brief opening and then we will go on to a question-and-answer session. Some of our questions are more like essays than questions, so my colleagues may slightly abbreviate the question when they ask it, but it will still cover the same ground as we have given you notice of. I do want to stress that we are focusing purely on the Commission's proposals and their acceptability, relevance and practicality, and we do not wish this inquiry to go into the wider areas of the debate. It has to be useful; it has to deal specifically with the impact of the Commission's proposals. Would you like to say anything to begin?

Professor Hammond: My Lord Chairman, first of all, may I thank you for giving us the opportunity to be here this morning. Perhaps by way of introduction I could introduce myself. My name is Professor Tim Hammond. I am Vice-President of Safety Assessment in AstraZeneca, which is one of the major pharmaceutical companies in the world, with research interests predominantly in Europe. I am here

today representing the Association of the British Pharmaceutical Industry with my colleagues, but I should also declare that I am Chairman of what is described as a priority action team, which is convened by the European Federation of Pharmaceutical Industries, reporting directly to the Chief Executive Officers of all the pharmaceutical companies with research interests in Europe. This is an unusual grouping that is brought together simply because of the concerns that are present within the pharmaceutical industry about the potential impact of the Directive on the pharmaceutical industry and the research base within Europe. As I say, we very much appreciate the opportunity to be here today. We would clearly like to recognise the opinion of the Committee. It is very important in giving a steer to Council as the discussion moves into the Council phase. Perhaps I could ask my colleagues to introduce themselves as well.

Dr Brooker: Good morning. My name is Dr Paul Brooker. I am responsible for the UK operations of Huntingdon Life Sciences, which is the largest contract research organisation (CRO) in Europe, and we also have testing facilities in the US. Just a note on contract research organisations in the UK: contract research organisations employ around about 4,000 specialist people in this arena of pre-clinical work and are responsible for exports of around £400 million per year.

Dr Dunn: My name is Dr Colin Dunn, my Lord Chairman. I work for Charles River, which is a company that breeds and supplies laboratory animals. I am Country Manager for the UK business. I am trained and I have practised as a veterinarian in the UK. I have a PhD in virology. Prior to my current appointment, I was head of the laboratory animal facilities at a large R&D site of a major pharmaceutical company. I am also here in the capacity of representing the Laboratory Animal Breeders' Association.

Q58 ***Chairman:*** From the evidence we have received, you seem to support the objectives of the Directive as they stand: to promote a level economic playing field in the EU; improve public confidence in animal research; promote the use of alternative test methods; ensure high standards of animal welfare; and promote high quality science. They are all very important objectives, clearly. Why do you think there is the need for this Directive?

Professor Hammond: Before I answer that question, perhaps I could just give you a little background. The existing legislation is over 20 years old, so clearly it is in need of updating in the light of developments over the last two decades. We are very supportive and very pleased to see a revision of the Directive. It is also important to say that during the process of the production of the text from the Commission and in the review of the text coming from the Commission, the bioscience sector—and that includes the pharmaceutical industries, the charities, the funding bodies—have come to a very high degree of agreement about the issues that the text raises, but it is important to note there are some good things in the Directive. The very positive thing that is coming out of it is the introduction of ethical review. For the first time we are seeing in formal legislation recognition of the principles of the 3Rs: refinement, reduction and replacement. In addition to that, there is also a mandatory requirement for increasing training. So we believe there are some very good and very positive things, but there are also some areas which are really quite concerning for us. These focus on the use of non-human primates and on definitions, particularly around severity classifications and the impact that the severity classifications may have on things like re-use, which is not something that you have asked us particularly to address but to which we would like to draw your attention. With appropriate definitions—as is currently within the amendments from the Parliament debate—that seems to be OK, but if those definitions are not correct, that will have a severe impact on welfare and we would like an opportunity to explain that. We are also concerned about the levels of bureaucracy that we currently have within the legislation surrounding the use of animals. This text, we believe, will increase that level of bureaucracy and that clearly then has an impact on competitiveness. The final area of concern we will touch on is around data-sharing and the issues around intellectual property and the protection of intellectual property. We believe there are some very severe risks associated with competitiveness if this Directive is implemented and taken through in an inappropriate way. In the documents we have put to you, we have used the word "proportionality" and we would like to emphasise that proportionality is what we would like to achieve. That is really a balance about the benefits of the research against the harm to the animals, the degree of harm that is inflicted on the animals being proportional to the level of control and administration. It is important, also, just to emphasise that the confidence in animal research that is often questioned is something that is very important to address upfront. We believe that animals play a very small part in the discovery and development of new medicines but a very crucial part, and if you take that part away and make that either difficult or impossible to conduct, the whole process of discovering new medicines and new treatments will be very severely compromised. As I have said already, we greatly welcome the greater emphasis on the 3Rs, but we would also like to emphasise that most of the activity that goes towards developing alternative methods comes from the scientific community. It does not come from bodies

which sit outside, separate from what we do in basic research and in the discovery and development of new medicines. The 3Rs' principle is an agenda which we drive and most of the advancements come from the academic or industrial scientific community.
Chairman: Do either of your colleagues want to say anything? They are content, so let us move on to impact assessment.

Q59 ***Earl of Caithness:*** The Commission told us that they have consulted widely and over a long period. Do you think that the bioscience sector has been properly consulted? The same question relates to your evidence. You did not like the impact assessment. Why is it so flawed in your opinion?
Dr Dunn: My Lord Chairman, it is certainly true the Commission had a very significant consultation with the bioscience sector, but our concern is, as you have stated, how effective this has been. In some of the consultations, and in the expert consultation performed in 2006, some of the questions lacked clarity and I think this did not lend itself to further objectivity. In the introduction to the impact assessment that the Commission have written, it is in fact stated that they did not have the data to back the findings that they had expected to get. I think that that illustrates itself where there may be issues. Indeed, in 2003, there were a number of technical expert working groups reporting, and I would draw one example being on severity. There were some very important aspects analysed about severity and about the use of animals and it appears that some of those findings have not been given full regard in the draft Directive from the Commission. We were certainly involved and certainly provided a great deal of input, but our concern is about what degree of weight our views and expert opinions were given.

Q60 ***Earl of Caithness:*** Are the Commission listening to your complaints about the Directive now? Having met them, do you have a working group with them?
Dr Dunn: The Commission clearly have set up, and the way things are going with the Council of Ministers, mechanisms to investigate more. There are expert groups being brought together for example to thrash out some of the issues around severity.
Professor Hammond: We do have a regular dialogue with the Commission and with the people who are actively involved in the drafting of the text. We are in regular contact with them, so they are aware of our views. As my colleague said, I think it is important to recognise that not all of those views are being reflected in the text.

Q61 ***Lord Palmer:*** Are some of your European counterparts also in this consultation process with the Commission at the moment?
Professor Hammond: Indeed. The group that I referred to at the beginning was the European Federation of Pharmaceutical Industries, which is a body that represents all of the pharmaceutical industries. Within that structure, pharmaceutical industries have also liaised within their countries with the bioscience sectors. The views that we have been expressing are the views that are widely held across the entire bioscience sector, across the entire European sector.

Q62 ***Earl of Caithness:*** That must be helpful.
Professor Hammond: We believe it is quite powerful if it is listened to.

Q63 ***Baroness Sharp of Guildford:*** In the evidence that you have submitted to us, you have raised concerns abut the impact of this Directive on the international competitiveness of the sector and particularly about competitiveness in relation to the USA, China and India. Other submissions that we have had have indicated that they do not think there is as much evidence as there might be to support this view. How would you substantiate your argument? What sort of data would you use from your own research in-house and from academic research or contract house research? To what extent is such research already being diverted to other parts of the world and for what reasons?
Professor Hammond: Most major pharmaceutical companies have research capabilities in multiple countries. Most of them have European bases and most of them have bases in the US. In the UK there are only four major pharmaceutical companies left conducting pre-clinical research in the UK. If you contrast that position to 20 years ago, the number was considerably higher. I would not venture to suggest that the reason for that has been due to legislation around animals, but it is a contributing factor when companies make decisions about where they will invest. It would be wrong to suggest that that is the major driver, but it is certainly a factor. I think it is also true to say that most major pharmaceutical companies are now investing in Asia. This is partly driven by access to emerging markets. There is certainly a contributing factor there—but it is also influenced very strongly, particularly, by access to non-human primates and developing the Asian market with particular reference to China. In my own company I can tell you that we are building facilities in Shanghai. Those facilities will focus on cancer research, but in addition to that we have a collaboration with a Chinese institution which is dedicated to construct a specific primate facility. The reason for doing that is largely driven by concerns that we have about the long-term sustainability, given the legislative framework, about investing in that kind of work in Europe. The evidence is quite clear that it is happening. It is already happening now.

Most companies are already in Asia, most companies are already in China. It is also important to recognise that one of the key features—and this will particularly influence the CRO industry which I will ask my colleague to comment about—is the level of bureaucracy. Where it does not carry a tangible animal welfare benefit—because companies are committed to furthering animal welfare programmes—it just becomes uncompetitive, and it becomes uncompetitive because you cannot respond in a global market in the way we should be able to respond.

Q64 ***Baroness Sharp of Guildford:*** In so far as Big Pharma have pulled out of doing pre-clinical research, how far is this contracted out to organisations like Huntingdon Life Sciences?
Professor Hammond: Big Pharma have not pulled out. We still maintain a very strong research base and most Big Pharma companies still have their discovery activities located internally. That is where most of the animals are used. There are some elements which are increasingly outsourced. That is a trend that is increasing and I believe it will continue to increase. Perhaps I could ask Paul to add something.
Dr Brooker: Baroness Sharp, there are 3 major pre-clinical CROs in the UK including HLS. All have facilities in the US and they either have now or are planning imminently facilities in China. CROs will have common animal welfare standards across their organisation, so there is no suggestion at all that we are migrating to where welfare standards are lower. We take our own welfare standards with us, which tend to be to the highest common denominator. But investment decisions will be taken on the basis of ease of doing business with our internationally based clients. If due to bureaucracy in the EU we can start a study earlier in the United States or in China, that will drive business out of the EU and into these other areas.

Q65 ***Chairman:*** The concern is not so much with standards but with bureaucracy. Is that right?
Dr Brooker: To illustrate the issue it is best to show an extreme theoretical situation. If, for example, you have a study where you need to write an amendment to a project licence in the EU it takes six months before you can do that work, whereas it will take six weeks in the US. If your pharmaceutical customer who is anxious to proceed with their clinical programme has the choice between waiting six moths or six weeks, they will virtually always go with six weeks. The welfare standards are the same but the time to start the preclinical study, and hence the subsequent time to get into the clinic and to start to see benefits for patients, will be reduced in areas where it is not quite so bureaucracy heavy.

Q66 ***Chairman:*** Is there an argument that if the work migrates to other countries, say to the Far East, there will be pressure on the welfare standards to decline?
Dr Brooker: I do not think that is true.

Q67 ***Chairman:*** Not from CROs operating internationally but from, I suppose, small jobbing outfits—not to be disparaging.
Dr Brooker: I certainly would say that large CROs and large pharma companies will take their own welfare standards with them wherever they are, and institutions such as AAALAC will ensure that their welfare standards are maintained. AAALAC is the Association for the Assessment and Accreditation of Laboratory Animal Care, which tends to be the international gold standard of approval. It is a US-based system. But you may be correct in terms of smaller non-AAALAC accredited organisations in local conditions, such as China.
Professor Hammond: One of the key issues that we have had to deal with in the programme that we have had in developing our capability in Shanghai is to ensure that the facility will work to our standards. The legal framework that they work within is completely different and far, far less bureaucratic. Your concern is justified. The onus is on us, if we are working in those areas, to ensure the standards are maintained.

Q68 ***Baroness Sharp of Guildford:*** In terms of bureaucracy, you were talking about making an amendment to a protocol or something like that.
Professor Hammond: Yes.

Q69 ***Baroness Sharp of Guildford:*** The time required to turn this around in Europe is considerably greater than in the USA, let alone in China.
Dr Brooker: Absolutely.

Q70 ***Baroness Sharp of Guildford:*** So it is really the flexibility on the part of he bureaucracy.
Professor Hammond: It perhaps links a little bit into the comments about the level playing-field. The time in the UK is considerably longer and the process more complex than it is in other European Member State countries currently. It is more difficult to respond in those timescales that are applicable in the UK than it is in Europe, and Europe is considerably more difficult than the USA, and the USA is probably a little bit slower than Asia.
Dr Brooker: Indeed, industry and academia have been in discussion with the UK Government in terms of better regulation over the past several years to try to ensure the correct oversight and welfare whilst maintaining as much flexibility and rapidity in the system as possible.

Q71 ***Baroness Jones of Whitchurch:*** If that is the case, why is there so much research still done in the UK?
Professor Hammond: The major reason that we continue to invest in the UK is because we can get access to world-class skills and world-class science. Our academic base in the UK is as good as anywhere in the world. Our track record is good. But it is under threat. We are seeing migration of skills out of the UK. We can provide you with evidence of that, if you would like it. That is happening.

Q72 ***Lord Brooke of Alverthorpe:*** We had the Commission representative with us last week and she denied emphatically that there was any evidence of transfer. You are talking about new business, are you, as distinct from transfer of existing?
Professor Hammond: Yes. One of the difficulties we have with this is that the impact of this is not immediate. If we were already investing in the UK, we will not simply close that investment, but when the next round of decisions about where we should invest will come, it will influence then.

Q73 ***Lord Brooke of Alverthorpe:*** The Commission view that was advanced was that other factors are at work over which you have no control; for example, the construction of new facilities in these Asian locations was cheaper than it would be anywhere in the West; the infrastructure operations were cheaper than they would be here; they were pushing to maintain non-human primate research there themselves and were refusing to release non-human primates for research elsewhere—particularly the Chinese; this is international competition and you have no control over it and this would not affect it.
Professor Hammond: Some of those points are absolutely correct. The Chinese are applying a quota system for exports. They are exporting primates but they apply a quota system. They are trying very hard to encourage investment in China because they want access to our science. They are doing a lot to try to attract us into China. They are a growing and fast-emerging market—there is absolutely no doubt about that.

Q74 ***Baroness Sharp of Guildford:*** So it is an attractive market for you anyhow.
Professor Hammond: Yes, absolutely. As far as the investment in the UK is concerned, in terms of building and capital, yes, it is cheaper to do it in China but not by very much. It is very much overstated. If you look at the prices and the costs associated with developing in Shanghai, they are extremely high. It is not cheap. If I may refer you to some internal experience I have with in my own company, I have invested $130 million in the UK in new facilities over the last eight years. Every time I asked for money to do that, I was never challenged about the need to do it; I was always challenged about why I needed to do it in the UK. The reason I gave was because I wanted access to the skills that we have available to us in the UK. Without that skill base, there is no reason to be here.
Lord Brooke of Alverthorpe: We will come to the issue of administrative burden later.

Q75 ***Chairman:*** When you are developing a primate facility in the Far East, and, I suppose, in the US as well, are, for example, the housing standards for primates the same in the three jurisdictions?
Dr Brooker: In terms of the local regulation, no.

Q76 ***Chairman:*** In terms of the industry standard.
Dr Brooker: In terms of the industry standard, I think there is a move which is becoming a very rapid move towards going to the norm of the European standard. If I take my own company, we conduct primate research in the UK, where we use very large cages, the animals are housed together, they have little verandas they can sit on and look out and so on. Our facility in the US has, until recently, had the local standard of having animals in smaller cages, although for the past twelve years we have allowed them to intermingle. We are now considering replacing all of our caging in the US with European-style housing. One room is already done, we are now reviewing the rest of the facility. Some of our customers are increasingly saying they will only place work where it is in European-style facilities, be that in Europe or in the US or in China. In planning facilities in China, there is no question that we would build new to European standards, to the standards we use in Cambridgeshire.

Q77 ***Chairman:*** Would that be the same for you, Professor Hammond?
Professor Hammond: Yes. We will ensure that the operation of the facility for work that is conducted by us will be done to European standards. What we cannot do is control the standards to which they operate for their local market and their local research groups. We can influence it and we do that.

Q78 ***Viscount Ullswater:*** Perhaps I could ask one more question about the provision of the animals. Is that cheaper in China than it is in Europe?
Professor Hammond: Is that in terms of the cost per animal?

Q79 ***Viscount Ullswater:*** Yes.
Professor Hammond: The answer is no. We have additional transportation costs to bring the animals from Asia to Europe, but I have to say that the cost of the animal is not a factor at all.

Q80 ***Baroness Sharp of Guildford:*** But it is easier to obtain the animal in Asia because of the Chinese export ban.
Professor Hammond: No. It is completely possible to obtain animals from China or Vietnam or Cambodia or Mauritius into Europe or the United States.
Chairman: Let us move on to one of the areas you have already identified is causing you concern and that is data-sharing. Lord Brookeborough.

Q81 ***Viscount Brookeborough:*** It seems there is divergence between what you say you and your colleagues have provided as evidence for going abroad and what the Commission believes. Are they simply not listening to you?
Professor Hammond: We have made our views very clear to the Commission.

Q82 ***Viscount Brookeborough:*** What do you think of their reaction?
Professor Hammond: It is difficult to comment. I think they are not seeing the reality that we are seeing.
Viscount Brookeborough: Thank you.

Q83 ***Viscount Brookeborough:*** On data protection, which you have already mentioned, I do not fully understand where the division or separation is currently between any data that might be shared and confidential data. From the point of view of my limited knowledge of the pharmaceutical industry, we sometimes see headlines that So-and-so has a magic new drug for such and such a thing, and this adds tremendous share price, it is tremendous business, and therefore it is obviously confidential. Where is this division currently?
Professor Hammond: This whole area of data-sharing is very complex, so perhaps I could take a few moments to try to explain the issues and illustrate some of the complexity. We have a little difficulty understanding why the need for data-sharing is being driven from a premise that there is widespread duplication. Within the pharmaceutical industry we work on chemicals which are protected by patents, so there is no interest, commercial or otherwise, for somebody else in another company to be working on chemistry which we in my company are working on. There is no benefit for them to do that, so we do not do it. We do not duplicate studies. We do not work on the same molecules. It is, commercially, nonsense to do that. We have a difficulty understanding where the duplication comes from. There is a view that duplication could be targeted towards duplication of the pharmacology that you are interested in. Again, we would take issue with that, because there are many, many examples where a very small change in the structure of a chemical will give you a very different biological profile, either in terms of efficacy or in terms of toxicology, and there are lots and lots of examples of that which are very, very well documented. Again, we do not believe that widespread duplication, in the strict sense of the word, occurs in the pharmaceutical industry. There are some areas where we acknowledge that there are studies which are repeated for, as we would see, no particularly good reason. The areas of major concern really come into some of the regulatory testing—and it really focuses on batch acceptance—where for movement of a batch of a vaccine, for instance, between Member States in the European Union or coming into the European Union, some of the Member States will insist that those batches are tested again. If the original test is robust, I think it is a legitimate claim to say, "That's unnecessary."

Q84 ***Viscount Brookeborough:*** That is revalidation.
Professor Hammond: It is not really revalidation. It is just acceptance into a different market. We would say that that is inappropriate and we would argue against that. There are some areas where data-sharing is something that we are already doing a great deal of within the pharmaceutical industry. Most drugs, when they are administered to patients, are administered in a formulation and there are excipients within that formulation. We spend a lot of time trying to make sure that the data that we generate to look at the safety of those excipients is shared across the industry, so that there is not repetitive testing for excipients that are widely used across the sector, but the active ingredient will be unique to an individual company and, therefore, it will not be subject to duplication.

Q85 ***Viscount Brookeborough:*** The data that is used in the initial research by your company is not shared openly with other companies until you have something—
Professor Hammond: No, absolutely not. That is our intellectual property. That is our value. If we are forced to put that into the public domain, we cease to become a competitive industry. If we are forced to put that into the public domain in Europe, it will simply mean that everyone else outside of Europe will have access to all our intellectual property and we will not have access to theirs. It would be absolutely untenable.

Q86 ***Chairman:*** "Freeloading" is a term that comes to mind.
Professor Hammond: Yes. It is untenable. No company will tolerate that. No company will do that.

Q87 ***Viscount Brookeborough:*** What sort of data do you think can usefully be shared? Can there be any increase in data beyond that which is currently shared?

Professor Hammond: We are already doing a lot. In the written submission that we have given, there are at least four examples we have quoted where there is a great deal of cross-collaboration, both in the pharmaceutical industry and also in the academic sector, to ensure that data that is generated which is non-competitive is put into the public domain and is shared. Part of that is to advance science, but also a very big significant part of it is to ensure there is no duplication of animal testing.

Q88 ***Viscount Brookeborough:*** How detrimental do you think these new proposals will be to you?
Professor Hammond: The proposals, we believe, are a significant threat and I would invite you to take some advice and some views from the academic sector as well. The academic groups live by publication and if they are forced to put things into the public domain at an inappropriate time, they will lose their competitive edge. I think the greatest difficulty that we all face is the publication of negative data—because journals do not like to take negative data. That is very difficult and so far has been quite an intractable problem. It is something that the sector is constantly talking about and trying to find ways to do it in a better way, but journals just are not interested in negative data, so it becomes quite a difficult thing to deal with.
Dr Brooker: "Negative data" meaning studies in which nothing interesting happens, rather than something negative happening.

Q89 ***Chairman:*** That sounds like what most of my research was like!
Dr Brooker: I sympathise with that.

Q90 ***Baroness Jones of Whitchurch:*** That is where the duplication happens. The evidence we received last week was that, because it does not get published and not a lot happens, people do not know that that research has already been done and so they repeat it and repeat it.
Professor Hammond: The provisions that were in place from the Commission text, and in particular the amendments from the European Parliament, will not stop that. It is predicated on you knowing that the data exists, and there is no way of knowing that that data exists, so people have talked about the establishment of databases to allow this to happen. If you look at the complexity of the data that is being generated, that is exceedingly difficult to do. In fact, we would suggest it is impossible to do. Attempts to construct these databases, even when the data is disciplined and very similar, have been extremely difficult. I would draw your attention to the genomic data and databases, where there is a great deal of stringency in the data and they have still been very difficult databases to construct. If you put that into a much more diverse biological system and try then to put formats out where that data needs to be shared, it becomes technically very, very complex. We recognise it is a problem but the legislation as it is now will not solve that.

Q91 ***Baroness Sharp of Guildford:*** The big problem arises from the revisions that came from the European Parliament.
Professor Hammond: The big threats to the industry certainly come from the revisions that came from the European Parliament, that is correct. I believe it is also true to say that what is being attempted in those revisions really has been lifted from legislation in other sectors—what you might call vertical legislation rather than horizontal legislation. Within particular sectors it may be appropriate to do that. The legislation around pesticides and chemicals has been put in place because most people were looking at either chemicals that would go into common usage or pesticides that had been reformulated and were already out of patent and people were reformulating, and that is entirely legitimate. We are not dealing with that in the pharmaceutical industry. We are dealing with proprietary intellectual property. The approach that has been applied there is just inappropriate.

Q92 ***Lord Livsey of Talgarth:*** Do you think the motivation for doing this is that some people in Europe, and possibly in the European Parliament, think that because of duplication, with cross-sharing not occurring, the cost of the end product is too high?
Professor Hammond: I do not know what the truth is. I do not know whether they are influenced by the cost of pharmaceuticals or not—and, actually, I am not best qualified to comment. I think it is true to say that the European Parliament and the people proposing the amendments were made aware of our concerns and we were not given any feedback that this was influenced by cost. It was influenced much more about a belief that duplication exists and we would challenge the concept that duplication exists. We would prefer to see a much more targeted approach. Where duplication is demonstrated and is clear, the legislation deals with that. It does not try to do a broad-brush approach, which is not appropriate.

Q93 ***Lord Brooke of Alverthorpe:*** Presumably the logic is that if you reduce the amount of research you reduce the amount of animals involved.
Professor Hammond: Yes.

Q94 ***Viscount Brookeborough:*** Their term "duplication" is really taken to be research into a particular ailment or disease rather than duplication of what is going on in the science.

Professor Hammond: My Lord, you make a very good point. One of the issues that we also need to be very clear about with duplication is the distinction between duplication and replication or validation. It is good scientific practice to be able to replicate your results, so it is standard practice that people will repeat work in order to ensure that it is robust and it is true—and it is true in multiple hands, it is not just true in one lab. There are many examples where data that has been published from one lab has not been able to be produced in another lab. It is a robust part of the scientific discipline to be able to replicate results. That is different from duplication.

Q95 ***Chairman:*** Could I just ask about the data-sharing of negative results. It is clearly the case that journals are not interested in publishing papers which lead nowhere, but surely there must be another factor as well. Particularly if you are a large pharmaceutical company and you have a trial or something going, and very expensively, and you come to the end of it and it has not done anything, are you going to be happy about using that information, knowing that your competitor most likely has to go through the same sort of series of experiments and if you release it they are just let off the hook in terms of funding a large study?

Professor Hammond: I think most people would accept that the true competitive advantage in the pharmaceutical industry comes from your clinical data, but you have to recognise it is a race. It is a competitive environment. Consequently, we do put quite a lot of our pre-clinical data into the public domain when we get to market, but we do not put the data into the public domain beforehand unless we want to control that release for particular reasons around supporting the clinical development of a drug. It would be wrong to say we do not put this data into the public domain. Any result from a clinical trial including those that are negative already goes into the public domain. That is already covered. The difficulty we have with the pre-clinical data is that a clinical trial may show a negative outcome in a particular indication but we may want to use that drug and take it into a different indication based on the pre-clinical data. We are very reluctant to put that into the public domain because somebody else will pick it up.

Chairman: Yes, I see that. Let us go on to another area of some controversy: non-human primates.

Q96 ***Lord Cameron of Dillington:*** You seem to have concerns about the limits being proposed on non-human primates: that is, to life-threatening conditions. Perhaps you could expand on your concerns here, bearing in mind that we have had written evidence from other parties suggesting that the use of non-human primates in experiments is not error free and the trials of TGN1412 and the various trials done on AIDS/HIV vaccines have not proven very successful. Perhaps you could expand on how you might refute those arguments.

Dr Brooker: The restriction to life-threatening and debilitating conditions causes much concern because it is not clear. It is not clear what is included and what is not. Perhaps we should make the point that restrictions on the use of NHPs should be considered in the light of the diseases that are under research. There are many areas of fundamental research that cannot be directly linked to a specific disease, and in many instances the benefit is only realised sometime after the original discovery. To attempt to legislate against use in this way will severely compromise the ability of science to identify and develop new treatments further down the line. We should emphasise the mobility of such research. If restrictions are put in place in the EU, again we are back to the situation where the research will simply relocate. We cite some evidence in our written evidence, in the footnote on page 16, that shows a progressive move of skills in neuroscience to the USA and anxiety about the research environment, including the potential for future restriction, as a contributing factor. In terms of specific disease areas that we would be concerned about, they would include reproductive health and the ability to develop protein therapeutics, and, most commonly, monoclonal antibodies, which would include therapies, including cancer research, rheumatoid arthritis and respiratory diseases. They would be the sectors that we would be concerned about. Moving on to your question about the validity of the model, non-human primates are never used where an alternative is available. It is prevented under the current ethical review and approval process in the UK and they are only ever used where a strong scientific reason confirms that the use of an alternative species is not appropriate. In the case of monoclonals, we confirm the pharmacology is not present in any other species by means of in-vitro screening before we go on to use the primate. On occasion, not even the primate for these monoclonals is appropriate, and so you have to go to a less precise model involving mouse homologues or transgenic animals, because there is no point in using the primate because the pharmacology is not demonstrated: they do not have the same receptors as humans would have. We only ever use a primate where we have good reason to believe that it is the best model for studies which inform decisions about clinical trials and there are no alternatives. As with all models, there are rare cases where the use of primates has not identified a cause for concern. My Lords, you have correctly pointed to the example with the TeGenero compound, TGN1412, where the primate research failed to predict the response. But it is also

true that there were a number of in-vitro alternatives carried out on that compound as well as the primate research which also failed to predict. I think this was a rare example. To keep this in context, animal research is critical in supporting first dose into man, and the record in ensuring safety for patient volunteers or healthy volunteers in phase one trials is very good. No models are 100 per cent and it is unreasonable to expect all models to be 100 per cent accurate.

Q97 ***Lord Cameron of Dillington:*** To move on to your concerns about the setting of dates for second generation in-captivity animals and why this particularly concerns you, if you have sufficient warning of it, it seems to me that you could build up the relevant stock and it therefore should not be a worry.
Dr Brooker: I think this is all a matter of timing. We are not opposed to the principle at all of the use of F2 generation primates—indeed, we use them whenever they are available. The issue is how to move to self-sustaining F2 colonies without causing major welfare and supply problems, bearing in mind that the suppliers are outside the EU, almost totally in Asia, and that the EU only takes five per cent of their supply. It is not as though this is something under our total control; we have to work with the suppliers to move them towards this position. There are concerns. It is not clear what will happen to the F1 males during this process and you may see a large culling of F1 males, which I do not think we would like to see. It is also not clear whether large closed colonies will compromise the quality of the animals and put undue pressure on the breeding female stock. We support the European Parliament position here in calling for a full feasibility study rather than the seven-year prescriptive time limit which the Commission's original proposals put in place.

Q98 ***Lord Cameron of Dillington:*** What about the techniques that were recently developed to create genetically modified non-human primates? How significant are these?
Dr Brooker: If you are referring to the development reported in *Nature* and the general press last week about a transgenic marmoset being produced in Japan, it is an interesting scientific development but it is really too early to assess its impact. I would just make the point that transgenic technology, usually using mice, has increased the number of animals being used, and, of course, if we can have transgenic NHP models it will be necessary to demonstrate that the objectives of any experiment cannot be achieved by using a non-NHP model. I think there is potential in the technology but it is far too early to assess the implications.

Q99 ***Earl of Arran:*** Can you ever foresee a time when the use of animals for scientific research will not be needed?
Professor Hammond: No. If your question is directed toward medical advancement for humans, then I think there is a prospect that that will happen but it is a very long way away, but we have to remember also that a lot of research is done on animals for the benefit of the animals. In that context, I think that will continue.

Q100 ***Lord Cameron of Dillington:*** Has their use diminished over the last ten years?
Professor Hammond: The numbers of animals that are used in research over the last 20 years has decreased, but over the last couple of years it has either plateau'd or risen, and it will probably rise again. That will be driven partly by the transgenic technology revolution and partly by the increase in productivity coming from the industry.

Q101 ***Chairman:*** In paragraph 81 of your evidence you have listed a series of areas of fundamental research that might be curtailed by the current draft in relation to primates. When we had the representative of the Commission here last week, she said, amongst other things, "In addition to life-threatening, we also talk about debilitating conditions in humans and Recital 16 further clarifies and says that it has to be a condition that has an effect on the day-to-day functioning of the person. We feel that, for example, infertility could be considered in this category. We have references to it being considered as a debilitating condition and we know that infertility can result in depression and it can result in psychosomatic disorders, therefore we feel that link can be made." She was then asked: "Under debilitating, I take it we would include diabetes and Parkinson's?" and, although the transcript is blank, she nodded and indicated assent. Do you take any comfort from those words?
Professor Hammond: I would take comfort from those words but I do believe we still have a problem that it is around definition. The terms "life-threatening" and "debilitating" to our knowledge are not present in any legislation, other than legislation that is associated with orphan drug status, and orphan drug status is really a very small niche area with particularly life-threatening outcomes. It comes back to the issue of terminology and definition. Our fundamental premise here is that we want to protect basic research that generates knowledge, because from that knowledge will come advancements in the future. To assume that any project that is done is justified purely on the basis that it will affect a specific disease fails to understand the way in which research operates.

Q102 ***Chairman:*** If you are not careful, you are asking for a blank cheque, are you not? Are you not in danger of saying, "We want to be able to conduct any research on primates if it advances knowledge"?
Professor Hammond: We are saying that if the ethical review can see the justification, and the harm to the animal is outweighed by the potential benefits that will come from that research, either direct or indirect, then it should be supported. If it does not, it should not be. That is the current situation.

Q103 ***Chairman:*** I would have thought that on fundamental research it is very difficult to know what the potential benefits are.
Professor Hammond: Usually we know enough now to be able to have some idea of what the benefits will be. I am not aware of any research in primates which is purely speculative.
Dr Brooker: I think you also run the risk, if you have unclear definitions, of differing interpretations in different Member States as to what that may be.

Q104 ***Chairman:*** You would hang it all on the ethical review approach.
Professor Hammond: The ethical review and authorisation approach, yes.

Q105 ***Chairman:*** Are you confident that that is robust enough throughout the Member States?
Professor Hammond: I believe the ethical review is not applied across all Member States. The Directive as it is currently written will introduce that, and if that is done properly, then yes.

Q106 ***Baroness Jones of Whitchurch:*** Is that not something that will create some of the bureaucracy that you were complaining about earlier on?
Professor Hammond: We certainly do not complain about any bureaucracy where there is a welfare benefit. All we complain about is the bureaucracy that is associated with procedures for which there is no welfare benefit: it is simply control and bureaucracy. We are not against bureaucracy where it is linked to very clearly tangible and evident benefits to animal welfare.

Q107 ***Baroness Jones of Whitchurch:*** An experiment could start in six weeks in China but it takes six months in this country, but surely part of that delay is doing the ethical review.
Professor Hammond: The ethical review can be done very quickly in most instances. There are some complex things where it would take longer and we would expect it to take longer, and that is fine.

Q108 ***Earl of Dundee:*** We learn that the Directive's provisions include immature forms of invertebrates and of certain live invertebrate animals. Those provisions, if unamended, how would they affect the research community?
Dr Brooker: We would invite you to take further evidence on this from our colleagues in the academic community, because it will have a much greater effect on them than it will on the pharmaceutical industry. One basic premise that I think the whole bioscience community would like the Directive to be placed on is that of sentience, and to prove that creatures are sentient before applying this legislation to them.
Professor Hammond: The evidence quoted by the Commission we believe is weak.

Q109 ***Earl of Dundee:*** Which amendments to those provisions do you think the European Parliament may bring forward?
Professor Hammond: We would like to see invertebrates where sentience has not been clearly demonstrated—and it is a very small number where it has—not to be covered by the Directive until there is scientific evidence that sentience is demonstrated.

Q110 ***Earl of Dundee:*** Would you like to see any other formal amendment brought forward by the European Parliament?
Dr Brooker: I think we are broadly in favour of amendments 30 and 31 brought forward by the Parliament. We have some minor issues with the wording, which are present in our written evidence, but in general we were in favour of those amendments put forward by the Parliament.
Professor Hammond: They could go further.

Q111 ***Chairman:*** When we are talking about experiments on invertebrates, which invertebrates are being experimented upon?
Professor Hammond: I think you would get a more authoritative view by addressing that question to our academic colleagues. The industry's major area of concern in relation to where this scope extends is that we have to conduct environmental fate studies for our pharmaceuticals, so we will, by necessity, need to assess the impact of our drugs when they get into the environment and, as a consequence of that, we will do fate studies and we will do toxicity studies on fish and on invertebrates. It is quite limited, but we do some.

Q112 ***Chairman:*** That is for the environmental impact.
Professor Hammond: Yes. As far as academic research, I think that is much more widespread and I would defer to the academics to answer on that.

Q113 ***Lord Livsey of Talgarth:*** We come to severity classifications and you have already mentioned this on a number of occasions. The proposal (Article 15) contains a system of "severity classifications" for

procedures (up to mild; moderate; severe; or non-recovery) which will determine important aspects of the application of the Directive. However, the criteria for these classifications are only to be finalised after adoption of the Directive. Would you like to see these agreed within the text of the Directive, as proposed by the European Parliament? What is your view of the definitions proposed by the European Parliament (amendment 161)?

Professor Hammond: The first thing I would say is that it is absolutely crucial to have full and accurate definitions in order to be able to interpret the impact of many of the articles within the Directive. We are very, very supportive of the parliamentary amendments which brought that clarity. We would like to see perhaps some very minor modification to the amendments proposed by the European Parliament, particularly in that the system that was proposed was largely based on the Swiss system and the Swiss system does not separate non-recovery. For clarity around how many parts of the text are written, it would be helpful to have that as a separate category rather than to re-write large parts of the text. But the principles behind it are something that we very strongly support. One particular area where it is absolutely crucial for us—and we believe this is a very big welfare issue—is around the subject of re-use. Re-use is quite complex. Perhaps I could take a couple of seconds just to explain. The reason we are concerned about re-use is that the Commission text limits re-use to one re-use only, and only if animals have been subjected to what is defined as a "mild procedure". If we were to adopt that, some of the advanced technologies that we have developed would become very difficult to apply. One example is telemetry. One of the things that we do now is to implant telemetric devices into a dog or into a primate. This is particularly important because it affects the higher-up species. Then we will collect data from that individual animal after repeated dosing of different compounds. We can look at heart rates, blood pressure: it is very sophisticated and you get very high quality data. The most traumatic part of that procedure is the surgery to implant the devices. If the text as proposed by the Commission is taken forward, we would have to do that on separate individual animals before we collected the data for each compound. The most difficult part of the procedure would be the surgery. It would increase the number of animals that we would use probably by ten-fold or more and it would cause major welfare issues for us—probably to an extent that we would not do it, we would move it, because we would find it very difficult to justify that. Severity classifications as they have been defined by the European Parliament, and allowing re-use up to moderate, would allow us to continue to do what we are doing now, which is seen as ethically acceptable, so we would very strongly support a continuation and support the amendments that have been put forward by Parliament in this area. There is a working party that will define severity classifications. We are concerned that if they come up with a set of definitions which are completely different from the ones which are currently proposed by Parliament it will again make interpretation of the rest of the text very difficult, and I think we will need to go back to square one.

Q114 ***Lord Livsey of Talgarth:*** Would it be correct to assume that you have made these points very clearly in the way that you just have?

Professor Hammond: Indeed. In terms of the severity classification that was proposed by the European Parliament, obviously, we were closely involved in that. We work very closely with our Swiss colleagues; we helped the Parliament to do that.

Dr Dunn: And, if I may add, my Lord Chairman, the Technical Expert Working Group report from 2003 is unambiguous in this area.

Q115 ***Baroness Jones of Whitchurch:*** Do you have a view on the fact that the criteria are not going to be established until after the directive has gone through?

Professor Hammond: I believe it is unacceptable. The parliamentary amendments are already tabled and I hope Council will adopt those or will adopt a minor revision of those that will come from the working party, but I think it would be wholly unacceptable to have the directive issued without having that clarity. It affects so many parts of the directive and the interpretation of the directive. It would be very unwise indeed in our view.

Chairman: I think the Commission also recognise that they have got a problem there on the basis of the evidence to us. Let us go on to authorisation.

Q116 ***Lord Brooke of Alverthorpe:*** Thank you, by the way, for your paper which I thought was very comprehensive indeed and also very helpful in the area of authorisation of decisions. The diagrammatical description of what life would look like if the directive goes through as at present defined though is not easy to follow. It would have been easier possibly if we could have had a diagram of what happens at the moment and what your alternative is by comparison with what happens now because I think there is a distinction between the two, is there not?

Dr Brooker: I think we can provide that subsequently for you if that would be helpful.

Q117 ***Chairman:*** That would be very helpful.

Professor Hammond: It is also worth commenting that we can provide that for you as to how it operates in the UK. It is important to recognise that across Europe it is widely divergent.

Q118 ***Lord Brooke of Alverthorpe:*** We are aware of that. How would you say the current procedures that we have in the UK will have to change?
Dr Brooker: This is hugely complex and we do not think that either the Commission or the Parliament has dealt with this topic adequately. This is why we suggest an alternative. However, to answer your question specifically, the following points would demand change of the current UK system. First is the separation of ethical review from authorisation, even though both could be done within one body. Our concern there is that the directive sets no time-limits on ethical review, which pertains to the previous point, that there are time-limits on authorisation but no time-limits on ethical review, so that would be a change from the current system. Project licences currently run for five years and the directive would change this to four. Currently they have two reviews, one in mid-life and one at the end. Annual review is proposed. A retrospective review is proposed. Currently this is not required unless a licence renewal is applied for. Severity is not reported retrospectively. Those are the specific changes that the current Animals (Scientific Procedures) Act would need to have made to it.

Q119 ***Lord Brooke of Alverthorpe:*** We chased the Commission representative quite a bit on this last week and I ended up with a question, "Would you argue then that the British Government's claim that this is a substantial additional bureaucratic charge which is going on to operations is quite invalid?", to which she replied, "No, I wouldn't go that far. I would like to discuss the details with the British Government. I think that would be the best way to say it", so it sounded at the end of the exchange we had that there was still an area for negotiation and discussion. Is that how you perceive it?
Dr Brooker: We feel that the current UK system is overly bureaucratic, which is why there have been discussions under the Better Regulation banner over the last several years, and I think the Home Office agrees with that. The fact that what is proposed here goes over and above the current UK system fills us with concern on the point about bureaucracy with no welfare implications that we were talking about.
Professor Hammond: The Commission so far have shown in our discussions with them no inclination to want to discuss this. They believe that they have already got sufficient flexibility, particularly through the designation of "competent authority" and allowing subsidiarity to give that flexibility so that Member States could implement this in a way which suited those Member States. Our difficulty is that, although that is true, there is a high degree of prescriptive requirement that comes from the directive which, if it is transposed into law, is then an obligation to fulfil. It is difficult for us to see how you would have that flexibility and that obligation.

Q120 ***Lord Brooke of Alverthorpe:*** The point about flexibility was made very strongly to us, that there is a degree of freedom for Member States to apply this as they see appropriate.
Professor Hammond: I can only comment that within the UK we are particularly anxious about it and we already have a very bureaucratic and difficult system to work with. Other scientific communities in other Member States see this as a major change to what they are currently doing.

Q121 ***Lord Brooke of Alverthorpe:*** Have you put your alternative to the Commission?
Professor Hammond: We have discussed it with the Commission, yes.

Q122 ***Lord Brooke of Alverthorpe:*** What kind of a response have you had from them?
Professor Hammond: So far we have no indication that they believe that this is something they would like to take forward.

Q123 ***Lord Brooke of Alverthorpe:*** And to the British Government too?
Professor Hammond: We have put this to the British Government as well.

Q124 ***Lord Brooke of Alverthorpe:*** And the kind of response?
Professor Hammond: The Home Office, I think, are probably still in need of convincing that there is a legitimate way to separate notification and authorisation and we are continuing to discuss that. The opportunities for proportionality, I think, are recognised by the Home Office. I believe they see that the level of control and of approval to conduct a non-human primate study and the processes that go towards supporting that should not necessarily be the same as if you were to apply for a licence to do a study on an invertebrate. Under the current directive there would be no distinction, so there is no proportionality between them.

Q125 ***Lord Brooke of Alverthorpe:*** Given that there is a wide variation in existing practices throughout Europe at the moment, particularly in regard to ethics, could you see a case to be advanced that there should be a programme developed whereby those at the bottom should be required to raise their standards, for example, introducing ethical reviews before further changes should be introduced across Europe?
Professor Hammond: That is an interesting question. I think the current legislation, Directive 86/609, already provides a framework and I think we have

seen that there has been a big difference in implementation across Europe so I am not sure how legislation is going to deal with that. I think the issue that we need to deal with is implementation and it is unclear to me how that would happen.

Q126 ***Lord Brooke of Alverthorpe:*** The case has been put that there is a wide variation in practices on the 1986 legislation and that it could conceivably become wider with the new legislation. We put that to the Commission. One of the ways that could be advanced to try to overcome the paucity of attention to animal welfare in some countries would be to insist at least that the 1986 Directive was introduced to narrow the gap.
Professor Hammond: I cannot disagree with that but I will just refer back. It is already there. It is about implementation. What appears to us is that the implementation across Europe has not been uniform. There are some countries which have implemented it fully and others which have not.

Q127 ***Lord Brooke of Alverthorpe:*** And would you wish to have seen those standards applied across Europe?
Professor Hammond: I think the standards, yes. The bureaucracy, no.
Chairman: A nicely nuanced answer, if I may say so!

Q128 ***Viscount Brookeborough:*** Are your colleagues in Europe fighting this as hard as you are or do you think they would just be quite happy if they were not implemented?
Professor Hammond: They are fighting this as hard as we are. As I said in my introductory comments, the views that are being expressed to you today are the views of the pharmaceutical industry; that is why we are here, but we are very consistent with the entire bioscience sector across Europe. It is not just in the UK and it is not just industry across Europe. It is the entire bioscience sector across Europe.
Chairman: We now come to care and accommodation standards.

Q129 ***Baroness Jones of Whitchurch:*** This follows neatly on because you say in your evidence that you think these standards should be guidelines rather than mandatory, but surely if we continued with it being based on guidelines we would get exactly what we were discussing just now, which is the gold standard in the UK and variable standards across Europe with some countries virtually ignoring the new legislation as they have the previous legislation. How can you justify that you only want it to be a guideline and not mandatory?
Dr Dunn: My Lord Chairman, the challenge with regard to the animal care and accommodation standards is that the ones that have been adopted as mandatory were in fact originally conceived as guidelines to be used in an informative as opposed to a mandatory way, so if they were adopted as currently indicated in the draft we would be losing a very considerable amount of capacity for rodent and rabbit stock, and that is even in comparison to the current well-enforced standards in the UK code of practice. It is certainly the case that it would encourage harmonisation but we would be harmonising to what is a very high standard. I draw your attention back to the impact assessment that was carried out where the costs of this have been very significantly underestimated and the welfare impact for these animals—and we are talking here, I would remind you, about rodents and rabbits—as stock animals is really not supported by the scientific evidence.

Q130 ***Baroness Jones of Whitchurch:*** I think you have probably answered the second bit of my question. Which is the bit of the new mandation that you particularly object to in relation to the care and accommodation for rodents?
Dr Dunn: It is very much around—and again I would like to be very specific—the cage space allowances. There are many aspects of the performance standards which are being adopted through ETS 123 Appendix A which are well supported, things like environmental controls, group housing, environmental enrichment, but the actual amount of physical space in centimetres squared for stock rodents and rabbits is posing quite a challenge.
Professor Hammond: If I could add one comment, it is important to recognise that these standards are engineering standards, so they are basically specifying space and humidity. In the original work that was done to try and look at this, there was a high degree of controversy around the evidence to support whether or not a particular cage size was better or worse than another particular cage size, so it is not a simple scientific argument to make.

Q131 ***Lord Cameron of Dillington:*** Your whole industry is obviously surrounded by controversy. It seems to me that objecting to these simple things, by saying that this is not proven by science, is not a particularly effective argument in this particular industry because it is more of a philosophical and moral argument, or the perception of it is.
Dr Dunn: My Lord Chairman, an important point to make is that we have tremendously positive experience for these species with the current provisions and that is an important factor, I believe, to be taken into account before making the argument and the case where we are being asked to elevate what we currently have.

Q132 ***Chairman:*** So you are not arguing against the concept of mandatory standards? You are saying the present mandatory standards are OK but the ones that coming through from the directive are the Council of Europe aspirational ones and you see no scientific justification for moving from one set of mandatory standards to a higher set of mandatory standards? Is that fair?
Dr Dunn: That is fair comment.

Q133 ***Earl of Caithness:*** But the current standards are not mandatory, are they? They are advisory.
Dr Dunn: If I may confirm, I am making the comparison between the UK code of practice which has the status of a code of practice, and the mandatory standard that would come through an A(SP) order.

Q134 ***Chairman:*** But you would not get a licence if you did not. Would you be able to function if you did not house using the code of practice standards at the moment? The present system is a code of practice.
Dr Dunn: Yes.

Q135 ***Chairman:*** If you did not operate at that code of practice would you be able to get the certification to carry out procedures?
Dr Dunn: I believe that it is the case that the Home Office inspectorate would enforce the standards that are in the code of practice, and my understanding is that the status of the code of practice would be that if you deviated from it you would need substantial reasoning why you did that, and it is very much related to the status of the code of practice as a statutory instrument.
Chairman: Thank you very much. We come finally to the 3Rs.

Q136 ***Viscount Ullswater:*** The 3Rs principle lies at the heart of the Commission's proposals and I think Professor Hammond, in a reply to my colleague, Lord Arran, said that total replacement was unfeasible, and I think you also asserted in your opening comments that the scientific community was the driver of the 3Rs principle rather than it being forced on them. How do you see these proposals? Are they helpful or do they hinder the adoption of the 3Rs principle?
Dr Brooker: We are completely supportive of the focus on the 3Rs that is within the directive. We think it is excellent and we think it appropriate. It is the means to achieving that that perhaps we take issue with, and their proposal to set up a series of national centres is one that we do not see as being particularly effective. We believe it is those directly engaged in the scientific practice that drive forward 3Rs and there are some examples we would like to leave with you of developments in the 3Rs that we presented to the European Parliament earlier this year. It is a booklet. We do not have time to do it today but we would encourage you to look at these examples, and we would perhaps point to the model in the UK where we have the National Centre for the 3Rs, which is funded mainly by government but with support from industry, and which, rather than being a separate, isolated laboratory working on its own, instead provides a forum for all practitioners to meet together under the guidance of the National Centre for the 3Rs which has a very clear drive towards reduction, refinement and replacement. It set up fora for sharing best practice, it set up particular work streams, and perhaps I could point you in particular to one that has produced some excellent work in the last two years on the use of primates in the testing of biologically derived molecules, and also funded research in a variety of different academic and individual laboratories which are centres of excellence for the work that they do. We do not think that setting up 15, 20 independent centres would work particularly well and nor would it be a good use of funds. The general principle we are completely supportive of. In terms of our incentives, which I think was another part of your question, the incentives are completely clear. It is ethically right and it is commercially sensible. It is actually much cheaper to run alternatives than it is to set up animal testing laboratories, so there is both a commercial and an ethical drive wherever we can either to use fewer animals, less complex procedures on animals, or indeed, where possible, to replace animals.

Q137 ***Chairman:*** Can I just raise one issue which is the interests of breeders? Are there any particular concerns that we have not touched upon that are specific to breeders?
Dr Dunn: My Lord Chairman, I think that you have given us a fair hearing with regard to the issues around the care and condition standards. That is the major challenge for the Laboratory Animal Breeders Association, and again I would stress that in the UK this relates very much to our capacity to hold stock of rodents and rabbits.

Q138 ***Earl of Caithness:*** What is the variance between our code of conduct and the European or American?
Dr Dunn: For the new standards that would be mandatory through Annex IV—

Q139 ***Earl of Caithness:*** Sorry, our existing code rather than the proposed one.
Dr Dunn: We would be talking about a gap of about 25–30 per cent capacity to hold stock.

Q140 ***Chairman:*** Are there any other points that you think should be brought to our attention that you have not had the opportunity to bring to our attention?

Professor Hammond: No. My Lord Chairman, I think you have given us a very thorough opportunity to explain the issues as we see them. I could recap very quickly if you like. It really focuses on the critical issues around the use of non-human primates, around severity definitions and re-use, around bureaucracy and around protection of intellectual property. They are the key areas that we are concerned about and they are the areas that could potentially have the biggest impact upon decisions to invest in the EU as well as in the UK.

Q141 ***Chairman:*** Thank you very much indeed. Can I say that I was particularly attracted to and interested in the somewhat metaphysical discussion in your evidence on whether death was a lasting harm.

Professor Hammond: It is actually quite an important point.

Chairman: Certainly for me it is! Thank you again.

WEDNESDAY 17 JUNE 2009

Present	Arran, E	Livsey of Talgarth, L
	Brooke of Alverthorpe, L	Palmer, L
	Brookeborough, V	Sewel, L (Chairman)
	Cameron of Dillington, L	Ullswater, V
	Dundee, E	

Memorandum by the Royal Society for the Prevention of Cruelty to Animals

SUMMARY OF EVIDENCE SUBMITTED BY THE RSPCA

Objectives of the Directive

— Replacing animal experiments wherever possible and maintaining good standards of animal care and welfare within research are not only moral obligations but also essential for good quality science.

— The RSPCA regards most of the proposed measures in the draft Directive as both necessary and proportionate in spirit, although problems with the drafting make some of them unclear.

— The UK Animals (Scientific Procedures) Act 1986 should not be compromised in any way by a Directive with lower standards.

International Competition

— Animal research and testing is exported to third countries for many reasons, many of which do not relate to animal welfare. These include lower staff and infrastructure costs, expanding markets, available labour and tax breaks.

— Many companies now state that high standards in animal use form a key part of their corporate ethical policies. Moving research and testing out of the EU and reducing standards would make nonsense of such statements.

Non-human Primates

— Far greater efforts should be made to phase out the use of primates in research, but the proposal does little to facilitate progress with respect to this.

— The restrictions in Article 8 would have no impact on primate use because the scientific community argues that all the research currently using primates is for serious medical conditions.

— The prohibition on Great Ape use is appropriate, as it should be unthinkable that any country would consider it morally acceptable to use them in experiments. The safeguard clause (Article 50) is therefore unacceptable.

— The capture and use of wild-caught primates is a major animal welfare concern. While primate use continues, there should be a move to the exclusive use of F2 animals as rapidly as possible and *much* sooner than the seven to 10 years given in Annex III to the Commission proposal.

Scope of the Directive

— The proposed additions to the scope of the Directive are all justified in the view of the RSPCA.

Administration of the Directive

— The level of administration that the Directive would require is wholly proportionate to its objectives, and is essential for good welfare and ethically sound, good quality science.

— Those who wish to carry out experiments that cause animal suffering—and profit directly or indirectly from it—must accept that an appropriate level of regulation and administration is required.

Provisions for Establishments, Projects, Persons and Inspection

— Many of the Articles relating to establishments, record-keeping and care and accommodation of animals require clarification and significant improvement.

— The proposed membership of permanent ethical review bodies at establishments is too limited and should include an independent "lay" member.

— It should also be made clear that an important function of these bodies is to review the harms, benefits and justification for each project.

Care and Accommodation

— The care and accommodation standards are based on those in Council of Europe Convention ETS123 Appendix A, which represent minimum requirements agreed as a compromise between stakeholder groups.

— Annex IV of the proposal omits critically important elements of ETS123 Appendix A.

— The timescale set for the implementation of Annex IV is far too long.

Alternative Methods

— The proposal identifies the main block to the introduction of alternative methods as the need for new methods to be developed. However, Article 45 gives no indication of how the Commission or Member States should address the problem, or how their efforts should be coordinated.

— The proposal for National Reference Laboratories addresses only test validation and is also an impractical proposition because not all Member States have laboratories with the required expertise, and it is not clear how the work would be coordinated and financed.

— The existing European Centre for the Validation of Alternative Methods should be given an expanded remit covering the development of alternative methods as well as their validation.

— The proposed EU Centre should be supported by a network of National Centres to assist in coordinating and commissioning research needed for both the development and validation of alternative methods.

Subsidiarity and Legal Base

— There are good reasons to regulate all of the issues covered in the Directive at the EU level, provided that Member States retain the flexibility to improve upon minimum standards. The Directive already sets out in its discussion of the legal elements how the proposal complies with the subsidiarity principle.

— Article 95 of the Treaty of Rome is the appropriate legal base, as the stated goal of the Directive is to harmonise and level practices such as the breeding, keeping and use of animals for scientific purposes.

EVIDENCE SUBMITTED BY THE ROYAL SOCIETY FOR THE PREVENTION OF CRUELTY TO ANIMALS

1. Representatives of animal welfare organisations and of the scientific community were in broad agreement about the principles and required content of the revised Directive during the discussions of the Technical Expert Working Groups that were convened prior to drafting. Unfortunately, many disagreements have subsequently arisen due to poor drafting of the proposal.

2. The principles that we believe still have very wide support, and which underlie the answers given below, are that:

(i) replacing animal experiments wherever possible, and ensuring good standards of animal care and welfare within research, are essential for good quality science. This is what the Directive is attempting to do;

(ii) ensuring a rigorous system of authorisation and control is a requirement for achieving good welfare *and* good science, and for developing public confidence with regard to the contentious issue of animal research;

(iii) ensuring that the necessity and justification for animal use is rigorously assessed through an appropriate system of ethical review provides a significant driver for improving both science and welfare, and helps develop public confidence in the ethical standards of industry, academia and regulators.

Objectives of the Directive

Question 1. *What degree of harmonisation of rules governing the protection of animals in research is required to avoid distortions of the Single Market? To what extent are such distortions causing problems at present, and is the draft Directive a proportionate response to those problems?*

3. The objective of the revision of the Directive is not only to strengthen the Single Market, and reduce unfair competition, but also to improve animal welfare and protection in line with the Animal Welfare Protocol annexed to the EC Treaty. The proportionality of the proposals must therefore be seen in the light of this dual objective. Distortions in the Single Market resulting in unfair competition arise where research organisations in one Member State can gain an advantage over those of another state where more stringent controls over animal experimentation apply. To remove such distortions by harmonising requirements to a low level would be contrary to the Animal Welfare Protocol.

4. Harmonising rules to achieve a high level of animal welfare and protection is the only option which will achieve both of the objectives of the proposed Directive.

5. In addition, harmonisation to a high standard of animal welfare is essential for maintaining the scientific quality and efficiency of biomedical research in Europe. The environment in which animals live has been proven to affect their physiology, which then impacts upon the data obtained from them. Research results obtained from animals kept in poor conditions are prone to be misleading, having potentially serious consequences for progress in biomedical research and the protection of human health.

6. To ensure high standards in animal care and welfare it is essential that the Directive specifies comprehensive controls and checks on establishments and personnel. In addition, training provided for researchers, veterinarians and animal care staff must be consistent in nature and quality, as the ability to perform these roles in a competent and empathetic manner is critically important if high standards are to be achieved. Furthermore, harmonisation of the decision making process relating to the necessity and validity of projects using animals prevents funds being wasted on research that is of dubious scientific merit.

7. There are already a number of working national laws that implement all of the above to a good standard, without disadvantaging the national science base. The UK legislation, the Animals (Scientific Procedures) Act 1986 (ASPA), is a good example. The ASPA, which was introduced and enacted by the UK Parliament in accordance with the will of the UK public, should not be weakened or compromised in any way by a new Directive with lower standards. To eliminate distortions in the Single Market, whilst ensuring high quality science and good animal welfare, the Directive should significantly raise standards throughout the EU.

International Competition

Question 2. *How might high(er) animal welfare standards in the EU impact upon the international competitiveness of the EU's private and public sector research base, and that of commercial establishments carrying out routine testing? Is there a risk of displacing research using animals to third countries and, if so, what would be the consequences of such a trend?*

8. Higher animal welfare standards in the EU will have a positive impact on international competitiveness because the quality of the science (and hence efficient use of resources) will be higher as a result.

9. The standards for animal housing and care set out in the proposed Annex to the Directive are taken from the recently revised Appendix A to Convention ETS123. The guidelines in Appendix A were drawn up over an eight year period by Council of Europe working groups comprising the full range of stakeholders (industry, academia, animal welfare and regulators). The standards were agreed as the minimum requirements to cater for animals' needs. Housing animals according to lower standards, for example by reducing space allowances below those in the Annex, will therefore, by definition, compromise animal welfare and hence scientific validity.

10. Animal research and testing is exported to third countries for many reasons. For example, a recent feature in *Nature*[1] quotes a number of pharmaceutical company executives explaining why moving research and development programmes to China is an attractive option. Reasons include the fact that clinical trials (using humans, not animals) are cheaper to run there, researching in China builds connections with the lucrative

[1] Cyranoski D (2008) Pharmaceutical futures: Made in China? *Nature* 455: 1168–1170

Chinese market for the future, and there is a large pool of talent in the form of Chinese researchers who have trained and worked in Western companies. Lower (and cheaper) animal welfare standards were not mentioned. Cheap labour, tax breaks, expanding product markets and easier planning applications for new buildings have also been cited as supporting work in other countries outside the EU such as Singapore.

11. Most pharmaceutical companies now state that high standards of animal welfare and careful justification of animal use form a key part of their corporate ethical policies and that they are proud of what they do in the UK and Europe. Moving research and testing out of the EU in order to reduce standards would make nonsense of such statements. It would also clearly demonstrate that maximising profits is more important than animal welfare and quality of science and hence the safety and efficacy of their products.

12. In any case, many pharmaceutical companies are multinational and already operate in countries outside Europe.

The Proposed Requirement to Restrict Research on Non-human Primates (Art. 8)

Question 3. *Are the proposed restrictions proportionate, and what might be their impact?*

13. Taking into account the level of cognitive development of non-human primates, their ability to suffer, the difficulty of satisfying their behavioural needs in a laboratory environment, and the high level of public and political concern about the use of these animals, the RSPCA would like to see their use phased out completely. The Directive should put in place a strategy for the complete replacement of primate use in research and testing. In that context, we regard the proposed restrictions only as steps in the right direction.

14. Article 8 (1): The scientific community argues that all the research currently done on primates is for serious medical conditions. Therefore, the restrictions in Article 8 would have no impact because their research would already be within the permitted purposes.

15. Article 8(2): The prohibition on Great Ape use is appropriate. However, the safeguard clause (Article 50) is unacceptable. Given the closeness of Great Apes to humans, their endangered species status and the level of international concern about their use, it should be unthinkable that any country would consider it morally acceptable to use them in experiments. It would also be impossible practically—there are insufficient numbers in the wild and it would be impossible to breed them fast enough to respond to an "unexpected outbreak".

16. Articles 10 and 27: The capture and use of wild-caught primates is a major animal welfare concern because of the level of suffering and mortality associated with capture, handling and housing of wild animals. This is widely documented and it is accepted that it is a significant animal welfare concern that must be addressed (see Annex 1 for a number of authoritative reports that recommend only using F2+ primates). The concern applies whether the animals are used for scientific procedures or for breeding. It is also recognised as an issue for human health and safety since wild primates are recognised to carry a number of diseases that are transmissable to humans.

17. The RSPCA therefore believes that, while primate use continues, animals should be sourced from closed colonies that are not supplemented with primates caught from the wild. There should be a move to the exclusive use of F2+ animals as rapidly as possible and *much* sooner than the seven to 10 years given in Annex III to the Commission proposal.

Extension of the Scope of the Directive (Art. 2)

Question 4. *Are the proposed extensions to the scope of the Directive justified, and what might be their impact?*

18. There are three major additions to the scope of the Directive, all of which are justified in the view of the RSPCA.

(a) Animals bred specifically so that their organs or tissues may be used for scientific purposes

19. The welfare of animals kept as a source of tissues or organs for research, whether or not they were bred solely for that purpose, is just as important as the welfare of animals used in scientific procedures. They are entitled to good standards of housing and care and humanely conducted euthanasia using appropriate techniques. The public is also concerned about the lives and welfare of animals killed for tissues and organs, as this is an aspect of the impact of science on animals. This should be reflected in the legislation, especially with respect to reporting on this use of animals in official statistics.

(b) Independently feeding larval forms or fetal forms as from the last third of their normal development

20. Fetal animals are capable of suffering under at least some circumstances. Although there is debate about fetal consciousness, it may well be the case that there are episodes of consciousness during gestation in which the developing animal could experience pain. It is also possible that stimulation caused by procedures could increase levels of consciousness, especially if the fetus is exposed to higher oxygen levels. In addition, events that occur during development can influence the welfare of animals post-partum, even though the fetus may not have consciously experienced those events at that time.

21. Taking all of the above into account, fetal forms should be given the benefit of the doubt and it is clearly not acceptable only to regulate procedures from birth or hatch. The proposed cut-off point of the last third of gestation or incubation is arbitrary, as is the current 50% cut-off point used in the UK. A solution from a legislative point of view would be to retain a generic cut-off point, but also include an Annex to the Directive listing species-specific developmental stages when fetal animals reach a stage of neural development when they could become capable of suffering. The Annex could be updated as new knowledge becomes available.

22. The use of larval forms of vertebrates requires regulation, because the alternative of licensing procedures once metamorphosis is complete is highly unsatisfactory. Independently feeding larval forms are responsive to their environments and react to noxious stimuli. Therefore, as for fetal vertebrates, they should be given the benefit of the doubt with regard to potential suffering. An Annex listing species-specific developmental stages when larval forms become capable of suffering could be added to the Directive.

23. The UK ASPA has regulated the use of fetal forms and independently feeding larval forms since 1986 and this has proved to be perfectly feasible and workable. One objection to the proposed Directive is that counting these organisms and reporting their use in statistics would be an unnecessary burden. However, they are not counted and reported and the same could apply to the Directive.

(c) Live invertebrate animals, including independently feeding larval forms, of those species listed in Annex I (Cyclostomes, Cephalopods, Decapod crustaceans)

24. Cyclostomes (lampreys and hagfish) are members of the class Agnatha, or the jawless fishes. Agnatha is one of the classes within the subphylum Vertebrata, of which the other six living classes are Chondrichthyes (sharks and rays), Osteichthyes (bony fish), amphibians, reptiles, birds and mammals. Cyclostomes are therefore vertebrates and as such their use should *already* be covered by the Directive.

25. Studies on crustaceans have demonstrated that they fulfil a range of criteria that are used to demonstrate the experience of pain. These are (i) a suitable central nervous system and receptors; (ii) avoidance learning; (iii) protective motor reactions including reduced use of the affected area; (iv) physiological changes; (v) trade-offs between avoiding a noxious stimulus and other motivational requirements; (vi) evidence of reduced pain experience with analgesia; and (vii) high cognitive ability and sentience[2,3] Studies on cephalopods have focused more on cognition, but have also shown that these animals fulfil many of the criteria for the ability to suffer[4,5]

26. The Directive should therefore regulate procedures on all animals that fulfil the criteria listed above. (There are other versions and approaches to listing criteria, which are broadly similar; eg see Smith & Boyd (1991[5]) and Nuffield Council on Bioethics (2005[6]).) This includes cephalopods and decapod crustaceans. Note also that the New Zealand Animal Welfare Act regulates research on crabs, crayfish, squid and octopus.

AUTHORISATION OF PERSONS, REQUIREMENTS FOR ESTABLISHMENTS, INSPECTIONS AND PROJECT REQUIREMENTS (ARTS. 20–43)

Question 5. *Are the administrative demands that the draft Directive would impose overall proportionate to its objectives?*

27. The level of administration that the Directive would require is wholly proportionate to its objectives, and is essential for good welfare and humane, ethically sound and good quality science. The wording is sufficiently flexible to allow interpretation by individual Member States when drafting national legislation.

28. Animal use causes suffering which is agreed to be a serious concern. Those who wish to carry out animal experiments—and profit directly or indirectly from it—must accept that a stringent level of regulation and administration is required.

[2] Elwood RW, Barr S & Patterson L (in press) Pain and stress in crustaceans? *Appl. Anim. Behav. Sci.*
[3] Sherwin CM (2001) Can invertebrates suffer? Or, how robust is argument-by analogy? *Anim. Welf* 10: S103–S118
[4] Mather JA (2008) Cephalopod consciousness: Behavioural evidence. Cons. Cogn. 17: 37–48
[5] Smith JA & Boyd KM (1991) *Lives in the Balance.* Oxford: Oxford University Press.
[6] Nuffield Council on Bioethics (2005) *The Ethics of Research Involving Animals* London: Nuffield Council on Bioethics.

Question 6. *Do any of the provisions relating to the authorisation of persons, the requirements for establishments, the inspection regime, or project requirements require further consideration and/or amendment and, if so, why?*

29. Establishments: The drafting of the Directive is unclear in places, particularly with regard to Article 24(1) on the requirements for personnel. This is confusing in that the introductory sentence suggests paragraphs a) to d) apply to animal care staff, yet the responsibilities described would require a wider range of expertise and a far greater level of overall responsibility.

30. Permanent ethical review body (Articles 25 and 26): The requirement for an ethical review body is welcomed.

— The proposed members in 25(2) are the minimum requirements and this should be made clear. An independent "lay" member should be added to this list.

— Article 26(1) is poorly drafted. It needs to be clear that one task is to review the harms, benefits and justification for each project. This is encompassed in 26(1a) but this needs to be more explicit.

31. Inspections (Articles 33 and 34): The inspection regime should be viewed constructively as a valuable means of promoting good practice, preventing infringements and facilitating the authorisation process.

32. Records on animals (Article 29): An important point is missing from the list of records. Paragraph 1a needs to include records of the numbers of animals used as well as those bred etc. This is the most important point.

33. Care and accommodation (Article 32): There are several very important points missing from this article.

— Para a): given current knowledge about the needs of animals, it is reprehensible only to state that they should be given "at least some freedom of movement". The thinking behind the revised Appendix A was that accommodation and care should satisfy the animals behavioural and physical needs and it should say this here.

— There should be a paragraph requiring the health and well-being of animals to be checked at least once per day.

— Para e) is wrongly worded; "defect" should be replaced with "pain, distress…".

— The timetable given in para (2) and Annex IV is unacceptable for the reasons given below.

34. Article 43: It is unacceptable for projects to be "deemed to be granted" if a member state does not make a decision within 30 days. Although this only applies in the case of procedures classified as "up to mild" and does not include primates, it would allow projects involving thousands of rabbits or dogs to go ahead unauthorised. This hardly reflects the tight system of regulatory control that the public expects and is used to in the UK.

Question 7. *Are the care and accommodation standards set out in Annex IV to the Directive appropriate, and will they produce an adequate level of harmonisation across the EU?*

35. The care and accommodation standards are based on those in Council of Europe Convention ETS123 Appendix A. These were developed and agreed in 2006 after eight years of work by Council of Europe expert working groups comprising stakeholders from industry, academia and animal welfare organisations, together with extensive consultation with the "user" community. It was understood that the standards would be translated into the new Directive.

36. In the RSPCA's view the standards represent a compromise between the stakeholder groups and represent the minimum requirements. With this proviso, applying Appendix A across the EU would produce an adequate level of harmonisation, although Member States should be able to improve upon the minimum if they wish. There are however two concerns:

(i) The housing and care standards set out in the draft Annex IV omit critically important elements of Appendix A. For example, the tables for cage sizes are of limited use without their accompanying text which advises how to meet the animals' physical and behavioural needs and why this is important.

(ii) The transitional arrangements that have been set for the implementation of the Annex are much too long. It was widely acknowledged over 10 years ago that husbandry and care standards in the Appendix and Annex were out of date and no longer appropriate in animal welfare terms. If animals continue to be housed according to the previous guidelines they will therefore be in sub-standard accommodation below the agreed minimum. This is not acceptable. There should be no fixed transition period, let alone another decade for facilities to provide animals such as primates and dogs with the new agreed minimum standard.

Alternative Methods

Question 8. *How satisfactory are the provisions on alternatives to animal testing and National Reference Laboratories (Art. 46)?*

37. We agree wholeheartedly with the statement made in the Explanatory Memorandum to the proposal that the ultimate goal should be to replace the use of animal experiments altogether. Unfortunately, the proposal contains little to enhance promotion of the development, validation, acceptance and implementation of alternative methods.

38. Recital 45 correctly identifies the main bottleneck to the introduction of alternative methods; *"there is an increasing need for new methods to be developed and proposed for validation."* Similarly, Article 45 requires the Commission and Member States to *"contribute to the development and validation of alternative approaches"* and to *"take such other steps as they consider appropriate to encourage research in this field."* However, there is no indication of how the Commission or Member States should contribute, or how their efforts should be coordinated.

39. The proposal for National Reference Laboratories (Article 46) addresses only validation, despite the fact that validation is not the bottleneck identified in Recital 45. Validation in essential in certain circumstances, principally for tests required to satisfy safety legislation. Such procedures account for only a small proportion of scientific animal use in the EU. Formal validation is not appropriate in most areas of biological research, where it is not simply a question of applying standard tests. Even in regulatory testing, potential test methods must be identified, developed and refined before they can be considered for validation.

40. The proposal for National Reference Laboratories is also rather impractical. Not all Member States have laboratories with the required expertise, and it is not clear how the work of such laboratories would be coordinated and financed.

41. The key to replacing animals in all forms of research and testing is the adoption and adaptation of new technologies. What is needed is a more wide-ranging and coordinated EU approach to promoting the Three Rs. To this end, we believe that the role of the existing European Centre for the Validation of Alternative Methods should be expanded to cover the development of alternative methods as well their validation. The expanded remit should include:

(i) defining and implementing strategies to develop the Three Rs in basic and applied biomedical research as well as regulatory testing;

(ii) identifying needs and priorities for research required to support the defined strategies, and coordinating research supported by the Commission and Member States;

(iii) coordinating and managing pre-validation and validation studies, and conducting such studies where appropriate;

(iv) providing information and advice on the availability and suitability of alternative methods, to support both scientists and Competent Authorities in the discharge of their duties under the Directive.

42. The EU Centre should be supported by a network of National Centres so as to coordinate research funded from national as well as EU sources. National Centres do not need to be based within laboratories, but should be able to identify suitable facilities for taking forward the recommendations of the EU Centre. National funding for research and validation should be channelled through the Centres.

43. The principal functions of the National Centres would be to:

(i) assist the EU Centre by providing suitably informed national representatives and information on relevant research programmes within their territory;

(ii) cooperate with the EU Centre in coordinating and commissioning research needed to assist the development of alternative methods;

(iii) commission pre-validation and validation studies to be conducted in suitable laboratories within their territory, under the coordination of the EU Centre.

Subsidiarity and Legal Base

Question 9. *Is it appropriate to regulate at the EU level—as opposed to lower tiers of government—in all of the proposed areas? Is the legal base for the proposal adequate in light of the content of the Directive?*

44. It is appropriate to regulate all of the issues covered in the Directive at the EU level, but with the proviso that individual Member States should retain the flexibility to improve upon minimum EU standards.

45. The reasons to regulate animal research and testing at the EU level, rather than solely at the national level, were established in the discussions on subsidiarity in the 1990s. These include the involvement of a trade element, the fact that legislating and enforcing legislation is more efficient at an EU level than at a national level, and compliance with the requirements of the Treaty of Rome, in that it aids the working of the internal market. The Directive already sets out in its discussion of the legal elements how the proposal complies with the subsidiarity principle and the following explanations can be made for this:

— there is internal trade in animals used for scientific purposes and an internal trade in products produced as a result of using animals for scientific purposes, so disparities between Member States should be eliminated;

— enforcement of the measures taken to protect animals used for scientific purposes is better regulated at a EU level due to the internal trade in products and animals;

— data collection of animals used for scientific purposes should be harmonised and collated at a EU level, in order to be able to compare practices within and between Member States;

— application of the 3Rs needs to be driven at an EU level to avoid discrepancies between Member States;

— the internal market would be distorted without minimum EU standards on authorisation and ethical review of the accommodation, care and use of animals for scientific purposes;

— there need to be common standards of education and competence to facilitate free movement of researchers, animal technologists and other relevant staff.

46. Although the original objectives of the European Community make no mention of animal protection, it has always been recognised (within certain limits) as a reason for prohibiting or restricting trade between Member States as under Article 30 of the Treaty. The agreement in 1999 on a Protocol for animal welfare contained two important language changes:

— it gave the first reference in EC legislation (whether normative or otherwise) to animals as *"sentient beings"*, altering the definition of animals;

— it asked for *"full regard to the welfare requirements of animals"*, establishing the need to protect animals as a moral issue rather than purely an economic one.

47. The Directive refers to the Protocol on animal welfare. Although the Protocol is now in place, and always referred to in the recitals of any proposal relevant to animal welfare, the introduction of animal welfare-related legislation at EC level is still based on other objectives within the EC Treaty. This is because there is no specific legal base for animal welfare in the Treaty of Rome (the Protocol is not a legal base).

48. To date, legislation dealing with animal welfare has used as a legal base Article 37 (common agricultural policy), Article 95 (internal market), Article 133 (common commercial policy), Article 175 (the environment) and Article 308 (other EC objectives in the course of the Common Market).

49. The reliance on Article 95 is the appropriate legal base here, as the stated goal of the Directive is to harmonise and level practices such as the breeding, keeping and use of animals for scientific purposes. Article 95 is there to ensure the proper functioning of the internal market. If the Directive did not exist, the internal market on the movement, use and keeping of animals used for scientific purposes and products made through the use of animals would not function effectively.

21 May 2009

Annex 1

USE OF F2+ PRIMATES

There are a number of reports that have a bearing on the capture and use of F2+ primates, including key documents from the European Council, European Commission and national level advisory bodies for example:

- Council of Europe Declaration of Intent concerning animals used for scientific purposes (4.12.1997).
- Council Decision of 23 March 1998 concerning the Conclusion by the Community of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes.
- The European Commission SCAHAW report on "The welfare of non-human primates in research" (2002).
- EFSA: Opinion of the Scientific Panel on Animal Health and Welfare on a request from the Commission related to Aspects of the biology and welfare of animals used for experimental and other scientific purposes (14.11.2005).
- The Animals Procedures Committee, UK (2006).

Relevant sections of these documents are quoted below.

- Council of Europe Declaration of Intent (4.12.1997) concerning animals used for scientific purposes states:

  "*The signatories to this Declaration of Intent …..agreed in collaboration and as appropriate to their competency:*

  — *to encourage initiatives and measures to end the use of wild-caught primates*."

- Council Decision of 23 March 1998 concerning the Conclusion by the Community of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes, states that:

  "*Whereas the use of primates for experimental and other scientific purposes has led to the catching of primates in the wild, and whereas this should be avoided whenever possible in view of the suffering and losses which can occur during catching and transport*;"

- The European Commission SCAHAW report on "The welfare of non-human primates in research" (2002) states:

  "*Breeding and supply*

  14. For as long as the use of primates in research is necessary, only purpose-bred animals should be used. Such purpose breeding should be planned in order to meet the projected research requirements and breeding centres should be accredited (Ch. 8, 12). Only animals of the second or subsequent generation bred in captivity should be accepted as being classified as 'purpose-bred' and supplied for research. Any exceptions should be based on their approval following an ethical review process (Ch. 8)."

- The revised Appendix A of ETS 123 states:

  "*Keeping non-human primates in the laboratory creates a number of problems which are not shared with other commonly used laboratory mammals. Non-human primates are not domesticated, but are wild animals; most are also arboreal. Their wild status means that they are more alert than domesticated species and thus are highly reactive to any unfamiliar and alarming stimuli. Unlike domesticated species, they have not been selected for friendliness to humans and low aggression. Early friendly contact between infants and care-givers will result in a less fearful animal, as the animals learn that familiar humans do not constitute a threat, but the animals will retain most of the attributes of their wild conspecifics.*

  Non-human primates used for scientific research should be captive-bred and, where practicable, reared on site to avoid transport stress. Captive-bred animals are of known age, parentage and health status and have been reared under standardised husbandry practices. Where non-human primates are to be imported they should, whenever possible, be obtained as offspring from established breeding colonies with high welfare and care standards. They should be free from zoonotic diseases. Wild caught animals should only be used in exceptional circumstances as they present health hazards to staff, have unknown histories and are likely to be more afraid of humans. In some instances there can be a significant mortality among the animals at the trapping site and during transfer to the source country holding site."

— EFSA: Opinion of the Scientific Panel on Animal Health and Welfare on a request from the Commission related to Aspects of the biology and welfare of animals used for experimental and other scientific purposes (14.11.2005) states:

"Capturing a species from the wild for use in a laboratory is a major welfare concern and is, therefore, an important criterion for inclusion of the species in Annex 1."

— The UK Animals Procedures Committee in its report on "Acceptance of overseas centres supplying non-human primates to UK laboratories" (2006) states:

"Capture of wild primates for use as breeding stock or for export for use in experiments has been identified as a particular cause of concern because of the additional distress caused to the animals (Prescott 2001, SCAHAW 2002)."

The PSC recognised that it would not be possible to immediately end trapping of wild animals without impacting on supply, but went on to say:

"In order to help discourage the use of wild-caught animals as breeding stock, and support the effort to eliminate early weaning systems (since in general, early-weaned primates do not become competent breeders) the following is required:

— *The UK should move toward a position where it will only accept as 'purpose-bred', animals of the second (F2) or subsequent generations bred in captivity. The PSC recognises that achieving the goal of defining 'purpose bred' animals as F2 or subsequent generations may take time, given recent experience of how this affects breeding performances and general well-being of the colonies. The UK should require any centre that traps from the wild to have a clearly defined strategy to decrease reliance upon wild populations and move to the supply of F2 animals only (for example by gradually decreasing their trapping quota and retaining a significant and increasing proportion of first generation offspring for breeding second-generation stock). The overall progress towards this goal for centres generally should be kept under review by the PSC. Due consideration could be given to other factors, for example, where, as part of their national authorisation to operate, breeders (at the present time) are required to trap a minimum quota of animals. The progress of individual centres should be reviewed by the PSC and the Home Office Inspectorate when assessing a centre for re-acceptance ie at intervals of not more than two years."*

All of the above reports accept that capture of primates from the wild is a major animal welfare concern that should be avoided. There are a number of scientific papers supporting this view that can be referenced on request. There are, in addition, associated issues relating to human health, the health status and quality of animals (and hence quality of science), and conservation of local primate populations, that argue against the continued capture of wild primates, that need to be taken into account.

21 May 2009

Examination of Witnesses

Witnesses: Dr Maggy Jennings, Head, Animal Research Department, and Mr David Bowles, Head of External Affairs Department, RSPCA, examined.

Q142 ***Chairman:*** Good morning and welcome. Thank you very much for finding time to come and help us with our inquiry and also for the written evidence you have previously submitted. It has been very helpful. I have formally to put on the record that this is an evidence-taking session for our inquiry into the use of animals for scientific purposes and research. A transcript will be taken and you will get a copy of it within the next few days. Perhaps you could read through it and correct any errors that have slipped in. The other thing is that we are being webcast, so there is a slim possibility that, somewhere, someone may be listening to what is going on; but I do have to say that we have never received any evidence that that is the case! Would you like to start by making an initial statement or would you prefer to go straight into the question-and-answer session?

Mr Bowles: Perhaps we may introduce ourselves to you, which might give you a little more background as to who we are. My name is David Bowles and I am Head of External Affairs at the RSPCA, which covers our European, political and campaign work, and obviously an important part of our work at the moment is on research animals. The RSPCA has had a long history of working on research animals. Our Research Animal Scientific Department is 30 years old. Dr Maggy Jennings is the head of that department and she will introduce her specific experience in a minute. Previous to that, we have worked for many years on animal experimentation. Even back in the days when the first legislation on animal experimentation was set up in 1876 we worked on that, and we had a large part to play in the 1986 Animal (Scientific Procedures) Act, although fortunately both Maggy and myself are far too young

to have done that ourselves! Maggy will be able to give you her own experience.

Dr Jennings: I do not want to give you a long CV but I thought it would help to put our evidence in context if I gave you some brief, relevant points. I have been at the RSPCA as Head of the Research Animals Department for 20 years. Previous to that I was a research scientist at a BBSRC research institute. I think particularly relevant to this work is that I spent eight years on the Animal Procedures Committee, chaired the Education and Training Sub-committee of the APC, and I am currently a member of the cross-departmental committee on efficient regulation. I was rapporteur to the Technical Expert Working Group on Ethical Review, which was set up to advise the Commission on the revision of the Directive, and a member of the expert working groups for the Council of Europe Husbandry and Care Appendix, which has now become the Annex. I am on the board of NC3Rs in the UK and on ECVAM's Scientific Advisory Committee.

Q143 ***Chairman:*** Thank you very much. It was very useful to know that background, because some of the questions are directly related to your own experience. Can I kick off and start right at the beginning and ask what is the case for a new Directive? Why do we need a new Directive, and what are the main faults with the existing system?

Mr Bowles: There are really three reasons why we need a new Directive. Obviously 86/609—it is self-explanatory—is 23 years old. The European Union has something like 30 different pieces of animal welfare legislation and this is the oldest piece of animal welfare legislation, which has never been reviewed. I think there are two reasons for that. The first is that it never had a review date built into it, and most of the other animal welfare pieces of legislation do have review dates built into them. We are therefore very happy that the new proposal does have that, because it will mean that, instead of waiting a further 23 years, we will hopefully only wait ten years or so before it is reviewed again. I think that it is past its sell-by date and the reasons for that is that people's attitudes have changed enormously. If you look at the recitals in the proposal, there is a lot on animals' intrinsic value and there is a lot on ethics—all of which would probably never have been in the old Directive. Certainly people's attitudes have changed and so it is important to reflect that. Obviously science has also changed enormously, and it is important that that is recognised. Finally, because we have not had any changes for 23 years, what then tends to happen is that Member States do their own thing. You have seen different countries changing their legislation and going higher, the UK being a very good example. I think it is entirely relevant that the Commission has looked at this. It has been a very long process of theirs, looking at this. They started about seven years ago. They have had an extremely thorough process of looking at a Directive and what they want, and I think that they came up with a fairly good proposal. We gave it about seven out of ten when the proposal came up.

Q144 ***Chairman:*** You have made the point, and I think it is a fair one, that Member States have done their own thing to an extent and have gone higher, as in the case of the United Kingdom. Is there any evidence that some Member States have fallen below the level of the Directive?

Mr Bowles: One of the problems with the Directive—and again I will make a comparison with other European animal welfare laws here—is that, with many European animal welfare laws, the Commission has an active implementation role, to check on what is happening with the implementation of the legislation. They do visits to countries to see what is happening on the ground, mainly with farm animal legislation, and then they produce reports which are very transparent; they are available on the website. Unfortunately, with the Animal Experimentation Directive there have been none of those visits; so we literally have not known what the problems have been. That is why, again, we welcome the fact that in the proposal it said that they needed to have specific tasking or visits for this, and we think that will make the process much more transparent.

Chairman: Let us move on to the problem of international competition and leakage.

Q145 ***Viscount Brookeborough:*** In your paragraph 11 you seem to reject the concern of the bioscience community that the Directive as drafted is likely to displace some of the research out of the EU. However, if that research was driven overseas to countries with lower welfare standards, what would be the net impact on animal welfare in your view? I am not sure from paragraph 11 what you have decided is your view on whether it is happening and to what extent.

Dr Jennings: My Lord Chairman, perhaps I could answer that question. The net impact on animal welfare would clearly depend on the standards in the countries that the research is transferred to, and we are not exactly sure which countries those would be. We were rather assuming that it would be countries in eastern Asia like China and Taiwan, because those are the ones that are normally quoted to us. I do have to say that we are seeing increasing interest in animal welfare and in understanding European and US standards in those countries, and David may like to comment further on that. However, we are somewhat puzzled by these sorts of comments, because the pharmaceutical industry is a global industry and already has facilities in countries such as China and

Taiwan. I know of at least one company that has sent a UK vet out to have a look at the facilities and he came back very impressed. It should be within the remit of a global company to ensure that its standards are similar across the board, and a number of companies make proud statements that that is what they try to do; so we would have thought that it should make little difference to the animal welfare standards in industry. As far as academic research is concerned, again the UK major funders—MRC, Wellcome, BBSRC—also make strong statements about the need for high animal welfare standards, the link between high animal welfare and good science, and the importance of issues such as ethical evaluation. Some of them make it clear that they would expect research done in non-UK/EU countries to conform at least to the spirit of the UK legislation. It should also be within the power of research funders, therefore, to ensure that the high standards that they expect in the UK are also applied to the research that the people they fund carry out in other countries. The last point I would make is that the European Community has agreed that it is important to improve current welfare, and there is a widely accepted link between good animal welfare and good science. It does not say much for science and industry if, given that that position has been agreed, they are prepared to go abroad to avoid high standards of welfare. I think that does not say much for what they think of the science, what they think of public opinion, and what they think of high ethical and animal welfare standards.

Q146 ***Viscount Brookeborough:*** I am not quite sure whether you believe that what the companies are saying is correct, about going abroad and the continued use of high standards. When we heard representatives from the Association of the British Pharmaceutical Industry last week they seemed to be quite clear that, if they were taking the business abroad, they would be insisting on the high standards. Otherwise all their research would be corrupted completely. What I am not quite sure of is whether you believe that the Directive, as it has been brought forward now, will push more of that abroad. I am also not quite sure whether you either have evidence or believe that the standards abroad will be as good as they are here—in which case it should not be a problem.
Dr Jennings: I would say that nobody has yet given me clear evidence that the Directive will push standards abroad. There is a lot of anecdote.

Q147 ***Viscount Brookeborough:*** We had it last week, from the Association of the British Pharmaceutical Industry.
Dr Jennings: Fine, but they have not given it to us and, until I have that evidence in front of me, then I am not inclined to believe it.

Q148 ***Viscount Brookeborough:*** I thought that, in the nicest possible way, the RSPCA often went and got evidence about things that it wanted to get evidence about.
Dr Jennings: David may have to answer that question.
Mr Bowles: I think that there are two issues here. The first issue is that, every time we get a piece of European legislation, whether it is on farming or research animals or even on wildlife, the one thing that always happens is that industry says, "This is going to outsource our good standards to somewhere else". I would point to two things that are happening at the moment. The first is that there is an OIE[1] process, which you are probably aware of, that is drawing up global standards for the use of animals in research laboratories. It is true to say that at the moment many of the OIE's 174 countries do not have good legislation or standards, let alone good enforcement of these standards. Once those standards are in place—and I hope that those standards will be agreed at the May 2010 meeting of the OIE—that will give us a very good baseline to make sure that every country is applying the same standards. The second thing I would say is that, as we have already discussed, the UK has one of the highest standards in the EU, indeed in the world. Has that led to leakage of UK science abroad? I have not seen any evidence of that. As Maggy rightly said, you have to try to separate out what tends to be a very knee-jerk reaction in terms of saying, "This will of course lead to leakage of science" and actually look at the facts. The facts are that, as we see it, there is no evidence that this has happened in the past where there have been different standards, and we do not believe that the Directive will lead to that.

Q149 ***Viscount Brookeborough:*** You have no evidence, where pharmaceutical industries have already outsourced it, as to any reduction in standards as a result?
Mr Bowles: No, because, as Maggy has said, they have to abide by the highest standards. Otherwise it will corrupt their research.

Q150 ***Viscount Brookeborough:*** On the basis of animal welfare, therefore, it is not an issue?
Mr Bowles: No.

Q151 ***Viscount Brookeborough:*** What efforts do you make in the world arena, in linking up with other organisations as far as future standards throughout the world?

[1] OIE: the World Organisation for Animal Health.

Mr Bowles: We do quite a lot of work in that and I am responsible for the RSPCA's international programme. We work in something like 30 different countries overseas and we have organisations that we work with in 130 different countries. I have just mentioned the OIE process. We are heavily involved in making sure that the OIE standards, when they are drawn up, are as high as possible, to give us a good baseline. In particular in terms of research animals, we have worked in some nine countries on helping them to improve their standards, improve their enforcement, or translate our materials. One of the things people tend to forget is that there is a lot of good information out there but all of it is in English. For instance, when you go to China the researchers and the government people do not necessarily read English; so we have translated a lot of our good practice guides into Chinese, into Polish, into Ukrainian, for them to use in those particular environments. One of the benefits of that, particularly in Europe, has been that the ethical review process in countries like Poland, Czech Republic and Hungary is as good, if not higher, than in some of the old Member States, partly because they have started from a clean sheet of paper and partly because they have had assistance from groups like us, going out there and teaching them how we do it in the UK.

Chairman: I think it is fair to say that the position of the industry, when we talked to them last week, was yes, they are operating globally; yes, they do take their standards with them; but the attraction of doing work in China and places like that is that the bureaucratic process is not so oppressive. There might be lots of things that are oppressive about China, but not the bureaucracy in terms of getting procedures agreed.

Q152 ***Lord Cameron of Dillington:*** They claimed that to get a licence in this country it took six months, whereas in the United States it took six weeks; and that very often influenced their decisions as to where they actually carried out their studies.

Dr Jennings: There may be other ways of sorting out that problem than merely taking their work abroad.

Q153 ***Lord Brooke of Alverthorpe:*** Tell us how it could be solved, because they were very concerned indeed about this disparity between application time and actually starting the processes here.

Dr Jennings: The Government does have its efficient regulation process, which is looking at issues like this. I think that there are three main problems with the system of authorisation in the UK, which clearly might translate to the EU. There is the actual process of completing a project licence and the difficulty of that—a lack of understanding of exactly what the Home Office requires and, in some cases, just getting down to filling it in. I think that it is a difficult document to fill in. I can understand the concerns, and more guidance on that would be helpful. I think that improving the efficiency of ethical review processes in the UK and how they handle project licences—which is something the RSPCA is working on jointly with the Laboratory Animal Science Association—will help. Also very important is looking at the education and training of prospective project licence-holders in the UK and helping them in how they approach completing project licence applications. There is therefore a package of measures that can improve upon the whole application process and the time that takes.

Chairman: Let us go to Lord Cameron on non-human primates.

Q154 ***Lord Cameron of Dillington:*** This is another area of controversy and possible "leakage"! You in fact would like to see the use of non-human primates phased out completely and the other side, for want of a better word, think that they are quite crucial; although last week the ABPI did admit that there were some experiments that could clearly be held out as being exceptions to that—phased vaccines, and so on—and the Directive has taken a compromise line. I was wondering if you could tell me how convinced you are that an end to non-human primate research would not prevent key research on life-threatening or debilitating clinical conditions in human beings taking place. What are your arguments for wanting to ban them completely?

Dr Jennings: We are not actually asking for an immediate ban. That is because we fully recognise why primates are used. We do not want them to be used; we would like them replaced with the humane alternatives. However, we recognise why it is considered necessary, which is why we are asking for a phase-out. What we would like to see is a more open-minded approach; more acceptance that the use of primates (given the nature of these animals) is a very serious concern; that aiming to end their use is a perfectly legitimate goal; and we would like to see people moving away from a defensive, "There's no way you can do it" answer to questions about ending their use, to a more positive, "Let's see what we would need to do to get to a position where we could do without primates". So we would like to see a greater recognition of the need to replace them and a strategy aimed at doing just that, within all the different scientific areas that they are used. We are not asking for an immediate ban, therefore. Furthermore, we consider that the Directive as it is written would not seriously limit primate research in this country or in the EU, because the scientific community argues that all the research that they currently do is for serious medical conditions. The wording of the Directive adds in the word

"debilitating", which merely means "weakening"; so in our view the current restrictions in the Directive would have no impact on primate use.

Q155 ***Lord Cameron of Dillington:*** What wording would you like to see?
Dr Jennings: We would like to see a clear call for a strategy to replace primates with humane alternatives as early as possible and for industry, the scientific community, regulators, all the stakeholders, to get together to see how they could achieve that goal—but we recognise that it is very difficult.

Q156 ***Lord Cameron of Dillington:*** That could happen outside the Directive itself. What you are asking for is a kind of longer-term position.
Dr Jennings: It could, but I do not know if David would like to comment.
Mr Bowles: You tend to get change happening when you put finite deadlines into legislation. We have seen that very clearly with the Cosmetics Directive, in that you could have a lot of fine words in there but, until there was a deadline included, nothing actually happened in terms of moving away from testing on cosmetics. I think that it is the same with primates. We were fairly happy with the Commission proposal on primates that gave certain deadlines in phasing out wild-caught primates. We were frankly astonished that the European Parliament weakened that. It was one of the main areas that they weakened, and this was the same European Parliament that, two years earlier, had passed a declaration on primates, saying that they wanted an immediate ban on the use of wild-caught primates. It was the same MEPs who, two years later, decided to weaken it. I was reassured when Susanna Louhimies from the European Commission said that was one area the Commission wanted to keep hold of. It is important to state that, if we are looking at drawing up a piece of legislation fit for the 21st century, it has to have some things in there which are fairly bold and fairly revolutionary. I think that the great apes issue and the primate issue are two of those. People understand those issues. They may not understand the ethical review process or the intricacies of the authorisation process, but they understand the issue about great apes and the issue about primates. Do not forget that the proposed legislation is there to achieve two objectives. One is to improve animal welfare and the second is to improve the Common Market position on the use of animals in experiments for companies. If we are going to do that and then refer back to the fact that animals have intrinsic value, where better to start than primates?

Q157 ***Lord Cameron of Dillington:*** Transgenic technology would be one of your solutions, would it? How do you arrive at your solution to end testing?
Dr Jennings: If we had a solution, I think we would be proposing it now; but I think that it would be arrogant in the extreme to think that we could sit here and propose the solution. It needs the input of scientists working on primates; it needs the input of regulators; it needs the input of animal welfare people—but it has to be a collective effort, I think.

Q158 ***Lord Cameron of Dillington:*** So there is a long-term gateway that you want to be closed. That moves on to the second part of my question about second-generation primates. It was put to us last week that it is pretty well impossible to breed enough animals in captivity in order to cater for the needs of the research. To do so under false circumstances or using all sorts of sources, shall we say, might hinder welfare standards. I wondered how you responded to all of that.
Dr Jennings: Those are interesting points. We have felt for a very long time that the capture of wild animals and confining them, either in a laboratory environment or a breeding environment, was a very serious stressor, and that has been echoed in a number of Commission and UK documents. We therefore definitely want to see an end to the capture of wild animals. However, I am not entirely sure what have been suggested as the welfare implications, of maintaining F2 animals. The two things that have been suggested to me are, first, that you would have an excess of male animals and that these would have to be killed as surplus. On that particular issue I did enquire with primate users within the academic research community, and they could not think of any reason why you could not use the surplus males in research. I also looked at the use of primates in the pharmaceutical industry, where I think the main use is repeat dose toxicity studies and safety pharmacology, and I could not see any requirement for an equal number of species or using only females. So again I would have thought that the males would have been moved into a research environment. That was one point. The second point was the issue of keeping more animals in long-term captivity. That is a difficult question but, against that, you have to weigh the serious suffering and stress associated with the capture of wild animals and the effect not just on the individual but also on the family groups that are left behind. In weighing those two things, we would consider that maintaining more animals in captivity, providing that it was a good environment, would be the lesser of those two evils.
Mr Bowles: You have to be very careful saying generically "primates", because there is a lot of difference between breeding marmosets and tamarins. I used to breed marmosets and tamarins and they are quite easy to breed. I also used to manage the breeding of macaques. Again, they were not difficult to breed. I go back to the point I made to

an earlier question: that if you have some challenging deadlines in this, the industry will respond to them.

Q159 ***Chairman:*** I do have to say I am slightly uncomfortable about the idea of killing off surplus males, but that may just be me! Let us take the issue of putting a challenging date in. The critical response to that is that it is really quite irresponsible, because you are putting a date down and then hoping something turns up. It is almost like "20 20 by 2020",[2] sort of thing. Is that not the danger? That you put a date in and, because you do not know now how to get there, you are taking an enormous risk?
Mr Bowles: The danger is that, if you do not put a date in, you have the status quo and nobody is incentivised to do anything. I go back to the Cosmetics Directive, which when it was passed in 1993 had a date that all cosmetic testing on animals would finish by 1998. The Commission looked at that and decided that science had not caught up, and therefore they would give them an additional 11 years. That date has now happened; it is in place; and the companies have had to react to that. Yes, of course, science sometimes takes time; but, if you have the flexibility to do that, I think the only way to get progress is to have dates in there. They challenge people; they focus people's minds; and I think that, if you had a date in there, it would focus the industry's mind very clearly.

Q160 ***Lord Brooke of Alverthorpe:*** Would not the focus be, when you are making future investments, to decide to make them in those countries where they may not have such legislation but will continue not just to keep primates there but to develop facilities with more of them in? Can I read to you some evidence we took last week? "In my own company I can tell you that we are building facilities in Shanghai. Those facilities will focus on cancer research, but in addition to that we have a collaboration with a Chinese institution which is dedicated to construct a specific primate facility. The reason for doing that is largely driven by concerns that we have about the long-term sustainability, given the legislative framework, about investing in that kind of work in Europe." So really they are setting their stall out for the future. If you give them a date they will do it even faster, will they not?
Dr Jennings: It is difficult to answer that question.

Q161 ***Viscount Ullswater:*** But that is realistic, is it not?
Mr Bowles: We come back to the discussion about global standards. I cannot predict what will be in the OIE standards, but I hope that there will be something in there about the improvement of housing standards for primates. There may not be a phase-out of primates but I hope that there will be something quite challenging on primates in there for people. I think countries, once they see that, will then all start to raise their standards. Their standards may still be below the EU standards, but they will all start to balance out. I go back to Maggy's point. We are talking about global companies here that have global CSR policies. I do not think that you can mix and match those global CSR policies to say, "We have one CSR policy for Europe and one for China". I think that a company has to have a global CSR policy, which is, for instance, that they are dedicated to improving animal welfare and giving the best care and attention to the animals, wherever they are.

Q162 ***Lord Brooke of Alverthorpe:*** That may be your wish but the reality is that, as Viscount Ullswater has just stated, in dealing with it they are going to the places where they can continue to use them.
Dr Jennings: If that is what they are doing, it makes nonsense of their corporate social responsibility policies, and we would condemn them for that.
Lord Cameron of Dillington: Not if they are using very high standards. It is an argument on the primate issue here we are talking about, not the standards. The standards are going to be high.

Q163 ***Lord Brooke of Alverthorpe:*** They are high standards, yes.
Mr Bowles: But, for instance, if they are building a primate facility, will it be a primate breeding facility or will they still continue to take primates out of Vietnam or the Philippines? I think that is an important issue. We are talking about several different things here. We have recognised, and Maggy said this, that you need to have a phased-in approach to this. The first thing you need to look at is the issue of wild-caught. How do you get away from wild-caught and are they dealing with that particular issue? The next issue is how do you get away from using primates in totality? We have accepted that it will not happen overnight. However, if companies start to recognise that—and I do not know this particular company in China but, if they are setting up a breeding facility, hopefully they have recognised that they do not want to use wild-caught, because of the welfare problems and because of the ethical issues involved—that would be a good thing.

Q164 ***Viscount Brookeborough:*** Is it not also the standards? Because wild ones do not have the standard for hygiene, and common breeding genes?
Mr Bowles: It is quite strange that the Directive since 1986 has prohibited the use of feral and stray dogs in experimentation, for instance, because of the very point that you have just made, yet we are still using wild-caught primates.

[2] See European Commission Communication COM (2008) 30, of 23 January 2008, as "Europe's climate change opportunity".

Dr Jennings: There are several issues here. One of them is the welfare standards. If the welfare standards are good and you do not have to transport primates across the world in order to use them—so if you have your breeding centre as part of your research facility, whatever country that is in—if the standards are high then, from a welfare point of view, that is fine. The issue is whether that sector of industry, the primate facility sector, operates in Europe or operates in China. That is of less concern to us because we are concerned about animal welfare and the welfare standards that apply.

Q165 ***Chairman:*** I thought that Lord Brooke's argument in quoting that evidence was that, as soon as you put a date in, say a phase-out date, the response of the industry to that will be to move offshore.
Mr Bowles: I am assuming that they have already made this decision before any date was ever discussed. I assume, because these things take so much time to put in place, they made their decision to do that maybe five years ago.
Lord Brooke of Alverthorpe: They have made those decisions for other reasons that we will come to later in the questioning, but they said that this was also happening in relation to the issue about whether they should be continuing experiments with primates or not—that the Chinese were developing facilities to have them available.
Chairman: Let us turn to the scope.

Q166 ***Earl of Dundee:*** We learn that the Directive would widen the scope to include live invertebrate animals of a number of species. What evidence do you think backs up the proposal for this inclusion?
Mr Bowles: I think it is perfectly true that there is evidence on both sides on things like decapods and cephalopods in terms of their sentience. We basically feel that the most important thing is to assess each of those species against a list of indicators to assess their sentience. For instance, can they feel pain? Do they have a nervous system? If you give them analgesics do they respond less to pain? That will give you a very good indication of the capacity of that animal to feel pain and therefore its sentience. This is one of the things that has changed a lot in the 23 years that the Directive has been in place. I think that it is quite valid to say that countries such as New Zealand, earlier in this decade, Austria in 2004 and Norway earlier this year, have all decided that decapods and cephalopods have the ability to feel pain, therefore they have sentience, and they have all put them into their legislation. The RSPCA feel that where there is a benefit of the doubt, that doubt should be given to the animals. That is why we were pleased that those animals have been included in the Commission's proposal. As I said, we already have one EU Member State, Austria, which already has it in their legislation; and I think it is good to try to raise that particular standard by giving a level playing-field.

Q167 ***Earl of Dundee:*** What other parts of the Directive or recommendations from it do you perhaps think may not be sufficiently backed up by scientific evidence?
Mr Bowles: The larval forms issue is obviously one where there is insufficient scientific evidence. Again, whether you decide, as in the proposal, that you make the cut-off point in terms of when the animal has ability to feel pain, that is up for debate. To be honest, I do not think that anyone has the science yet on any of the larval forms to say when that particular cut-off is. However, going back to the UK legislation, it already has requirements on this. They have not seemed to be that onerous in terms of the industry. We have not heard any evidence that they are that onerous. Therefore, why not bring the rest of Europe up to the same level that the UK has?

Q168 ***Earl of Dundee:*** You mention UK legislation in this context. Would you like to talk about the legislation of any other state which is as good as ours or better?
Mr Bowles: I have mentioned New Zealand. As you know, the Animal Welfare Act in the UK does not include non-vertebrates and ASPA, as it stands at the moment, includes only *Octopus vulgaris*. However, the New Zealand Act includes octopus, squid, crab and lobster and, as I said, the Norwegian Act includes decapods and crustaceans. There are not that many, therefore, but we found three pieces of legislation that were above the ones that we presently have—just focusing on scope.

Q169 ***Chairman:*** Does the Directive also include plankton?
Dr Jennings: No. I think you have to be realistic in this. We recognise that with the larval forms of decapods and cephalopods it is difficult to argue that they have the same suffering as adult animals, and that you would have to have a legal cut-off point. We were therefore looking at adult decapods, adult cephalopods, and not looking at planktonic forms.

Q170 ***Chairman:*** You have mentioned crab and lobster.
Dr Jennings: Yes.

Q171 ***Chairman:*** Mussels?
Dr Jennings: No, we are talking about decapods, decapod crustaceans. That would be crabs and lobsters mainly.
Mr Bowles: As far as I am aware, no legislation in the world includes mussels at the moment.

Q172 ***Chairman:*** Any read-across to the catering industry?
Dr Jennings: We would rather that the catering industry humanely killed the crabs and lobsters that people eat, but you have different legislation for different animals. I think that is true across the board, in farming, in research and in companion animals, and we are specifically looking at this particular piece of legislation.
Mr Bowles: I do not know whether you are aware but there is now a device called the CrustaStun, which humanely kills lobsters. That is something the RSPCA was involved in drawing up; so there is now a humane killer for things like lobsters in the food industry, which therefore also recognises that they have the ability to feel pain.
Dr Jennings: As a conclusion from all of this, we would not argue that there is conclusive, scientific evidence that these animals can suffer, but we think that there is sufficient scientific evidence to give them the benefit of the doubt. We think that the consequences of not including them, if they are subsequently proven beyond reasonable doubt to suffer, are worse than the consequences of including them if they are subsequently not shown to have the same capacity to suffer.
Chairman: Let us go on to the severity classifications.

Q173 ***Lord Livsey of Talgarth:*** I note that in your summary of the objectives of the Directive you say, "The UK Animals (Scientific Procedures) Act 1986 should not be compromised in any way by a Directive with lower standards". I am pleased to see that, but it comes as rather a jolt that it was the first piece of legislation I was ever involved in here and I had forgotten that it was 23 years. It is a long time, even in politics. Cosmetics and other controversial matters were very much to the fore in those days and subsequent legislation seems to have got that right. In terms of the severity classifications, the proposal contains a system of severity classifications for procedures, up to "mild", "moderate", "severe" or "non-recovery", which will determine important aspects of the application of the Directive we are considering. However, the criteria for these classifications are to be finalised only after adoption of the Directive. First, do you agree with these classifications?
Dr Jennings: I think that it is ridiculous to agree them after the adoption of the Directive, because so many of the articles within the Directive depend upon them; so that is one point. We prefer the wording in the text of the Directive and the classifications they use to the amendment suggested by the Parliament, without doubt. The wording in the text is fine[3], although we would have split the "moderate" category into two: into "lower moderate" and "upper moderate", because we feel that is too broad. We welcome the Commission's intention to set up a working group to look at the classification system, and we have been invited to be part of that working group.

[3] However 'up to mild' needs to be 'up to *and including* mild'. (RSPCA annotation)

Q174 ***Lord Livsey of Talgarth:*** You make your view pretty clear. You clearly would like to see these agreed within the text of the Directive. However, in relation to the definitions proposed by the European Parliament, amendment 161: from what has been said just now am I correct in thinking that you prefer—and I just want this underlined—what is actually in the Directive already?
Dr Jennings: Yes. I am puzzled by why amendment 161 was put forward, because what the Parliament seems to have done is to take just one system from one country, without an awful lot of thought. Severity classification is in itself difficult. I think that it is difficult to operate in the UK. It is difficult to understand where the different cut-off points are; it needs careful guidance. For a long time we have believed that it would be useful to harmonise severity classification across Europe and we still believe that, but I would not go about it by taking one Member State's system and putting that into the Directive. I think that it requires much more careful thought. If you look at the wording that supports the individual classification in the proposed amendment 161, it is muddled and I think that it would be difficult to interpret. We would rather stick with the principle you have in the current text therefore, and then go with the working group to work out the final details.

Q175 ***Lord Livsey of Talgarth:*** I got the impression, when the pharmaceutical industry were here, that they preferred the wording in 161 to what was in the Directive.
Dr Jennings: Really?

Q176 ***Lord Livsey of Talgarth:*** Why do you think that is?
Dr Jennings: I have no idea.
Lord Livsey of Talgarth: I think I am correct in saying that.
Chairman: I do not think it is a major issue. Can we go on to re-use?

Q177 ***Lord Palmer:*** As things stand at the moment, the proposal under Article 16 would allow an animal already used in a procedure to be used in a further procedure in limited circumstances, all linked to the severity classifications as they stand in Lord Livsey's question. In what circumstances would you consider that the re-use of an animal should be permitted?

Dr Jennings: This is a difficult question. You always have to balance the welfare cost of bringing a naïve animal into a laboratory environment and carrying procedures out on that, and thereby increasing the numbers of animals that you would use, against the welfare cost of repeated procedures on a single animal. I think that balancing is difficult to do. I think that the UK system works well and we would support it. We would like to see the same sorts of principles as we have in the UK within the EU Directive. That means the requirement to authorise re-use in advance through the project licence; using criteria that are thoughtfully and carefully developed by animal care staff and veterinary staff; that re-use should not be authorised if the animal has undergone substantial procedures, which the Directive currently would not allow anyway; that the animal should not have suffered any significant adverse effects and its health and welfare had been returned to normal; and that there is good guidance on interpreting the clause. I understand that the Directive as written, in excluding re-use of animals that have undergone moderate procedures, could result in a considerable increase in animal use in certain areas, and that would concern us. It might seem a strange position for an animal welfare organisation to take, but we would be prepared to look at the idea of animals being used in moderate procedures, depending of course on an appropriate definition of "moderate" and on there being a well-monitored system of control taking into account all of the above provisos.

Q178 ***Lord Palmer:*** But you said earlier, did you not, that you reckon that the "moderate" ought to be split into "semi-moderate" and lower moderate.
Dr Jennings: Yes, I did, but at the moment it is not. Looking at the current Directive, therefore, we would accept re-use of animals that have undergone moderate procedures, in certain circumstances that are carefully controlled. If there was a lower and a higher "moderate", obviously we would have to look at that again.

Q179 ***Viscount Ullswater:*** Is that on the basis of reduction, because otherwise you might have to use double the number of animals?
Dr Jennings: It is partly on the basis of reduction but, even so, that would always have to be balanced against the effect on an individual animal. An individual animal that was having trouble existing long-term in a laboratory environment clearly would not be appropriate for re-use. That is why I think the criteria, and veterinary and animal care control of the criteria, are so important.
Chairman: Let us go on to the issue of the authorisation process and ethical review.

Q180 ***Lord Brooke of Alverthorpe:*** To a degree, this links to the exchanges that we were having earlier about international competition. The joint submission that we received from the bioscience sector, which I was talking about and whose evidence we had last week, suggested an alternative approach to authorisation, based on the principle of notification, for projects containing only mild procedures, and that institutional ethical review should be time-limited for all projects. The bioscience sector argues that a notification process for mild procedures allows rapid progression of projects, while still giving the competent authority the chance to intervene. What is your view of their suggestion?
Dr Jennings: We are extremely concerned about that suggestion. Of all the suggested amendments and suggestions for changing the Directive, it is probably the thing that concerns the RSPCA most. We feel that would be a serious step back in the regulation of animal experiments in the UK. There are a number of points that I would make on that. First, this would be a serious weakening of standards in our view. The research community and the Government, whenever they are challenged on animal experiments, always say proudly that the UK system of licensing and control is good, strict regulation and requires the highest standards. It therefore seems somewhat surprising to me that people are seeking to weaken that legislation.

Q181 ***Lord Brooke of Alverthorpe:*** Could you say what the consequence would be if it was weakened?
Dr Jennings: I think that it is very important for all research, regardless of the level of suffering, to go through a proper system of ethical review and authorisation. There are problems about the category "mild": how you determine "mild"; how you predict and assess adverse effects and whether they really are in the mild category. I think that there is an issue of numbers of animals. For example, you could cannulate a peripheral vein in 100 dogs -that would be a mild procedure, according to the Home Office definition. Or you could carry out a skin irritation study on 1,000 rabbits. That would also come into the definition of "mild". I do not think that the public would accept that that type of experiment should be subject to a less stringent nationally focused authorisation system than any other experiments. I think that it would have serious consequences in terms of public confidence in the legislation, in terms of the attitude to the legislation, and the controls for animals.

Q182 ***Lord Brooke of Alverthorpe:*** More generally, how content are you with the Commission's proposals on ethical review and authorisation?

Dr Jennings: We are very supportive of what they have got. We feel that it is very positive. We support the idea of a central, focused authorisation system and that that should include an ethical evaluation. We are very supportive of the concept of local ethical review processes—or "bodies" as it is called in the Directive—and it is something that the RSPCA has promoted and been involved in for a long time. Good ERPs make a very real difference to animal welfare, to science, to the local culture in research establishments. We sit on a lot of ERPs ourselves and see that happening. However, we also feel it is important to have an overarching national ethics committee, where you can bring issues of public concern; where you can incorporate a wider range of stakeholders and offer different perspectives on things such as the development of transgenic primates and whether that is a permissible use of animals. We therefore think that the proposals are very positive. I suppose the problem is that the text is not terribly well drafted in places, there is inconsistency between articles and it is a little ambiguous. We would have liked to have seen better drafting, therefore.

Q183 ***Lord Brooke of Alverthorpe:*** Would you accept that the level of bureaucracy under the proposals is likely to increase or diminish?
Dr Jennings: I would have thought that for the UK the level of bureaucracy will not increase.

Q184 ***Lord Brooke of Alverthorpe:*** Will it surprise you to learn that the Home Office thinks that it probably will and that most certainly the industry, which gave evidence last week, thinks that it will increase substantially, with costs going up too?
Dr Jennings: It slightly surprises me that the Home Office thinks that. I would be very interested to see what particular aspects they think will increase, and how one could work to avoid any problems that might cause.

Q185 ***Lord Brooke of Alverthorpe:*** I am a little muddled. I thought you started at the beginning with a very positive statement about how you thought changes could be introduced, and were needed with the present practices in the UK. That was when you set out your three points.
Dr Jennings: Oh, yes, without doubt.

Q186 ***Lord Brooke of Alverthorpe:*** I listened very carefully to those. I also listened very carefully to your CV and where you are involved with the Better Regulation review. I hear the Home Office concede when they came before us that they believe there are areas in which there can be improved operations. I hear evidence last week from the pharmaceutical industry itself that they believe a change is required but it is very difficult to move. You are in favour of change. Why is there an impasse then in moving forward?
Dr Jennings: To answer that question I need to know where the impasse was and exactly which piece of the bureaucracy was causing the problem. I think that the Home Office efficient regulation task force is trying to sort these things out. The three points I made about improving ethical review, improving the project licence application process and improving training for licensees—I think that all those will have a very positive impact and are extremely important. We would support all of those. What I do not quite understand is why you feel there is a problem between that and my answer on the European legislation.

Q187 ***Lord Brooke of Alverthorpe:*** Because both of the parties I have just mentioned maintain that the European legislation will further increase the amount of bureaucracy.
Dr Jennings: Again, I would need to talk to the Home Office and see exactly what part of that bureaucracy would be increased. Often it is how these things are implemented in practice, rather than the actual legislation itself. We certainly are not trying to increase bureaucracy for its own sake. One would look for ways of facilitating the implementation of the Directive, so that welfare, science, ethics and public acceptability would benefit, rather than causing unnecessary bureaucracy.
Mr Bowles: Perhaps I could add one small point on the ethical review process. This is one area where we have seen an enormous change happening in the last few years. We have seen a cascade effect coming out of countries like the UK, which was one of the first countries to do the process, and into many other countries—even in the EU. I mentioned earlier in the evidence that the ethical review process in many of the new Member States is superior to that in the old Member States. This is also having a cascade effect on the candidate countries. We work a lot in Turkey, Croatia and Macedonia, and they see the way things are going. They are already setting up these ethical review processes. We are also working in Korea, Taiwan and other countries, to try to get them to do the same things. Hopefully this will be a real improvement, because not only does it put in a good standard and check/balance process; also, importantly, it opens up transparency. When you get people from animal welfare organisations, industry and other experts in the same room discussing this, I think that can only be good—to get everybody to understand their different points of view.
Lord Brooke of Alverthorpe: I think that a common view has been held on that, My Lord Chairman, in the evidence put to us.
Chairman: I think that is right. Let us move on now to care and accommodation standards.

Q188 ***Earl of Arran:*** We have been in and out of this already. You support a compromise to the current proposal but worry that the provisions might not be tough enough. To expand on that from the point of view of your concerns there are two questions. First, on what grounds is it possible to demonstrate the animal welfare benefits to be derived from the proposed standards? Secondly, do you really think that these standards could readily be implemented in the UK? Surely is there not a risk that such research work might leak to other parts of the world with inferior standards?
Dr Jennings: We have covered the latter part of that question quite a lot. Going back to whether it is possible to demonstrate the benefits of animal welfare standards, what I would say is that the standards we now see in the Annex were taken directly from the Council of Europe Appendix. Those standards were put together over an eight-year period and involved experts in animal welfare of each of the species in question from all of the main stakeholder groups. We therefore had representatives from the Home Office in the UK who were expert in husbandry and care; we had animal breeders; we had people from user establishments in industry and academia; and we had people from animal welfare organisations, including myself and other people from the RSPCA. The decision was taken by those experts to base the standards that they put forward on information from the scientific literature, and I know that very thorough scientific reviews were done. The second point that the standards were based on was the expertise of the people around the table with regard to current good practice. I was on the rodents and rabbits group. We went to rodent breeders and had a look at hamster accommodation and mice and rat accommodation, animals in different-sized cages, to look at what you could provide for them. So it was information from the scientific literature; information on best practice from those people who were keeping animals; and factored into that were the constraints that there would be on keeping animals in a laboratory environment and the economic factors. Of course, once the expert working groups had put those standards together, they were then debated extensively within the Council of Europe multinational consultation process with input from experts from all of the Member States. I think that you therefore came out with a pretty good compromise of what those groups of experts thought was best for animals at the time. We would always push further for animal welfare, and that is why I said we accepted that it is a compromise. We have stuck with the agreed compromise position because we felt it was the right thing to do. I hope that has answered your question about the welfare. As far as whether they could be implemented in the UK, I felt sure that they could be. One of the reasons for that was that the Home Office were very assiduous in the consultation they did of UK breeders and users before the standards were accepted. I know they did that conscientiously and well and, if there were problems, I am puzzled that they were not raised at that point. Furthermore, the UK codes of practice are over 20 years old and for quite some time it has been signalled that eventually they would be updated; so people have seen this coming. Bear in mind that the whole process of revising the Appendix started in 1998. That is a very long time for people to have been thinking about what they need to do. Our main concern with that Annex, therefore, is that it only contains the tables from the Council of Europe Appendix and we believe that it should include much more of the text, which explains the basis for the standards and how people might implement them in practice.

Q189 ***Earl of Arran:*** If what I therefore pick up from your answer is that these are passing concerns rather than grave concerns, would I be getting the wrong impression?
Dr Jennings: No, I think we would support the standards as being what has been agreed as current good practice—a compromise position but we support it. We were part of it and so we would continue to support it. Our problem is that all the explanatory text has been omitted, which we felt was an important part.

Q190 ***Chairman:*** Could I ask what is the status? The Council of Europe Appendix that all this comes from—what is it?
Dr Jennings: It is not legally binding.

Q191 ***Chairman:*** The requirements in there, the targets in there, were aspirational, were they?
Dr Jennings: I never viewed them as aspirational.
Mr Bowles: When you have a process of negotiation over many years, you do not tend to have aspirational standards at the end; you tend to have the lowest common denominator at the end. I think that is what Maggy was saying has happened with that process.

Q192 ***Viscount Brookeborough:*** Just to look at the accommodation standards in comparative terms—how do they compare with pet shops and private ownership of animals and any regulations that there are? Because when we went to the University of London I was really impressed by the amount of room that they had. Does it compare, or are there any regulations for having private pets or pet shop accommodation?
Mr Bowles: The Government at the moment, as you are probably aware, is drawing up its position on primates under a primate code under the Animal

Welfare Act. As the RSPCA, we have been arguing very strongly that there should be certain restrictions on what primates people can have as pets. Also, there should be some very strict guidelines in terms of accommodation and in terms of what information they get from a pet shop, if they decide to have a pet primate. Pet primates is something that we are very concerned about. The evidence seems to show that there is an increasing number of primates being kept at pets and we are concerned that many people do not have the expertise to deal with that. One other crossover area is obviously zoos. We have the Zoo Licensing Act in the UK which is now nearly 30 years old and that has some fairly good specific housing and care standards on primates. I would not be able to give you an exact comparison between a laboratory cage and a zoo cage but I would imagine for many zoos the accommodation is probably better in terms of enrichment.

Q193 ***Viscount Brookeborough:*** What about mice and rats?
Mr Bowles: Zoos do not tend to keep mice and rats.

Q194 ***Viscount Brookeborough:*** In pet shops especially with the mice and rats and hamsters, they seem to have reasonable room.
Dr Jennings: You see all sorts of elaborate cages.
Viscount Brookeborough: I was just wondering—
Chairman: Intriguing as pet shops are I do not think it is relevant.

Q195 ***Viscount Brookeborough:*** But that is the way the public looks at it and if they see them in acceptable circumstances they are then maybe led to believe that in these other experimental circumstances it is good.
Mr Bowles: One of the issues that we have been looking at is not necessarily space but also enrichment. There is a real problem with giving enrichment because of hygiene levels and things like that in laboratories whereas obviously in zoos there is now a recognition that if you want a healthy and well-adjusted primate particularly you have to give it good enrichment.
Dr Jennings: Could I just say that I do think that the research community in the UK does very well with its husbandry and care standards. We have seen great improvements over the years and I think we do operate to a good standard in this country.

Q196 ***Lord Palmer:*** Could I ask a quick supplementary? Has this subject always been under the domain of the Home Office or did it years ago come under the Department of Agriculture?
Mr Bowles: You have probably got a great deal more experience than we have in this room but as far as we can remember it has always been under the Home Office.

Q197 ***Lord Palmer:*** In your view is that the right Department?
Dr Jennings: It is difficult to imagine it not being the Home Office.

Q198 ***Lord Palmer:*** Defra presumably would be an alternative?
Mr Bowles: There have been discussions on moving it across to Defra at certain stages and, you are right, Defra would be an alternative, but the Home Office has a huge amount of experience on this and I know that Defra and the Home Office do talk about animal welfare issues, so hopefully we get good crossover, like we were just talking about with the primates issue where you have Defra introducing regulations for primates as pets and the Home Office introducing them for laboratory use. I think it is important we get good communication between different departments when responsibilities fall between different departments.
Dr Jennings: I think one of the issues is that the Home Office does not actually fund any research so it is independent, and Defra actually does, and so you would need it in an independent government department, which I think is important.
Chairman: OK, alternatives and Lord Ullswater?

Q199 ***Viscount Ullswater:*** The Commission maintain that the 3Rs principles of replacement, reduction and refinement lie at the heart of their proposal, with which I think you concur, but you consider that the proposal is drafted in a way that is insufficient, and I think we went into some of the areas of the deadlines and things like that. You also propose as a solution to expand the role of the existing European Centre for the Validation of Alternative Methods. We know that the European Parliament also took the same position. Could you expand a little bit on the comments that you make in your paper, outlining how you see the role of the ECVAM changing and how national centres would work with those European centres and how that network would assist the research community to develop alternative methods?
Mr Bowles: As you all appreciate, this year is the 50th anniversary of the 3Rs and it is quite interesting that 86/609 almost falls exactly in the middle of that 50-year period. The language in 86/609 is quite similar in parts to the language in the present proposals, that Member States should try and work towards the 3Rs—replacing, refining and reducing the use of

animals—but the key thing to look at then is how are you going to actually implement that, how are you actually going to make that happen. If you look at what has happened in the last 23 years with 86/609, we were going through a process of reduction in the use of animals in Europe and then it suddenly went up again, mainly because of the GM issue, but the trend is now going up rather than going down so you could argue that the 3Rs policy in 86/609 had very little effect in terms of that. Then you have to look at why did it have very little effect. ECVAM was set up in 1992 so it is 17 years old. What they have tended to focus on in these 17 years is just one of the 3Rs which is replacement, because their work has been all about validation of alternatives. That tends to look at just one very small area of the use of animals which tends to be in toxicity testing. We think probably about eight per cent of the animals used in the EU are on toxicity testing. What ECVAM has been doing for the last 17 years is looking at trying to replace—just one of the 3Rs—animals for eight per cent of the experimentation. It is not surprising therefore that the number of animals being used in experiments continues to rise. The key thing is how do you reverse that. What we have suggested is we certainly support what is in the Commission proposal about national centres although we do not necessarily believe that those centres should just be in laboratories; they could be anywhere. What you need to do is get all 27 Member countries and the expertise and the scientists in those countries working together to actually think of ways of reducing, refining and replacing. To do that you have got to have a central co-ordinating body, and we think ECVAM would fit that role very nicely. So you would have all the national centres in the 27 countries beavering away and giving ideas, and you would have ECVAM at the centre of the web doing the strategy and getting the information back from those centres and then saying how they want to actually progress that in the future. I think that is one of the ways that hopefully you can actually get the 3Rs implemented and translate the very good language in the Directive to let us all do the 3Rs, but at the moment I am afraid I think a lot of lip service has been paid to that. What you have got to do is to get concrete action happening as a result of that. That is why we have proposed ECVAM in that particular role. One of the good things that we believe happened in the Parliament discussions was that they accepted that, and we were really pleased that the parliamentarians focused a lot on the 3Rs. It is very, very important to them. They wanted to have a better role for ECVAM, they wanted to have more funding going into the 3Rs, and they also wanted to look at other issues such as biobanks. All of those things together provide us with some really good concrete examples of how we can translate the nice words about using the 3Rs into actual action.

Q200 ***Viscount Ullswater:*** On another related topic, what is your view about revalidation of scientific procedures which produce a drug in one country and then when it is imported into the EU it has to be revalidated with further use of animals? I suppose it is important to make certain that it does what it says on the tin but what is your view about that?
Dr Jennings: Just that I think animals would be better served by greater harmonisation of standards and acceptance of data between countries.

Q201 ***Viscount Ullswater:*** So that is a data-sharing issue?
Dr Jennings: It is not just data-sharing; it is data acceptance so, for example, if vaccines are tested in a particular country and they are authorised for marketing there, you would want the UK to accept that authorisation for marketing rather than requiring its own set of tests. I think the issues are harmonisation of standards and greater acceptance of other countries' data.

Q202 ***Viscount Ullswater:*** Does the Directive really focus on that?
Mr Bowles: Again I think the Directive has very fine words on data-sharing, and that is great, but then you have to look at what lies underneath that, how are we actually going to do that and I think in that respect it falls short because it does not actually say what the steps are to actually achieve that, and I think that is going to be a real challenge. I know you have discussed that in some of your evidence sessions with other people as to how they are going to do that.
Dr Jennings: Also data-sharing will not be the only answer. The Directive cannot provide all the answers, so issues such as acceptance of data for vaccines, or whatever, and harmonisation will probably be dealt with by other Directives and in other fora. You cannot expect this one to do everything. The important thing would be for the principles within the animal experimentation Directive to be co-ordinated with other Directives.
Viscount Ullswater: I accept that.

Q203 ***Lord Brooke of Alverthorpe:*** On the same subject, you say the key to replacing animals is adoption and adaptation of new technologies. Could you develop that a bit further for us, please?
Dr Jennings: Probably with difficulty since it is not my area of expertise. We have a specialist on alternatives and particularly toxicology within the department and it is his particular field of interest. I do not think I should pretend to try and have the expertise to answer that here but I could always provide additional information later.

Q204 ***Lord Brooke of Alverthorpe:*** Could you say then if you have, in the course of the consultations with the Commission on the development of this particular Directive, put in your views—
Mr Bowles: Yes!

Q205 ***Lord Brooke of Alverthorpe:*** —on the new technologies that should be used and whether in fact they have been heard and whether there has been any move to translate any of that into words in the Directive?
Dr Jennings: We have put forward views on general principles but I do think that one has to be careful about pretending to be an expert in everything. With a lot of these issues we would actually go to experts in the field, to discuss them, to develop ways forward, and to enable us to contribute further, and that of course requires time and a dedicated programme of work to do.
Mr Bowles: If it would be helpful for you we can go back and give you some information on the new technologies.

Q206 ***Viscount Brookeborough:*** Could I ask you very quickly about data-sharing, I think you said that some countries do not accept data from other countries. However, most of this data comes from the big pharmaceuticals. Is data produced and then tagged with a national identity tag so that for instance, if Glaxo, say, were operating in China, would the data that the company obtained through experimentation in China have a different status from data obtained in this country?
Dr Jennings: I think it depends on the sort of data you are talking about. What I was actually thinking about was not so much company dependent data, it was more in relation to health and safety in the UK and the requirements of government departments, for example whether a vaccine that was tested in, say, Belgium would be accepted in the UK without the need for further testing.

Q207 ***Chairman:*** I think that is it. Just before we close is there anything that you think that we ought to hear that we have not heard or any final points that you would like to make?
Mr Bowles: No, I think you have been extremely thorough and thank you very much for inviting us in to hear our evidence. I wish you luck in producing your report!
Chairman: Thank you.

WEDNESDAY 24 JUNE 2009

Present	Arran, E	Dundee, E
	Brooke of Alverthorpe, L (Chairman)	Livsey of Talgarth, L
	Caithness, E	Palmer, L
	Cameron of Dillington, L	Sharp of Guildford, B

Examination of Witnesses

Witnesses: SIR MARK WALPORT, Director, Wellcome Trust; SIR LESZEK BORYSIEWICZ, Chief Executive, Medical Research Council; and PROFESSOR MAX HEADLEY, University of Bristol, representing the UK Bioscience Federation, examined.

Q208 ***Chairman:*** Good morning, gentlemen. Thank you for your joint evidence which you submitted to us in advance. The session has been arranged to take formal evidence for the Committee's inquiry into the proposed revision of the Directive on the protection of animals used for scientific purposes. A transcript of the evidence will be taken and you will have an opportunity within a few days to look at it and to make any corrections, if any are necessary. I should also mention that the session will be webcast, but not broadcast on television. I wonder if you would like to start by introducing yourselves and also if there is any additional statement you might wish to make, supplementing the written evidence you have put in before we get to the questions.

Sir Leszek Borysiewicz: My name is Sir Leszek Borysiewicz and I am Chief Executive of the Medical Research Council. I am here wearing three hats, I believe. The first of these is as Chief Executive of the MRC, where we spend about £600 million a year on biomedical science and about 20 per cent of the projects involve the use of animals. We therefore have a real interest in this particular issue. Secondly, I house and am charged with financially supporting NC3Rs, as the organisation that sits within the MRC Head Office, supported in large part by the MRC. We also scrutinise the performance of that organisation and ensure that its findings are brought into good scientific practice within the projects that the MRC itself supports. The third element that I am involved in is that I am Vice-President of EUROHORCs, an organisation you may not be aware of but it is the organisation in Europe that represents all of the national funding agencies that are publicly funded, which in essence accounts for 85 per cent of all European science funding, as opposed to the nine per cent that is funded through the Commission. This is therefore an international organisation. I am also the United Kingdom representative on the Council of the European Science Foundation and the European Council of Medical Research Councils; as well as coupling that as the representative for the international and European agendas on behalf of all research councils in the UK. It is this last aspect that I would particularly like to address. First, we are all supportive that the Directive needs to be reconsidered, because of the period of time that has passed. I am particularly pleased, as I think are virtually all the organisations, with the higher prominence given to the 3Rs in this activity. However, the point that I would like to make from the heads of European research councils—it is available on the website and I can furnish additional information—is that I was mandated as Vice-President of that organisation to seek the advice of all the major member countries in Europe as to their national funding bodies' opinions in relationship to this particular documentation. There are 36 organisations enshrined within EUROHORCs from 24 countries. We received responses to our suggestions in relation to 19 out of the 36 organisations, representing 15 countries. The major concerns that we identified as an organisation were in relationship to non-human primates; the severity levels; the restrictions on re-use; the extension of scope to invertebrates; and particularly the care and accommodation issues that are there. In summary—again, I can provide further detail—19 out of 19 respondents agreed that there were significant problems in relationship to security, to severity levels, the extension of scope to invertebrates, and particularly the care and accommodation standards. In other words, there was no agreement with the proposal as it was placed before the European Parliament. Eighteen out of 19 wanted to distance themselves entirely from the proposals around non-human primates, in view of the impact it would make on the science programmes in Europe, and 17 out of 19 were opposed to the issues on restrictions proposed on re-use. In addition, eight out of 15 countries were convinced that their governments would follow the line that these organisations are proposing directly to their governments. In France, Germany, Poland and Sweden, the views of the relevant councils would be the views expressed by those member countries in considering this documentation. The point that I would therefore like to make to the Committee is that the views we

expressed in our joint statement are views that are supremely and very widely held by all research organisations that utilise animals right across the European Union, and the UK's position is not an isolated one in this context.

Sir Mark Walport: My name is Mark Walport. I am the Director of the Wellcome Trust and have been so since 2003. The Wellcome Trust funds approximately £600 million of medical research each year. To put that in context, approximately 30 per cent of the grants that we award involve some animal research. The vast majority of that animal research is in small rodents, particularly mice. Overall, as I am sure you will have heard from others, non-human primates account for less than 0.2 per cent of animal research, though an extremely important component of that—as I am sure we will come back to later. I agree entirely with what Sir Les Borysiewicz has said; in particular, I would like to emphasise that the response to this Directive has been very consistent, not only from the nationally funded research councils but also from the charity sector and also the industry sector. We all support conducting animal research to the highest possible standard. Indeed, again as you will have heard from others, the UK has the highest standards of animal research. I think that we all recognise that the Directive is out of date and does need to be brought up to date. However, my final comment at this stage is to say that more bureaucracy does not equate to better standards of animal care, and I think that there is considerable confusion between the two in the way this Directive has been put together.

Professor Headley: My name is Professor Max Headley. I am a veterinary surgeon by training and a professor of physiology at the University of Bristol. Over my career, I have held all the different roles that are required under the Animals (Scientific Procedures) Act, except that of being a Home Office inspector; so I come as a doer across the board. I am here representing the Bioscience Federation, which increasingly is representing all the different sectors of bioscience across the UK, from academia through to the funding agencies, patient groups and, increasingly, industry. I would like to support what Mark Walport has just said: that there is a remarkable degree of unanimity across the sector in terms of our approach to the legislation that has been put in front of us.

Q209 ***Chairman:*** You say 19 out of 36 organisations or representative bodies were approached. Could you give some indication of what kind of bodies did not respond and what kind of countries they represent?

Sir Leszek Borysiewicz: I will group them in two and I will certainly make the specific evidence available to you. They fell into two groups: those research bodies which primarily funded physical sciences, like CNRS in France. In some countries, particularly France, one body, Inserm, is charged with responding on behalf of all French funding agencies, therefore the others did not respond. There are one or two smaller countries like Slovenia, Slovakia and others, which did not respond to our request for information around this area; but the responses covered countries as diverse as Hungary through to Portugal at the other extreme of Europe, in terms of the views that were expressed. As I said, I could make available to you the complete list or I could read that list out, if you would like me to.

Q210 ***Chairman:*** You have covered your concerns there on the non-human primates, on the alleged growth of bureaucracy and the severity of definitions as well, I think.

Sir Leszek Borysiewicz: Yes.

Q211 ***Chairman:*** What about data-sharing? It is an issue that has been drawn to our attention.

Sir Mark Walport: The first thing to say is that research funders as a whole are very strong supporters of the fact that research is not completed until it is published. We have a grant condition that says that, within six months of publication of papers from the research we fund, all publications must be made available on the internet to anyone who wants them; so the scientific community works on the basis of sharing data. Again, the issue is proportionality. Just because data is shared, it does not mean that it is necessarily useful data. What we support, therefore, is data to be shared of properly completed research. The idea that every piece of data about every animal experiment should be made available would neither improve animal welfare nor would it realistically increase transparency. I think that one has to get behind the issues around data-sharing. One of the allegations that has been made is that there is a great deal of duplication of work. The reality is that that is not the case. When we make funding decisions, part of the peer review process actually says whether there is any evidence that the work has been duplicated or not. We do not fund duplicated work. The costs of research are high and therefore it is not in the interests of researchers to do it. Equally, it is not in the interests of industry to duplicate the work needlessly. I think that this is therefore trying to crack a problem that does not really exist. The other thing to say is that some duplication is appropriate. Science advances on the basis that people make observations that can be verified; so from time to time things are repeated. That is deliberate and it is either to confirm or refute important findings. The answer, therefore, is that the general principle of data-sharing is one that we support, but we do not support data-sharing as an unalloyed good, as it were. One has to recognise that there is work that is done in industry which is competitive, which has to be finished properly and

the intellectual property protected, before it is made public.

Q212 ***Chairman:*** There is also the argument, from people who are concerned about the numbers of animals used in experiments, that there are many experiments that take place which never reach the point where there is any published report on what has happened because there is no outturn which is of public value, and these do not surface in any way, to be counted in terms of the number of animals involved.
Sir Mark Walport: That is not really the case as far as research funders are concerned. When we make a grant to someone which involves animal research, that is expensive research. It would be a very disappointing outcome if there were no published outcome. It would not be good for scientists in terms of their future prospects of getting grants. People do work very carefully with the aim to get it published. I therefore think that there is a minority of animal work, as it were, that is not published because it does not reach any useful conclusion.

Q213 ***Chairman:*** To what extent have differences in the way the 1986 Directive has been applied across Europe had an impact on the academic research sector?
Professor Headley: There have been and continue to be significant problems with the implementation of ASPA, as it is referred to colloquially—the Animals (Scientific Procedures) Act. It is very restrictive and that causes enormous frustration. If you are doing an experiment today as an innovative scientist, you want to be able to modify in the light of today's experiment what you do tomorrow. Not to be able to do so without having to go through the application procedure for amendments and obtaining appropriate approval to do so causes enormous delays. It is one of the reasons why people are increasingly going abroad, to collaborate and do their animal-based research abroad rather than in this country. That is largely because of the level of stipulation of detail that has been required since the 1986 Act came in, although that has increased progressively over the first ten years of the operation of the Act. I am happy to say that, over the last year or two, the Home Office has started to reverse that trend and is now tending to reduce the amount of information that is required in licences, which allows the scientists a little more flexibility. That has not gone far enough, however, and there is still a great reluctance to engage in risk-based assessment, the controls should be greater for those procedures that are more likely to cause an animal suffering than those procedures that are not likely to. To take the example of a so-called non-recovery experiment—one that is undertaken exclusively under anaesthesia with no recovery at the end—it seems inappropriate to demand the same level of bureaucratic control for that situation as for more serious procedures that will cause significant welfare deficit. We therefore do still need to have a greater degree of proportionality in the system than we have currently. So, yes, I would argue that there have been and continue to be significant problems with the implementation of the 1986 Act.

Q214 ***Chairman:*** Could you say something about the German position of academia? As I understood it—and I asked some questions of the Commission about this and they were not themselves able to give us an immediate example—we had been led to believe that the 1986 Directive did not apply to German academic research.
Sir Leszek Borysiewicz: That is the position as I understand it in Germany at the present time, but the DFG, the *Deutsche Forschungsgemeinschaft* organisation, has engaged with us as EUROHORCs, and part of the evidence that it has provided is the impact that this would have on research in Germany as well; so they are engaged with the process. However, as I understand it, formerly the 1986 Directive did not apply to academic research in Germany.
Professor Headley: I think it is true that they all have controls; the difficulty in understanding it is that it is based on the *Länder*, the states. They vary very considerably according to, in simple terms, the balance of political parties in the local parliament. The political influence on the decision-making process on animal research is therefore quite heavy.
Sir Leszek Borysiewicz: We should not run away with the view here that the standards therefore applied in Germany are any the less stringent. I think it is true to say that many of the *Länder* have far more stringent requirements than the 1986 Directive. It is very important therefore that this is not counted as a negative against those investigators working in Germany, who work to very high standards by and large. That is very clear in the responses that we have received from DFG and the Max Planck Society.

Q215 ***Earl of Caithness:*** Professor Headley, you have made it clear that the Home Office have gold-plated the European Directive of 1986, and what you have said about Germany is interesting. There are two countries that have ratcheted it up above the EU level. What about the other countries? Have the other major players, or are we facing huge discrepancies across Europe?
Professor Headley: Yes, we are facing considerable discrepancies and therefore there is considerable export of animal research, not just to non-EU countries but also to Europe. There is much more flexibility in quite a number of EU countries, including some states in Germany, than there is in the

UK. So, yes, we do not have a level playing-field at the moment, and that is one of the advantages that we see in terms of the potential revision of the Directive.
Sir Leszek Borysiewicz: This is precisely the view across all of the funders in Europe. While we all agree that a revision of the Directive is necessary, we have had new Member States coming into the European Union, some of which perhaps do not have as stringent requirements in this area. Ensuring that they are up to speed, to ensure that we have uniformity of view, is considered to be generally a good. What is important is that that is reached through appropriate debate and discussion over a period of time, to ensure that this very important area is covered right across the board. However, there is no disagreement between any of the countries that this does need revision at this point.
Chairman: Professor Headley has just referred to considerable export of animal experimentation, so I think that we will move on to talk with Lord Livsey about international competition.

Q216 ***Lord Livsey of Talgarth:*** On 10 June, Professor Hammond told us that the UK's academic base is "as good as anywhere in the world" but he also said, "It is under threat—we are seeing migration of skills out of the UK". Your written submission stresses the need to ensure that the UK's and the EU's "brightest and best scientists have sufficient incentives to remain within the EU". What evidence is there of a brain drain out of the UK to other parts of the world?
Sir Mark Walport: I can comment on that in relation to non-human primate work, where a combination of costs and regulation has meant that there is a significant decrease in the amount of neuroscience that involves non-human primates. I think that, increasingly, youngsters who are looking to a career in neuroscience will look to the States as the place that can provide that. In the context of rodent research, there is no doubt that the UK is in the world forefront of research involving rodents. None of us dispute the fact that this work has to be done to the highest standards across the board, and I think that we have a model that works very well. One of the benefits of the EU Directive if got right, and it is far from right at the moment, would be, for example, the incorporation of ethical review. The issue is much more that people make judgments about the quality, appropriateness and the standards of research, rather than trying to write down the precise letter of what is and is not allowed; because then you get into enormous bureaucratic knots. The issue for the UK is to make sure that the processes run smoothly and rapidly. That is the issue. I do not think that researchers mind the fact—in fact they applaud the fact—that research is well done and well judged; but there is a duty on the bureaucracy to work efficiently, and I think that has been one of the challenges. We are less qualified to speak for industry; they can speak for themselves. However, as regards the decisions about where industry locates its R&D—which are absolutely crucial to the economy of the UK since the pharmaceutical industry is one of the major economic platforms in the UK—they look at the bureaucracy around animal research and they make judgments, which could be harmful to the UK. In terms of an academic brain drain, this is not happening on a large scale but there is no doubt that people are making decisions, particularly if they want to work on primates. However, there are very significant threats in the Directive about imposing time lines and bureaucracy, which actually will not improve animal welfare.
Sir Leszek Borysiewicz: Regarding the issues here in relation to species other than primates, I think the evidence is very patchy and there is very little evidence that regulation is playing a significant part. In relation to primates, a very eminent journal has already quoted the issues about people emigrating to the United States. I had the privilege recently of being in Shanghai and having some discussions, probably with the very centre that was mentioned in the evidence previously provided. There are issues that some countries are using their position in relation to primate research as a way of attracting industry away from the UK. However, as my colleague Mark has said, the real issue here is that all investigators want to work to the highest possible standards. It is not about dropping standards; it is about making sure that the bureaucracy is appropriate to the work that is being done. Clearly, in some parts of the world where high standards are also in place, it is easier to conduct some of this work than it is in the UK. I am very concerned that, for example, the expertise we are likely to lose particularly in the primate area. Young staff numbers training in these disciplines in the United Kingdom is falling, as is the use of primates for particular procedures in the UK; whereas the evidence from the United States is that it is static or growing slightly. This is very important to maintaining the UK's competitiveness for the future.
Professor Headley: We should be mindful that we are talking about two different things. One is migration of people, lock, stock and barrel. The other is people based in the UK but doing their animal-based research, or some of it, abroad. From my perspective, I see that as the bigger problem or, shall we say, the more extensive problem; because it then starts to lose the skills base which the ABPI and others have emphasised in recent years is severely lacking in this country. If we start to export the work, we will simply fall further behind on that score. Getting evidence of that is quite tricky. That is because few of the people who do this are willing to stand up and be counted, because they still have animal operations in the UK. They are nervous about the way that the Home Office

inspectorate would respond to the fact that they are starting to do some work abroad. I have asked repeatedly, through the Bioscience Federation, for people to stand up and be counted and to give us examples. Although I know of many cases ad hoc, it is quite difficult to collect the evidence.

Q217 ***Chairman:*** So in a sense it is being outsourced?
Professor Headley: It is being done by collaboration. It depends what you call outsourcing. It is not so much that you say, "Go and do this for me" but "Let's do it together, but I'll do it in your lab rather than you doing it in my lab".

Q218 ***Lord Livsey of Talgarth:*** Clearly this is a very big subject. If one factored into this an article in *Nature* published in October which says "Made in China?" it goes on to say that the companies see opportunities abroad and that "The combination of desperation outside China and promise within has convinced almost every big pharmaceutical player, including Roche, Novartis, GlaxoSmithKline, Eli Lilly and Pfizer, to collectively invest hundreds of millions of US dollars into research operations there . . . ." That clearly must be a factor which we cannot ignore. You have given a lot of causes of migration. We are very interested in what evidence there is that controls over the use of animals in scientific procedures are at all a significant factor. In particular, are there scientific procedures which cannot be done in the UK now, or which could not be done under the revised Directive, which UK scientists would take abroad?
Sir Leszek Borysiewicz: I think that there are several issues here. What is very difficult is to tease out the various incentives that countries like China and India are now putting to scientists in order to recruit them to work in China. The attractiveness of China certainly to academics is that they are providing facilities that are second to none. Many of those are being built at cost, with very little cost to utilise the facilities; so there is widespread subsidy in order to attract that kind of business into China. The animals are very often treated to very high standards in many parts of that country, certainly the ones that I visited, but clearly it is just one part of a major incentive to attract that research to China. In order to maintain our competitive edge, it is very important to retain this activity in the United Kingdom. While we are talking about non-human primates, I would have to stress that, as currently formulated, the withdrawal from the capacity to study non-human primates for primary biology in order to understand the very basic processes that can lead to future discovery, as highlighted by the article yesterday by Lord Rees in *The Times*, is something that is a very real threat. Certainly all the countries with which I have corresponded and engaged see this as an absolutely unacceptable part of the proposed Directive that non-human primates should only be used in very specified areas. I also have some views about the restrictions on great apes, because again it is trying to predict what is required when it is impossible to make that prediction in our current state of knowledge. I do not accept that we have yet reached the point on replacement where we could replace non-human primates adequately with alternatives. That is a very real anxiety and the fundamental worry that underlies the problems in the Directive around non-human primates.
Sir Mark Walport: May I add three things to that answer? The first thing is to make absolutely clear that research funders would not agree to something being done overseas that was considered unethical to do in the UK. That is a very important principle. The second thing to say is that if the Directive was implemented as is proposed at the moment, then for primates the specification is that research could only be done if it related to life-threatening or debilitating clinical conditions. Frankly, that would impose restrictions that would make no sense. For example, the use of deep brain stimulation in Parkinson's disease, which is helping many people worldwide, depended on fundamental research on the rate of neuron-firing in the brain. Again, it comes back to my point earlier that we have a system in the UK which, if used well, means that people use judgment when they are considering whether experiments on primates are justified or not. Trying to define whether a condition is life-threatening or debilitating is not something that can be readily done by statute. The third thing which I think would cause major problems is that some of the proposals—and you may wish to ask questions specifically about this—that specify, for example, the precise cage sizes would, in a non evidence-based way, add approximately 25 per cent to the costs of mouse research. That in itself would make it uneconomic for the research funders in the United Kingdom. There are some very major threats here, therefore.

Q219 ***Earl of Arran:*** How much, if any, is the remuneration package a draw to researchers working out of the UK?
Sir Leszek Borysiewicz: At the moment, I think there is very little evidence that for UK-based researchers this is a major consideration. China has a very favourable remuneration package to attract back Chinese workers who were particularly based in the United States, and they are given very special consideration within the Chinese system. However, there is no evidence that, outside that grouping, this is a major factor. We have done several studies to try to look into this in our trainees. It is the availability of facilities, the ability to undertake work and, frankly, the availability of money from the academic

sector in order to conduct that research through funding agencies in those countries. There are other incentives obviously for industry and other sectors that would have to be taken into account, including tax breaks, facilities and aggregates on large science parks. All of these have played very well into the scale of developments taking place in China, India and Singapore.

Q220 ***Lord Palmer:*** I was going to ask the same question as Lord Arran but, just going to the other end of the scale, are you worried about the number of undergraduates who are going into the medical research aspect, or might this be a worry in, say, five or ten years' time—that there will not be enough of the likes of you, with your expertise?

Sir Mark Walport: This is something on which we are working very hard. The problem starts in schools and probably goes far beyond this Directive. I think that there is quite clear evidence that there are fewer youngsters going into university to read the pure natural sciences—so physics, chemistry, mathematics—and these are all absolutely key skills for the biosciences in the future. We are working very hard to remedy those problems. I would have said that this is a relatively small part of that particular puzzle about people going into research and medical research in particular.

Sir Leszek Borysiewicz: We have looked at this area in particular and the real anxiety here is people who have specific expertise in physiological models, which is of particular importance to the pharmaceutical industry and elsewhere. There does appear to have been a trend that fewer and fewer of the young scientists who come in at university level and then want to take on a professional career want to do so in the context of animal research. There are a variety of factors, not least among which are the climate in which animal research takes place. However, we have instituted special measures, alongside the industry, in order to train more people in these aspects and creating specific units that focus on these areas, because we do consider research in this area as an absolutely critical part of future advances in biomedicine. Whatever we say, animal research is an absolutely integral part of all biological research moving forward, both in gaining a better understanding and in being able to alleviate disease.

Sir Mark Walport: Perhaps I may add to that. This is an important point. When we were undergraduates, part of the training of a medical student did involve undertaking physiological experiments using animals. That hardly happens now. If these regulations were to be put in place, students would not even be able to do experiments on some decapod species. Shrimps and other species are used in undergraduate experiments. This would make that extremely difficult. It is a continuation of a long trend, which I think would be very damaging.

Professor Headley: It is certainly true that if you want to have the next generation, you have to engage interest at a relatively early stage of people's careers. It is not something you can bolt on at post-university level. However, it has become increasingly difficult to expose undergraduate students to this sort of work, for a combination of reasons. Part of that is cost; part of it is the absurdity, for instance, that the annual licensing fee for personal licences does not match the academic session. You therefore end up having to buy two licences in order to expose your undergraduate students to one year's worth of training. Significant are the cost of animals and also the restrictions that there have certainly been—which I am happy to say are slightly relieved now—about getting a project licence through the Home Office in order to allow you to undertake relatively small numbers of demonstration-type experiments with undergraduates. That has been a major difficulty. It is becoming somewhat better. Indeed, there is a workshop taking place in September with the Home Office in order to try to promote that operation of licences involving teaching—but it has been a major problem.

Q221 ***Baroness Sharp of Guildford:*** Your final remarks pick up the question I wanted to raise with you. It is clear from the evidence you have given that from your point of view it is the implementation of ASPA and the directives by the Home Office that is the crucial issue, and you do not feel that the bureaucracy that they have in place is as helpful as it could be. I was going to ask you if you could give us some examples and whether there was hope that, in discussions with the Home Office—you were indicating that it has got easier in the last two years—one might be able to get procedures that were more friendly towards research in this sense.

Professor Headley: It is certainly true that ASPA has been one of the major difficulties in this area since 1986. That has waxed and waned with the level of risk aversion within the Home Office, in terms of the threat of dissent by antivivisectionist groups, et cetera. We are in a slightly more positive environment now and, as I intimated just now, we hope that that will improve things. That is not a complete solution as yet. At my University, for instance, we have just had to renew our project licence for undergraduate training. We still had to have three circuits round, about addressing the aims and objectives, making sure they were sufficiently precise, and so on; none of which has the slightest impact on welfare, particularly since most of the experiments that we are undertaking are mostly non-recovery. Even with the renewal of a licence with virtually no extension, therefore, there were still many hours of academic

time being put in to make this work. That seems quite unnecessary. We have to try to move to a system which is related to the welfare impact of procedures, rather than dotting Is and crossing Ts in the way that the Home Office has felt obliged to do under the current Act.

Sir Leszek Borysiewicz: There is a big concern among investigators about an issue underlying this Directive, which is that the imposition of additional bureaucratic steps—over and above the ones that we already have, on which we are negotiating and working very hard together with the Home Office—will add an additional burden. There are statements, requirements, authorities and authorisations in here that do cause a lot of anxiety in academic investigators that this will just make it bigger without actually improving the animal welfare side, as my colleague pointed out in his opening statement. We are very concerned that a linkage is being made that bureaucracy in some way reflects animal welfare. We absolutely refute that there is any association between these two. Bureaucracy has to be appropriate to the level of animal welfare that you want and not be overwhelming.

Chairman: I think that you are getting your message through! Can we go back to non-human primates, with a question from Lord Cameron.

Q222 ***Lord Cameron of Dillington:*** Perhaps I could first say that I am a farmer and so I understand that any representative body always resists change like mad, particularly if it is being foisted upon us by our political masters, shall we say. I wonder if I could start by asking if you accepted that minimising—and you can interpret that word in whatever way you like—the use of non-human primates must be part of the acceptability by the general public of all the work you do, not least in connection with the question being asked by Lord Palmer.

Sir Mark Walport: I think that we would agree with that completely, and we would go further and say that minimising the use of all animals has to be the goal. One then has to recognise that one needs to make judgments and it is actually about proportionality and deciding on a case-by-case basis whether the experimentation is justified or not. In parenthesis, it is worth noting that research on agricultural animals is something that would become almost impossible under these regulations. The housing conditions that are required would make agricultural work almost impossible. You would not be able to release animals back into your farm afterwards. There seems a slight paradox that this, which has come from a committee that ought to know about agriculture, has completely neglected it in terms of the regulations.

Sir Leszek Borysiewicz: Could I add that every funder from the Association of Medical Research Charities as well as the public bodies, as part of the application form where there is a request for "use of animals", stipulates that there has to be a specific justification, which is tested by peer review as to why those experiments are to be conducted in animals. The numbers are strictly tested, both for the ethical considerations in relationship to the use of the animals as well as to the numbers actually required in order to achieve the end goals of the proposed studies. It is not just something that we aspire to, therefore; it is something that we have inherently in our funding practices that is tested grant by grant, application by application, as it comes to every funder.

Q223 ***Lord Cameron of Dillington:*** This is an area that obviously divides the two sides pretty thoroughly, but even the RSPCA last week were saying that they do not want to ban experiments on non-human primates; they are just looking for ways of minimising them. Clearly, as you said, the draft Directive restricts [non-human primate] research to life-threatening and debilitating clinical conditions, although that was broadened by the Commission, when they gave evidence to us, to include conditions such as infertility, diabetes, Parkinson's and so on. On the other hand, two weeks ago Professor Hammond, who perhaps more represents your position, was saying that they wanted to "protect basic research that generates knowledge", which is pretty well a free-for-all as far as we were concerned. How would you minimise the use of non-human primates?

Sir Mark Walport: I think the short answer is that it is not a free-for-all, because we review this extremely rigorously. We have scientific review, which asks the question "Will this fundamentally add to knowledge?" In the case of primates we also add an additional level of peer review in that the MRC, the Wellcome Trust and other funders send the applications to the National Centre for the 3Rs for an additional layer of peer review; so we are therefore extremely careful. Let me give you another example that has recently been discovered. There are these neurons called "mirror neurons". If you are looking at someone moving, there are neurons that respond to that. That is relevant to the understanding of autism, which is an extremely important condition; but I do not necessarily think that the researchers doing that research at the time would know what the clinical implications of the research are. A fundamental understanding of the brain is therefore absolutely crucial to the understanding of neurological conditions, which are a huge burden of ill health. We are very careful that, when a research question is asked, it is an important question. In other words, if it is answered it will tell us something which we did not know that is important about how the nervous system works. That is not a free-for-all by

any means at all. It is very tough to get the money; it is very expensive for us, actually.

Q224 ***Lord Cameron of Dillington:*** Where would you draw your line? How would you reduce the use of non-human primates?
Sir Mark Walport: We would reduce it by the use of the judgments that are done at the moment. In other words, the UK system, which has peer review, it has ethical review and, in the case of non-human primates research, it has a further review of animal husbandry. We would still believe that asking wise people to make judgments on a case-by-case basis is the best way to do this.
Sir Leszek Borysiewicz: There would be two elements that I would like to add to that. First and foremost, please do not underestimate the potential ingenuity of applicants for grant applications. If you put in stipulations such as proposed in this legislation, you can begin to contort and convert any sort of basic research that you wish to undertake to having some downstream benefit. We all believe that there should be absolute transparency as to the purpose of an investigation, which is clearly outlined in the grant application, rather than creating a fantasy in order to fulfil rules. That transparency is tested in the UK system very clearly and very rigorously, particularly as it applies to primates, as my colleague has outlined. It is therefore very important to do that. Secondly, the numbers of primates in use in experiments in the United Kingdom has fallen, for a variety of reasons. Therefore, the trends in terms of utilising alternative models are already there and reasonably well established within the community. I would therefore say that we are already on a trajectory whereby we are seeing that minimisation, through the processes that my colleague has already identified.

Q225 ***Lord Cameron of Dillington:*** Can I touch on the F2 question, where the problem lies and how we cannot work towards a date whereby we are using only captive-bred animals?
Sir Mark Walport: The first thing to say is that there is actually no evidence that suggests that animal welfare is any better by using F2; in other words, entirely captive-bred animals compared with others. The second thing to say is that in principle it does seem a sensible direction in which to move; but we are a long way from having the capacity to do that and, frankly, it remains enormously expensive. The question therefore is, in a world where there are other economies, if it turns out that F2 animals are very much more expensive than animals bred elsewhere, then I think the community will vote with its feet—particularly the pharmaceutical industry. So I think that this could be dangerous to the pharmaceutical industry. As I say, we do support it in principle, but I think that there are questions. In particular, there is the question as to what the evidence is that it is necessarily any better for animal welfare to be dealing entirely with captive-bred populations. We do not know that.
Professor Headley: Could I add that, from a veterinary perspective, there are potential problems that are beginning to surface in some colonies about having rather small groups, and the genetic inbreeding that is likely to result from those, that may have problems as you start to get through the generations. That is beginning to surface. We really do need to have, as was proposed by the EU Parliament, a clear scientific review of that situation before there is any enforced implementation. It is notable that the Commission itself commissioned a report, the SCHER report that was released only in January this year, which does delve into a number of these issues in quite some detail and is rather antithetic to the position that was taken by the Commission in the original November draft. That is a mistiming that is somewhat unfortunate, because one would have hoped that the content of that SCHER report would have been reflected rather more in the draft Directive.

Q226 ***Chairman:*** Could we stay on the subject a little longer, on breeding? We have a later paper in evidence from the Medical Research Council and the Wellcome Trust, "Principles of appropriate levels of scrutiny, checks and balances for the use of animals . . . ", which has come to the Committee this morning. In paragraph 13 you say, "If the grant contains rhesus macaques, the main funders of non-human primate research in the UK stipulate that researchers must source animals from the UK-based Centre for Macaques (CFM)". Presumably this is something that you run yourselves?
Sir Mark Walport: Yes, that is correct.
Sir Leszek Borysiewicz: Yes. It is a centre that we look after. For obvious reasons, I am not going to disclose locations and so on—but, yes, we do. We support that centre.

Q227 ***Chairman:*** You do have the fullest opportunities then to explore some of these issues?
Sir Mark Walport: Yes, we do. Indeed, one of the challenges of that is that the costs of macaques being produced by that centre are enormously high. They are at present in excess of £20,000 per animal, and that does raise quite important questions about the long-term viability of that as a simple solution.

Q228 ***Chairman:*** Do you have second-generation?
Sir Leszek Borysiewicz: There are numbers of second-generation animals, but at the present time the numbers produced by that centre would in no way be able to provide the supply that is required in totality

within the UK, not just in the academic sector but in the wider CRO sector.

Professor Headley: Could I make one extra point in relation to the NHPs? Something like 70 per cent of the NHPs used in this country are for regulatory purposes. The numbers that we are talking about that are discretionary, if you like, in terms of fundamental research or applied research, are really very small. Whilst there is therefore this stipulation from the major funders that the CFM should be used for the supply of NHPs in that fundamental work, it cannot apply to the majority use, which is in industry; because the supply is not there and the costs would be prohibitive.

Chairman: This is an important area.

Q229 ***Earl of Arran:*** We have been touching on this for much of the morning, on authorisation. This terrifying set of procedures here on page 27, which has secured the criticisms from many organisations as "pedantic", "bureaucratic", "slow-moving", to put it politely. I do not want to put words into your mouth, but how much of a problem is this at the present time? Do you at all see the existing consultation process currently going on as a way of improving this, of simplifying this? Would the proposals for the revised Directive make matters worse or, on the other side, might they help by standardising procedures across the EU?

Professor Headley: As I hinted earlier on, I think we do have an over-regulated system in the UK that is not sufficiently proportional to the welfare costs involved. In terms of what is being proposed now, we have this, as you say, very complicated mechanism that would make that situation significantly worse. That said, we do see the introduction of a new Directive, and the implementation into the UK legislation subsequently, as an opportunity to get it right. We would very much like that to take place and have been working hard with the Parliament, and now the Home Office which acts through the Council of Ministers to try to get our views across. The issues are, on the one hand, harmonisation; so, yes, we would like there to be a level playing-field across Europe of both animal welfare standards and the ethical review process and support for the 3Rs. There is no attempt at any stage by our sector to try to dilute the welfare standards that should be applied to animal research. What is sadly lacking in our view from the draft Directive, is any sense of proper proportionality—the point I was trying to make earlier on—whereby the level of regulation should be proportional to the welfare impact of the procedures that are taking place. That is what we would like to see and what is singularly lacking. We have therefore been trying to make the point that we have to have that. One of the aspects that our sector proposed to the European Parliament—and that the Parliament in our view happily adopted as one of its amendments—was the notion of "notification" of the least welfare-costly procedures. That is part of this argument about proportionality. Nobody is suggesting that any research worker can do anything just because it happens to fall within the notification that is submitted. We still have the local ethical review process that would be undertaken. We still have a licence that needs to be prepared. We still have the issue of funding, and animal research is not cheap. So the idea that notification would somehow immediately permit huge numbers of irrelevant experiments to be undertaken is rather fanciful. What it would mean is that those experiments that are of zero or minimal welfare impact would simply be more adaptable. The other point that I would like to emphasise there is that we have always argued for advance notification, not for retrospective notification. What we are basically saying is that you go to the local institutional ethical review group; you write your application; you send it in to the competent authority—in our case the Home Office—and you say, "I intend to start this in a week's time". You therefore have your advance notification. That still allows the competent authority to come back and say, "Hang on a minute. I think you have got your severity classification wrong. We need to look at this a little bit more". I think that check is still something that would be very important to have, for public confidence, and to make sure that individual institutions do not drift too far sideways from what is permitted. We are still in favour of that, therefore. What we are trying to achieve, however, is the flexibility for research to move and adapt rapidly, in order not to hinder the advance of research in the way that we have currently.

Q230 ***Earl of Arran:*** Much of the criticism is levelled against the Home Office. Who advises the Home Office? Where do they get their advice from? It would not be from your good selves, would it?

Professor Headley: Over the last four years or so, we have had a lot more input. That started with the Government's Better Regulation agenda, to which we made a formal submission as a sector, and also the Davidson Review on the implementation of EU legislation, where we also made a submission. Since then, we have had much more of a dialogue with the Home Office than was possible beforehand.

Q231 ***Earl of Arran:*** Where are they getting these ideas from?

Professor Headley: I suspect a lot of it is the lawyers. It is the threat of challenge from antivivisection groups and the way in which that can lead, as we have seen, to judicial reviews—which are hugely time-consuming in terms of Home Office staff time and disruption to research on the ground. We have seen

that taking place and it is the concern over that happening again, which means that the lawyers say that they have to close things up all the time.

Q232 ***Earl of Arran:*** Do you think they regret that decision at the Home Office at times, and they blame those down the corridor? Is there any sign of that?
Professor Headley: I think the fact that we now have, I would not say killed the antivivisectionist problem, but we at least have it in far greater control than we did up to about five years ago—that has made a huge difference to the ability of the Home Office to take a slightly more risk-based approach and to relax the controls a little bit. However, there is still the looking over the shoulder and the concern that the way in which ASPA was worded does not allow for adequate risk base. Can I exemplify that? There is one word in ASPA that has caused more problems than just about the rest of the Act put together. That word is "*may* cause pain, suffering, distress and lasting harm". Not "is likely to" or "is expected to" or "will", but "may". "May" can be interpreted as being a one per cent chance, a 0.1 per cent chance, somewhere, some time, something will happen. It leaves one open to having to close all the possibilities of something going wrong, in a way which is extremely pedantic. Indeed, some of the changes we successfully encouraged Neil Parish to adopt in the amendments to the draft were to substitute "may" with "is likely to" or "is expected to". That would be hugely helpful in terms of promoting the intent of the legislation.
Sir Leszek Borysiewicz: Maybe I should add that the Home Office seeks guidance and advice through a number of advisory committees. In order to get that advice, we are consulted in specific areas and I know that the Trust is consulted in specific areas.

Q233 ***Earl of Arran:*** And presumably it has served on them as well?
Sir Leszek Borysiewicz: Absolutely. Particularly on non-human primates, we are actually providing advice and guidance and it does seek that advice and guidance very widely. I think that at the top level of the Home Office a lot of this is taken on board. What is important here is that the relationship between the guidance and the investigators and the Home Office allows for a to-and-fro, in order to get to a position which is both equitable with the legal requirements that are there, and rightly there, to protect suffering in animals and the ability to carry out and conduct scientific experiments effectively and well. That is a particular area of importance. The concern most investigators have is that the imposition of the additional directives on top of that will add a significant second tier of activity, which will then be very counterproductive towards retaining Britain's competitive position, both commercially and also in terms of scientific competitiveness, to be able to maintain our pre-eminent position in life sciences internationally.

Q234 ***Earl of Caithness:*** That is the very point.
Professor Headley: We should also acknowledge the role of the Animal Procedures Committee, which is advisory to the Home Office in this respect and has given some very useful advice over the years; admittedly not always with great alacrity, so a lot of the reports from the APC can take a year or two to come back. That in itself has caused problems, and continues to do so.

Q235 ***Lord Palmer:*** I want to talk about data-sharing, but you have already answered my first question earlier on about duplication; so I have only two questions left. Do you believe that there are opportunities for more data-sharing, particularly within the field of negative data? What would the impact of a mandatory data-sharing approach be on academic intellectual property?
Sir Mark Walport: As I have already said, as funders of research we do encourage the sharing of data. I think that the scientific community is increasingly responsive to this, and I will give you one practical example. There are two very large international consortia which are basically trying to delete a number of important genes in mice, so that one can understand the function of these genes. Those are working at the level of international collaboration; so instead of individual groups trying to knock out genes—and occasionally that does result in duplication—this is now a co-ordinated universe; there is sharing of results; there is sharing of both positive and negative results. We are therefore encouraging the creation of databases where the results of animal experiments can be put. In general terms, therefore, we think that the sharing of data is something that should be encouraged and we work hard to increase it. However, one can also share data in a mindless fashion. The danger of what is proposed here is that the sharing would be the end in itself. Very large databases could be created at both very large opportunity cost and financial cost, which would then add very little value. Ensuring that sharing adds value is in itself a highly technical thing, which the Wellcome Trust strongly supports. For example, we and the MRC fund the European Bioinformatics Institute. In terms of the sharing of negative results, that has been an issue particularly in the clinical trials area; but, again, I think that great progress has been made and, increasingly, there are clinical trial registration processes, which means that both positive and negative clinical trials results are accessible. The idea that, as it were, every single animal experiment would appear on a database somewhere does not really make sense. We have to be sure that the data that is shared means something and

can be interpreted. What we are concerned about here, therefore, is a blanket diktat to do it but not actually to do it well.

Q236 ***Lord Palmer:*** Which would have nothing to do with the protection of animals?
Sir Mark Walport: It would have nothing to do with the welfare of animals at all, no.
Sir Leszek Borysiewicz: Could I deal with the issue you raised on intellectual property, my Lord? I am afraid that this is often used as a red herring. Intellectual property is intellectual property, whether it is commercial or academic. In terms of the normal restraints that universities applied, from my previous experience as Deputy Rector of Imperial College, even when we entered into commercial contracts as an academic institution, there was a delay put in place in terms of publication and making data available, in order to allow protection of intellectual property by that institution. Therefore, as funders of research we certainly would allow a reasonable delay in order to allow intellectual property to be registered, but it cannot be an end in itself that you can delay indefinitely in order just to claim "This is protecting intellectual property". Beyond that reasonable time limit, academics are free to publish. There is a time factor here that is often not considered when that question is asked.
Professor Headley: Could I add that one should remember that it is the nature of academics to sing from the rooftops the wonderful results that they are achieving. That is deep in the psyche of the people who go in to do this sort of research. One has a whole industry of international conferences to which scientists go, in order to broadcast their latest results. That then spawns a network of informal contacts between the scientists working in cognate areas; so that you can pick up the phone and say, "Have you ever tried this?" and get the information that is supposedly, if one read the draft Directive rightly, not available to anybody. It is available through this informal networking, which is actually quite effective in the way that it operates.

Q237 ***Chairman:*** I think that there is a concern, though, that there are many experiments that take place where people do not achieve successful results, so that they do not want to broadcast it, for very obvious reasons. There is a fear that these take place on animals which are subject to experimentation. I take your point that to try to record every one would be difficult. This is a concern, though.
Sir Mark Walport: I understand that it is a concern, but it is also a concern for the people who fund research. We worry if we fund a grant and no results appear. The pressure on investigators to make sure that the results do appear is actually very high, and we do look into grants where nothing happens.
Professor Headley: There is a serious scientific difficulty with negative results, in knowing whether they are meaningful negatives or whether they are negative simply because the experiment did not work—in which case one learns nothing from broadcasting the information. It can be very difficult to know which of those two is the case when something has not worked out properly. That is one of the reasons why people are reluctant to broadcast; they just are not sure. They might discuss it informally but they will not put it down on paper, because they do not know to what extent it was simply a failure of the techniques in some way or whether it genuinely meant that that is not the way the system operates.

Q238 ***Chairman:*** Professor Headley, you originally intimated that you may want to leave around 12 o'clock. Are you staying with us?
Professor Headley: I am afraid that I do need to catch a train and I need to leave in ten minutes.

Q239 ***Chairman:*** In which case, is there anything before you leave that you particularly wanted to draw to our attention which you have not had an opportunity so far of expressing?
Professor Headley: Perhaps we could touch on the severity classification a little more?
Chairman: Which is the next set of questions.

Q240 ***Earl of Caithness:*** The Commission gave us a very good exposition as to why their severity classifications were right and justified. Sir Leszek said this morning that 19 out of 19 of his reporters said they were ghastly and horrible and needed to be changed. What is the true situation?
Professor Max Headley: There are two different things. One is whether the number of bands and the names that one gives them are appropriate; the second is the definition of what falls into those different bands. The names that the Directive gave us were reasonable, but what it did not do at all was to describe where the boundaries between those bands are. That causes major problems for the interpretation of the rest of the Directive. If you do not know when you are designing the rest of it [the Directive] what is a mild procedure and what is a moderate procedure, then how can you start to design and interpret those articles that refer to this terminology and make sense of it? The argument that has come from the sector, therefore, is that it is crucial to the design of the rest of the Directive that we have a well-designed and described set of procedures that fit into each of those severity bands. In the sense that the Parliament's amendment gave us the beginnings of that description, we supported it. In the sense that it did not include non-recovery as a category and did not separate out humane killing as a category, we did

not approve of it. It was a step in the right direction of descriptions but it did not get it right. I emphasise that it is very important that we have non-recovery and humane killing as separate categories to serve the 3Rs function; because if you do not have the lesser welfare impact procedure separated out, you remove part of the incentive to refine from a more vigorous procedure to a less vigorous one. We therefore consider it hugely important in terms of animal welfare to ensure that we have non-recovery and humane kill as identifiable bands that are separate from the "mild" category, but that was not separated out by the amendment. In that sense, we support to a greater extent the Directive's wording but we feel that there must be a description of that wording within the Directive, so that the terms of the other articles can be interpreted appropriately.

Sir Leszek Borysiewicz: Perhaps I may come back, My Lord Chairman. It was said that it was ghastly, but actually the proposition that we discussed and considered was that it was critical that the definition of the severity band was included in the main body of the Directive. What is particularly disliked by the group is that in some way there will be a Directive and, somewhere downstream, there will be a few committee meetings that will then put in those definitions, which can then be gerrymandered and moved around as required. The lack of clarity as to what those boundaries are, if it is not in the Directive, then makes the definition of when can re-use of animals be reasonable extremely difficult. The re-use issue was one of particular concern to the member organisations that I referred to.

Q241 ***Earl of Caithness:*** I will come on to re-use, but are you taking part in the EU working groups and is the Commission listening to you and your concerns?

Professor Max Headley: I do not think we know the answer to the latter question but, yes, we are all contributing to the meeting that is taking place in July. We are restricted in the numbers of members that can take part, but we have one member of the Bioscience Federation who is contributing and Roger Lemon, who is unable to be here this morning, is contributing as a representative of the European Science Federation. There is no restriction on the number of NGOs across Europe that can contribute to this discussion, but there is a limit on the national representatives that can go. We are restricted to one member from our sector, therefore.

Sir Leszek Borysiewicz: The representation, both through the European Science Foundation and elsewhere, is well established on these committees. However, your second point is valid because this is one of the major concerns that certainly European members have expressed, as well as a real concern to us in the United Kingdom. We had a Directive drafted from the Commission. That was very carefully considered by the European Parliament. Statements emanating from the Commission are that they will tacitly ignore everything that the Parliament has suggested or that has been debated; they will be going back to their original submission and are just going to drive it through willy-nilly. Therefore, while we thought that a great deal of debate had happened around the consideration of this Directive by the European Parliament, it transpires from statements currently emanating from Brussels that actually they are just ignoring all of that particular discussion. That is causing a great deal of disquiet, because it seems that we have to go through the process all over again at the second reading, when that comes forward to the European Parliament. We do not feel that that is an appropriate way for the Commission to behave, in something as important as this Directive.

Q242 ***Earl of Caithness:*** Could you tell the Committee what your thoughts are on the proposals for the limitations on the re-use of animals?

Sir Mark Walport: I think that there is a fairly general agreement that these may be counterproductive to animal welfare. A very good example is that, in order to study a drug that may alter blood pressure, telemetry devices can be implanted that will measure blood pressure. The idea that, rather than re-using an animal that has had a device implanted, a new animal would have to be used each time is actually deleterious to animal welfare. We basically support the position that examples of re-use need to be looked at carefully, but there are many cases where re-use will improve rather than harm animal welfare, and I think that is one area where the evidence has been fairly uniform from all the communities that have responded. Again, it is a question much more of using judgment rather than trying to have a blanket rule that says that re-use is not sensible; you have to look at it on a case-by-case basis. There was some criticism of the Home Office before, but I think, actually, we have a system that the Home Office is operating and is responsive to the scientific community which actually depends on proper review where people form judgments, and there is nothing like a group of wise people looking at something and determining, on a case-by-case basis, whether it is the right approach or not.

Q243 ***Chairman:*** Presumably, there is a case against re-use.

Sir Mark Walport: There is a case against re-use under some circumstances. So it is on a case-by-case basis. There should neither be a blanket ban on re-use or a blanket permission that says that re-use is OK. One has got to look at it on a case-by-case basis.

Q244 ***Chairman:*** Should there not be an attempt to define the circumstances in which—
Sir Mark Walport: Very difficult to define because the second you try and do that you run into all kinds of knots; it is much better to think about whether re-use is appropriate or not and make a judgment on a case-by-case basis.
Professor Headley: That is, to our mind, the function of the ethical review process that takes place, which every study is subjected to. There somehow seems to be a view that re-use would bypass that ethical review and authorisation process, which is not our intention in any way at all.

Q245 ***Earl of Dundee:*** You express concern about the Directive's intention to include immature forms of vertebrates and certain live invertebrate animals. If such proposals should remain unamended what impact will they have on the research community?
Sir Leszek Borysiewicz: I think this is quite an important area and there are two distinct areas that we have to consider: one is larval and embryonic forms of animals, which are very important, for example, for studies of development and other conditions; and then there are the invertebrates themselves that are actually employed in experimentation. The argument seems to come down to two areas. One is whether this should be recorded. In practical terms, it can be extremely difficult for free-swimming larval forms in a variety of tests to estimate how many larval forms are exposed to particular conditions. So there is a practicality that is extremely difficult to pertain here. Secondly, the question of whether there is sentience within some of these lower forms of life is inherent as to why they should actually come under this particular Directive. The evidence base on which that is based is very limited indeed, and is, in fact, very difficult to prove one way or the other, in some of these animals. The problem is that many of these animals will also form the basis on which we can eventually look for substitutions of non-human primates and other species, so that if you begin to restrict their potential use and investigation in this area it does cause major problems for reasonable movement in the 3Rs direction. That is the main reason why I, in particular, find that extremely difficult to engage with. These are the major areas that I would identify as to why this is not a practical proposition as enshrined in the Directive, and these issues have to be considered in far more detail than has actually been conveyed in this Directive.

Q246 ***Earl of Dundee:*** On scientific evidence relating to sentience, which you point out is very thin—there is not much to go on—would you forecast that that will—if there are no signs in the next five or ten years of such elements, following on from the nature of certain experiments that may be ongoing—improve or would it be very unlikely?
Sir Leszek Borysiewicz: If I had to make a guess, and it can be no more than that, I would think it is going to be extremely difficult in some of these forms to actually prove sentience. What is important is that we are aware of the evidence that comes forward and that you have a series of directives which are able to be flexible enough that it can be assumed and that changes can be brought in pretty rapidly if such evidence exists, rather than trying to take the other position which is to say: "Let's consider all forms potentially sentient until you prove the negative. So, from my point of view, it is about remaining open to the possibility of sentience; if it is observed and if it is seen and the evidence becomes firm then you take action at that point, and bring it in. The Directive seeks to be a blanket cover with a whole series of assumptions for which the scientific evidence is very limited indeed.

Q247 ***Earl of Dundee:*** A moment ago you warned us that the record, so far, in the Commission may not be terribly good in paying attention to the European Parliament. Nevertheless, to protect your concerns in this case, which amendments would you like to see being introduced?
Sir Leszek Borysiewicz: I can provide you with the detail of that. I have not got the specific numbers but it is where the definitions are in terms of decapods, in particular, that this is seen, because the evidence for sentience in that group of animals is extremely thin. There are some arguments one way or the other around cephalopods and there is some evidence of rudimentary sentience in some of these animals; so it is a matter, again, of not trying to provide a blanket definition and a blanket ban, if you like, on particular groups of invertebrate but being aware of evidence as it arises, and taking note of it when it is actually there and available.

Q248 ***Chairman:*** There is a list in Annex 1 of those that you mentioned. Would you remove this or would you amend it?
Sir Leszek Borysiewicz: I would look towards amending it; I would certainly look towards the removal of the decapods. I think the issue should be open; it should rather be provided as guidance to countries so that they can begin to take a view on, for example, cephalopods, since, as I say, there is a reasonable case that we may need to look quite carefully at some of the higher level cephalopods.

Q249 ***Chairman:*** Have you put these views to the Commission?
Sir Leszek Borysiewicz: We have put these views to the Commission; we have put them to the rapporteur and to the European Parliament as well.

Q250 ***Baroness Sharp of Guildford:*** Earlier on you have indicated that the proposals for the minimum standards of care and accommodation were going to cause difficulties. I wonder whether you could spell out for us some of those difficulties. Secondly, how far were you consulted about these standards? Again, we gather that they were agreed by the Council of Europe expert working groups that included representatives of industry, scientists, academia and animal welfare organisations. How far did you play a part in consultations earlier and how far do you feel that your views were in any sense listened to when these standards came out?

Sir Mark Walport: The first thing to say is that a lot of this was based on a document called, I think, ETS123, and there were expert advisers who participated in that. I think that they all acknowledged, as part of the work, that the scientific basis for making these decisions was virtually absent. In light of that, their view was that these should be recommendations. Of course, what has happened is that they have been changed from recommendations into absolute standards. In some cases, it is absolutely clear that for some of the larger animals the cage sizes specified were actually much too small. In other cases, particularly in examples of cage sizes for rodents, the cage sizes would be larger than those used, at the moment; they would be weight-adjusted, really, on the basis of very little evidence in terms of animal welfare and, indeed, some evidence that suggests that, actually, rodents prefer to be at high-density in relatively small spaces in terms of free living rodents. The issue here is that the scientific expert group which produced the document said: "This is the best we can do but we believe it should be recommendation and not statute," but this has been transposed into a set of rigid cage sizes, where, as I say, in some cases, welfare would be reduced and in other cases costs would be added with absolutely no welfare benefit whatsoever.

Q251 ***Baroness Sharp of Guildford:*** Picking up another issue which we have already touched on, do you endorse the assurances given by the ABPI's representatives on 10 June that the UK-based researchers (whether commercial or academic) would require standards of care and accommodation to be maintained at UK levels, even if the work were conducted overseas? As, again, we touched on earlier, there is a lot of collaboration taking place now, and within those collaborations the experiments might take place—

Sir Mark Walport: I can speak for my own organisation, which is a research funder, and it is one of our grant conditions that we would only award a grant if it was going to be conducted at the standard which was considered to be acceptable by UK standards. Equally, industry is dependent on the results of their research being sufficiently good for drug development meeting the regulatory standards, and therefore it is in no one's interests, actually, to conduct work at low standards.

Sir Leszek Borysiewicz: We have entirely the same procedures within the Medical Research Council that they have to be at the standards that are required in the UK. We actually fund very little animal research overseas; we try to ensure that much of it is conducted within the UK. However, there is something else that we have to be really clear about here: that good animal welfare and paying attention to good animal welfare does give the best and most credible scientific results at the end of the day. Therefore, when you challenge most animal investigators, it is extremely important—cost is just one factor—that you conduct the experiments on the minimal number of animals, with the minimum amount of suffering that is required in the best possible conditions to ensure that the results that you get are as valid as possible. I think it is extremely important to remember that the debate that we are engaged in around the issue of the Animals Directive is not about, in any way, reducing the welfare standards not least because it is not in investigators' interests to reduce the welfare standards; it is around other aspects.

Q252 ***Baroness Sharp of Guildford:*** I have one further question, if I might, which is actually off this particular subject but which I am quite interested in. You mentioned the NC3R centre, which is a UK-based centre which, as I understand it, is funded by the Research Council.

Sir Leszek Borysiewicz: Through the Medical Research Council, yes.

Q253 ***Baroness Sharp of Guildford:*** Is there anything equivalent at a European level?

Sir Leszek Borysiewicz: There are some centres which are becoming involved at a European level in terms of the 3Rs. What I would say is that I believe this is an area where the United Kingdom is providing enormous leadership. This is an extremely important organisation; it funds a lot of research; it is helped by a large number of very eminent scientists who have served on panels of both the Wellcome Trust and elsewhere. What is more important is that its work is open and open to scrutiny so that they ensure that the research that is conducted in the 3Rs area is conducted, also, to the highest possible scientific standards, so that makes its application all the more important. The research boards within the Medical Research Council certainly use evidence coming from the NC3Rs when we consider any applications which utilise animals, as to whether it is, in fact, the best involved. In relation to higher animals, particularly non-human primates, as my colleague has already pointed out, we utilise and provide advice that it is, in

fact, the best and only way in which this research could be conducted. So it is Britain's leadership here that is important, and all I can say is that I think they are doing a fantastic job. One of the important things about this Directive is that it does support the 3Rs, and if we broaden that activity around the European Union I would just say "Amen".

Baroness Sharp of Guildford: I was going to ask whether it provided something of a precedent that actually could be extended across the EU.

Q254 ***Chairman:*** Are you content with the proposals in the Directive or do you think they should go further?

Sir Leszek Borysiewicz: I am reasonably content with them. It is important for two reasons: firstly, it is about highlighting to the academic community that there is real research to be done in this area, and that research is vital in order to progress the goals of the 3Rs. In some areas of the Union (I am glad to say that is not part of the United Kingdom), that is still, if you like, a missionary activity—to actually say: "This work really matters because it then tells us what is the best work to do with animals". There is, however, an increasing tendency to propose national laboratories in this kind of activity. Now, I do not believe that that necessarily is the best way to go forward. One of the things that we have seen through the 3Rs programme in the United Kingdom is that what is important is to engage scientists who really understand the area that they are working in, so that they understand both the deficits of animal models in particular conditions and, also, could then be able to start looking at how best to replace them. So it is the scientists who work in a particular condition or in a particular field or a particular physiological system who are often best placed to advise and consider what are the best experiments to be done to consider replacement, rather than an arbitrary creation of a national physical centre which brings in experts who may not be expert in the specific field that you are trying to replace. I am not in favour of these sort of big, national laboratories in this area; I would like to try to promote the way in which this is conducted in the UK which, of course, you may say: "I would say that, wouldn't I?" but I do think it is a particularly good example of where the UK has led.

Q255 ***Chairman:*** How does one translate that into not just an exhortation on a European-wide basis but a practical reality? Could that be achieved to a degree by having time limit targets?

Sir Leszek Borysiewicz: I think the best way that a lot of these issues can be dealt with in the Directive is, firstly, not to put rigid timelines on when the Directive is imposed. This Directive is an important one; it is recognised by the community as being important, but adequate time should be given for debate around many important issues that this raises, and not to set arbitrary timelines in the way that appears to be happening at the present time. There is a huge amount of debate, and I believe that one can convert many of the ideas that are coming from national bodies, national agencies, governments and other bodies into a real discussion, and then, if you like, to translate it into Euro-speak in a way which allows guidance and recommendation rather than directed initiatives which, I think, could be counterproductive in many of the areas where the proposal is seeking to obtain real benefit.

Q256 ***Chairman:*** Surely, was that not a failing of the 1986 Directive—that it was written precisely in those terms?

Sir Mark Walport: My Lord Chairman, you cannot put timelines on discovery. Of course, we would all like to live in a world where it was possible to discover new drugs and cures for diseases without the use of animals, but the practicalities are that we cannot prescribe a timeline for the discoveries that are needed to make that happen.

Sir Leszek Borysiewicz: Nor in discoveries in 3Rs with which we will be able to replace some elements. If you take it at its extreme, the understanding of the human and mammalian brain, particularly neurosciences, where so much disease is affecting our communities, I would frankly have to say I would be very hard-pressed to see in any of those disorders any situation that will arise where we will be able, in my lifetime, to see a reduction in the use of non-human primates, which remain the only species that are capable, in some areas, of utilisation in this area. I wish it were not so, but, nonetheless, we have to be realistic as to where the priority has to reside, and that priority has to be tested application by application, not by directive and diktat from a centralised position.

Q257 ***Chairman:*** Could I go back to where we started? You mentioned that you chaired a group of state researchers on a European-wide basis. Is there an international grouping?

Sir Leszek Borysiewicz: We conduct and discuss this at meetings of the Heads of International Research Organisations—HROs. They tend to be rather more selected, in the European Union. Here we virtually have every single country, including countries outside the European Union (such as Turkey and Switzerland) that engage with this wider grouping. Internationally; HROs it is more of a mixed bag; it includes many countries of the former Commonwealth, the United States and other countries like China and India who are engaged in these discussions. So, yes, these debates do happen at that level but there is not an international consensus building up in this area. We have raised this particular issue for discussion, and we have considered, within

that organisation, this Animals Directive and how far it impacts on other countries, but, at the moment, I do not think there is any consensus emerging on the wider international stage.

Q258 ***Lord Cameron of Dillington:*** You have, basically, said that you approve of efforts to harmonise procedures and authorisation procedures across Europe, and so on. However, you have not really touched on the whole question of harmonising of enforcement and policing in different Member States. I was wondering whether you would like to comment on that area.
Sir Mark Walport: The issue is whether it is true harmonisation or whether there is the opportunity for gold-plating, because, of course, if different EU countries gold-plate in different ways then that destroys harmonisation. Equally, I believe there is the possibility that Member States can set their own penalties. So I think it all depends on what one means by "harmonisation".

Q259 ***Lord Cameron of Dillington:*** I was thinking more of bringing the minimum up to the current average, rather than the other way round.
Sir Mark Walport: Of course we would support that, and I think that that is the strongest argument for there being a new Directive—that, actually, it is a long while since the Directive was first introduced and there does need to be greater harmonisation.

Q260 ***Lord Cameron of Dillington:*** Is it a problem with the different enforcement in different countries at the moment, would you say?
Sir Mark Walport: I think it is difficult to comment from a UK perspective. We operate within the UK system, largely, which does work very well.

Q261 ***Lord Cameron of Dillington:*** I was thinking from the European experience.
Sir Leszek Borysiewicz: From the European experience, I think it is a patchwork. In different countries there are different levels of inspection, regulation and enforcement. There is going to be a very real European issue here, under that awful word subsidiarity, as to at what point does a recommendation actually require the country itself to enshrine the requirements of a Directive within the legal structure of that country. I would argue that the United Kingdom, I think, has, by and large, reached a position where there is a good inspectorate service that looks after animal welfare well. In some European countries, I think, one would have to say that may not reach the standards that we have in the United Kingdom.

Q262 ***Lord Cameron of Dillington:*** Would you like to highlight a particular problem country?
Sir Leszek Borysiewicz: No, I would not, at this point.

Q263 ***Chairman:*** Could you explore the possibility of suggesting ways in which the policing could be improved to make sure that they do raise the standards without having to identify any individual countries?
Sir Leszek Borysiewicz: I think the answer is yes that can be done, but I think it is best done by consultation with those countries as to the areas they accept from such a Directive. It stresses the need for the Directive to be clearly and carefully thought through, such that it is acceptable to the widest possible community in Europe, and the best way, I believe, within Europe that you achieve that level of agreement is by getting that to the position of consensus, instead of what we have, at the moment, which is basically camps that are in very different positions as a result of this Directive. If we can get to that position of consensus then I believe the implementation would follow downstream, because I cannot believe that any country that is a member of the European Union would want to be far away from the standards that are recommended within such a Directive as being appropriate in terms of its own internal structures. So I do think you have got to rely on those countries to uphold a Directive which is virtually universally seen as being of benefit in this area, which is why we support the need to revise the 1986 Directive.

Q264 ***Chairman:*** Some people could argue that can lead to the lowest common denominator, though, and, indeed, that this is being used as an opportunity by the industry in this country—to some extent supported by academia—that we should reduce standards to a degree.
Sir Leszek Borysiewicz: No, I would not accept that. I think, for the reasons that I have already said, particularly in the academic sector, which I can speak for best, it is extremely important that the value of the experiments that you conduct are conducted in the best possible circumstances and tested in those situations. There is very little advantage in the competitive world of science to be conducting experiments that are subsequently shown to be erroneous or wrong, which often could result. So scientists, by and large, will always move to very high quality standards, which we uphold and the Home Office upholds in the United Kingdom. Could I be certain that that is happening in 27 countries of the European Union? The answer is no, I cannot be, but I do believe the only way we are going to get that to happen within the jurisdiction of individual countries is to ensure that you have a Directive that is bought into by the widest possible community in Europe. Then you can begin to have the debate and discussion to ensure that appropriate levels of scrutiny are in

those countries, and then you can hold out bad practice and put the searchlight on bad practice quite openly in relationship to such an agreed Directive.

Q265 ***Chairman:*** Do you not think that, in examining the appropriate levels of application, we should be ensuring that is in the Directive, in the first instance, once you have reached the consensus?
Sir Mark Walport: We clearly do not want the lowest common denominator. I do not think anyone would argue for that.

Q266 ***Chairman:*** It has been alleged that—
Sir Mark Walport: I think we would say that is not what we are arguing for. I think what we are arguing for is the best regulation, and that should not be equated with the most regulation.
Sir Leszek Borysiewicz: We also have to be very careful as to how far a Directive of this sort should, for example, interfere with the internal governance of Malta or Cyprus or other countries. What we have to then do is examine what practice is put in place in those countries, and it is reasonable for the Commission to ask for guidance as to how far an agreed Directive has actually been implemented in those countries, but not to be directive in how a country actually polices it. Every major country in the European Union has its own structures in place. I believe the ones in the United Kingdom are very good and might serve as a model for other countries in the European Union.

Q267 ***Chairman:*** I think the suggestion is that it should be reviewed every five years. Do you think that is appropriate? I know you have unhappiness about timescales.
Sir Leszek Borysiewicz: I have unhappiness about timescales because I think some countries may take a lot longer to achieve the sorts of standards that we would want, from my own knowledge of the system.

Q268 ***Chairman:*** As we have seen from 1986.
Sir Leszek Borysiewicz: However, we also must remember that since 1986 we have had a large number of countries who have joined the European Union, and we do have to ensure that they are brought into the discussions that are currently taking place.
Sir Mark Walport: In ensuring that, we should be constantly alert, so it is not a question of saying there will be a review in five years because if something arises in one year which resulted in an improvement in animal welfare it should be implemented. I think it is a question of a constant awareness rather than, again, a rule-based system. There is a certain irony that we have been discussing the welfare, for example, of decapods, when, of course, the biggest harm to decapods comes from the millions of them that are consumed across the restaurants of Europe, where welfare standards do not really form part of the discussion at all.

Q269 ***Chairman:*** There are still a few contradictions around.
Sir Mark Walport: There are indeed.

Q270 ***Chairman:*** Gentlemen, you have been very helpful indeed. Are there any final comments or points you may wish to bring to us?
Sir Leszek Borysiewicz: From my perspective, my Lord Chairman, I think the most important issue to remember is that, by and large, we are all agreed—and the point I have made across the countries—that actually there is a need for a revised Directive. This one still falls well short of where we believe it should be; that we should give adequate time in order to have the debate and discussion around the very important issues that this Directive has, and I believe that that this process, eventually, will give the best opportunity for full implementation right across the European Union. So engaging in that discussion and engaging in that debate is extremely important. What I am more concerned about are the diktats that are enshrined in this Directive, as currently drafted, and the failure of the Commission to take on board the very real discussions that took place in the Agriculture Committee of the European Parliament and others with a large number of amendments accepted through those committees and, indeed, some of the statements coming from the Commission, basically, just saying: "We will carry on as if that debate had never happened."
Sir Mark Walport: The only thing I would like to add—because I think it has not really come up in much in the discussion—is that it seems curious that this is a Directive that has come from Environment DG rather than from DG Research. One thing that it would be helpful for you to enquire more into is to what the extent of the involvement of DG Research was in the formulation of this Directive.

Q271 ***Chairman:*** We are going to Brussels fairly soon, so we will raise precisely that question.
Sir Leszek Borysiewicz: Anecdote suggests that there was very little involvement of DG Research in any consideration of this, in the first instance.
Chairman: Nothing more from the Committee? Thank you very much indeed.

Supplementary memorandum by the Wellcome Trust

Principles of Appropriate Levels of Scrutiny, Checks and Balances for the use of Animals, Including Non-human Primates, for Research

1. The current process for the approval of animal research proposals in the UK demonstrates that the use of animals in research only occurs where it is ethical, and scientifically justified. This includes ensuring that the use of animals for research is only permitted when no alternative research techniques exist. A brief summary of this process is outlined below:[1]

Institutional level

2. A scientist typically formulates a research idea in collaboration with internal and external colleagues.

3. Proposals to use animals in scientific projects are individually scrutinised by the UK competent authority, the Home Office, and are regulated by the Animals (Scientific Procedures) Act 1986 A(SP)A. Project licences and personal licences are only granted subject to conditions of the A(SP)A,[2] including those relating to animal welfare.

4. An "Ethical Review Panel" (which includes a lay member) within the researcher's institution approves project licences for research and provides comments and guidance on the ethics of the application, but not normally on its scientific merit.

5. The Home Office Animals (Scientific Procedures) (ASP) Inspectorate closely monitors and inspects all licensed laboratories to ensure the appropriate standards in animal research.

Funding body level

6. In some instances, a researcher may submit a short preliminary application to assess the merit of their research idea and to develop the proposed application. This is compulsory for all proposals requesting the use of non-human primates.

7. A Grants Advisor reviews a main grant application. As part of the application process, the proposal is sent for scientific assessment by independent expert peer reviewers, who may include scientists who are not animal users.

8. If the application contains cats, dogs, equidae or non-human primates, the grant is also referred to the "National Centre for 3Rs" (NC3Rs).[3] The NC3Rs provides advice and expertise to funders in the areas of animal welfare and the 3Rs. This helps ensure consistency across funders in approving grants containing these categories of animals.

9. Comments from both peer review and the animal welfare assessment are collated and reviewed.

10. Where NC3Rs has reviewed the grant, outstanding questions or refinements are passed to the grant applicant. Dialogue between applicants and the NC3Rs will continue via the funding agency until NC3Rs is satisfied.

11. Following peer review, the grant is sent to the appropriate Funding Committee for consideration and for a decision to approve, or reject, the grant.

12. The final decision on a grant is subject to the researcher holding the necessary and appropriate Home Office licences and in compliance with Trust policies on animal welfare.[4] Grants containing non-human primates (NHPs) are additionally subject to the NC3Rs guidelines: "Primate accommodation, care and use".[5]

13. If the grant contains rhesus macaques,[6] the main funders of non-human primate research in the UK stipulate that researchers must source animals from the UK-based "Centre for Macaques" (CFM).[7] The researcher contacts CFM pre—and post-approval to discuss requirements for their research proposal.

[1] This summary is from the perspective of an applicant to the Wellcome Trust, though the process is broadly similar for applicants to other academic research funders including the Medical Research Council.
[2] www.homeoffice.gov.uk/science-research/animal-testing/
[3] www.nc3rs.org.uk National Centre for the Replacement, Refinement and Reduction of Animals in Research
[4] Based on the principles set out in the document "Responsibility in the use of animals in bioscience research: Expectations of the major research council and charitable funding bodies" (www.wellcome.ac.uk/About-us/Policy/Policy-and-position-statements/WTD040129.htm)
[5] http://www.nc3rs.org.uk/downloaddoc.asp?id=418&page=277&skin=0
[6] Rhesus macaques are the predominant species of NHP used in academic research.
[7] The Trust, and the Medical Research Council have provided "core funding" to CFM since it was founded in 2002 to ensure the highest level of welfare and quality of animal.

Post-approval

14. During the life of a grant, Grants Advisors maintain a "watching brief" on the grant. Refinements to the research are subject to approval by the Trust.

15. In the case of NHP grants, a site or office visit is conducted within 12–18 months of the start of the grant to discuss progress. For international awards, this visit may take place prior to final decision by the Funding Committee.

16. For NHP grants, the Trust additionally requests that applicants specify individuals who will be involved in the research and make the Trust aware of any change in post-holders or if any serious difficulties arise in the conduct of experiments.

17. At the end of grant, the researcher completes an "end of grant report", which includes an assessment of numbers of animals used and 3Rs principles applied to the research.

June 2009

Supplementary memorandum by Professor Max Headley

NOTE OF CLARIFICATION IN RELATION TO ENCOURAGING THE BEST REGULATORY SYSTEM FOR EUROPE THROUGH THE REVISION OF DIRECTIVE EU 86/609

1. This note is intended to follow-up and clarify aspects of the oral evidence given by Professor Max Headley to the Committee on 24 June 2009.

2. Our primary concern is to ensure that the revision of the Directive 86/609 allows Europe to develop a good regulatory system for animal research. The views of the UK bioscience sector are closely aligned with those of the UK Home Office in seeking a Directive which is clear, proportional, consistent and not overly-prescriptive.

3. As the evidence from the UK bioscience sector pointed out, the current proposal is confusing and introduces a number of unnecessary new bureaucratic and restrictive measures. These could both generate unnecessary administrative burdens and impose restrictions that would hinder research despite not serving to promote animal welfare or the 3Rs.

4. In many ways, the proposal from the Commission matches aspects of the Animals (Scientific Procedures) Act 1986 in principle. The UK is widely regarded as already having a strict regulatory system. As a result, Home Office officials have considerable experience in how such a regulatory system can work in practice, and how it can best be applied. We therefore greatly value their input to the process of the revision of the Directive, and indeed have liaised closely with them in developing our input to the EU Parliament and are continuing to cooperate in their development of strategy via the Council of Ministers.

5. It is widely acknowledged that both the original wording and the application of the UK regulatory system under ASPA resulted in a number of problems with respect to administrative burdens. This was highlighted in 2002 by the House of Lords Select Committee on animals in scientific procedures, as well as by the Davidson review in 2006. We have welcomed the commitment of the UK Government to a better regulation agenda and the establishment of a dedicated Home Office "animals in scientific procedures better regulation program", which we strongly support. Indeed, over the last two to three years we have been working progressively more closely with the Home Office in addressing these issues. We are pleased to see that just last week the Home Office proposed a new project licence application form, which looks to be a significant improvement on the previous version. We are confident that this, in addition to other measures (some already delivered), can help to reduce the regulatory burden in the UK.

6. We recognise concerns that better regulation should not undermine animal welfare standards. Indeed, we would hope the opposite would be the case—namely that with less time spent on bureaucracy, more time and effort can be spent by both the Inspectorate and scientists improving animal welfare and applying the 3Rs. In that light we have welcomed the constructive input from other organisations, including the RSPCA and the NC3Rs, into the better regulation program.

7. We emphasize that our concerns over the current operation of ASPA are being addressed via other fora. We cite our experience over the wording and operation of ASPA only to inform our approach to the revision of the Directive. We believe that this experience is important in highlighting pitfalls that in the combined interests of better science and better welfare should be avoided in the revised Directive. We believe the Home Office shares this aim.

8. In this light the following table shows in simple terms some of the bureaucratic and restrictive measures in the draft Directive which exceed ASPA, and that we consider would be likely to significantly hamper research.

SUMMARY OF BUREAUCRATIC AND RESTRICTIVE MEASURES IN DRAFT DIRECTIVE EU 86/609

Proposed measure	*Problem*
Increasing scope to invertebrates and immature forms	Bureaucratic burden, scientifically restrictive, impedes 3Rs agenda, unworkable
Inclusion of animals bred for tissues	Bureaucratic burden
Restrictions on re-use	New restriction—would undermine 3Rs
Restrictions on use of NHPs	New and seriously problematic restriction without clear policy objectives
Compulsory move to F2 +	New restriction which could undermine supply and may not serve welfare
Restrictions on humane killing to listed techniques in Annex	New restriction which could undermine 3Rs
Restriction on prolonged suffering	New restriction which could seriously impair research
Mandatory sharing of organs and tissues	Bureaucratic measure with minimal benefit
Authorisations for all projects, including those involving invertebrates	Bureaucratic proposal which lacks proportionality to welfare costs
Withdrawal of authorisation	Bureaucratic proposal which lacks proportionality
Care and accommodation—mandatory standards for cage sizes with no scientific justification	Administrative and cost burdens, together with lack of flexibility; lack of clear legal basis
Application for ethical evaluation and authorisation	Excessive, confusing and bureaucratic information requirements
Retrospective assessment	Bureaucratic burden with unproven benefit
Retrospective reporting	Bureaucratic burden with unclear objective
Mandatory data sharing	Bureaucratic burden with unclear objective and unworkable implementation
National reference laboratories	Expensive, duplicative, misunderstands nature of 3Rs research
National animal welfare and ethics committee	Overly prescriptive proposal
Poor drafting	Lack of flexibility and likelihood of legal challenges delaying research

Submission developed between Max Headley and Understanding Animal Research

July 2009

WEDNESDAY 1 JULY 2009

Present	Arran, E	Jones of Whitchurch, B
	Brooke of Alverthorpe, L	Livsey of Talgarth, L
	Brookeborough, V	Palmer, L
	Caithness, E	Sewel, L (Chairman)
	Cameron of Dillington, L	Ullswater, V

Examination of Witnesses

Witnesses: **Dr Vicky Robinson**, Chief Executive, and **Dr Mark Prescott**, Programme Manager, Representatives of the National Centre for 3Rs, examined.

Q272 ***Chairman:*** First of all, thank you very much indeed for finding time and coming to see us and help us with our inquiry. We have taken quite a bit of evidence already from various interests and I think that it is very important to address the issue of the 3Rs. There are two formal things that I have to say. One is that this is a formal evidence-taking session, so a note will be taken and you will receive a transcript of the evidence in the next few days and will have the opportunity of correcting any errors that have crept in. The second point is that we are technically being broadcast through the webcast system. This should not necessarily fill you with fear or thoughts that you are going to get people writing in as fan mail though we have had recent evidence that one or two disturbed, poor, sad individuals do listen to us, but not very many. Would you like to start by making any brief opening statement or would you prefer to go straight on to the questions and answers?
Dr Robinson: I think an opening statement.

Q273 ***Chairman:*** Please, do.
Dr Robinson: Good morning and thank you very much. I am Vicky Robinson and I am Chief Executive of the NC3Rs. I am a molecular biologist by training; I spent 10 years as a research scientist before moving to work at the RSPCA's research animals department. I was appointed to head the NC3Rs in 2004.
Dr Prescott: My name is Mark Prescott and I am a programme manager at the NC3Rs. My training is as a zoologist and primatologist; I have a PhD in primate behaviour and ecology. Previous to the NC3Rs, I too worked at the RSPCA in their research animals department. I was a member of the technical expert working group convened by the Commission to begin the process of revising the Directive and I was also involved in the revision of Appendix A to the Council of Europe Convention ETS 123, as a member of the primate expert working group but also as an observer to the multi-lateral consultations representing the World Society for the Protection of Animals.
Dr Robinson: May I add a few words about NC3Rs in general because I am conscious, having read some of the evidence you have taken already, that you have heard a little bit about the organisation and I think that it would be helpful in terms of the framework for the answers for our questions today to have a little bit more information about what we do. We are an independent scientific organisation and we were established in 2004 by Lord Sainsbury when he was the Science Minister. The establishment of the centre really reflected a recommendation in a report by a House of Lords Select Committee which looked at the use of animals in scientific procedures and said that there really should be more put into the 3Rs and, in order to facilitate that, it was necessary to have a national centre and, as a result of that, the NC3Rs was launched in 2004. Our role is really to drive the uptake and the development of the 3Rs across the life sciences and we do this because we believe that it benefits science and innovation and improves animal welfare. The approach that we take I think is different to many organisations in that we want to work with and engage with the scientific community because really, if you do not harness the expertise of the scientists and the knowledge that they have, then you are really missing an opportunity. Our work really revolves around aligning the best science, the best technology and the brightest minds with the 3Rs and I think that that has worked very successfully. We are largely funded by the Government through the Medical Research Council, the BBSRC, the Home Office and we also have funding from the pharmaceuticals and chemicals industry and the Wellcome Trust. We have an independent board which oversees what we do—that used to be chaired by Lord Turnberg—and we have a relationship with the MRC in that we sit in its building—that is where we live—and we have a service level agreement with them to provide some services and support and processes. Our work is divided into two. We are a research funding body, so we invest in research in universities and in industry. It is high-quality research; it has to meet a very high threshold equivalent to the Research Council threshold for

funding. We have awarded 41 grants to date totalling £8 million across a whole range of disciplines in the life sciences. The aim is delivering advances in the 3Rs. We also have activities led by the office and these very much focus on working with scientists and universities and industry, working with regulators, working with learned societies and research funding bodies to look at new opportunities for the 3Rs, to provide a safe forum for data sharing, for exchange of ideas, knowledge and concerns. We have a whole array of relevant programmes from looking at how you minimise the use of primates in the development of new pharmaceuticals through to how you would replace the use of animals in nausea and vomiting research. So, very different types of projects and again very much a scientific basis for our discussions and our work, and I think that this has proved to be very successful. We are not part of the regulatory process in the UK. We obviously work alongside the Home Office and work with scientists who use animals but we also work with scientists who do not use animals because that is also important in terms of horizon-scanning and accessing other types of technologies. Those are a few words of introduction.

Q274 ***Chairman:*** Thank you very much; that is very helpful. I would like to go straight to the Directive. Do you think that the case has been made to have a new Directive? Do you agree with the Commission in their statement that the Directive provides a solid basis for a full implementation of the principles of the 3Rs?
Dr Robinson: To answer your first question, I think it is timely to review the Directive. I think that things have changed over the last 20 or so years and it is important to reflect on those changes and to make sure that we have a regulatory framework that provides for legitimate scientific needs and protects animals. So, we fully agree with the need to revise the Directive and we are very supportive of that. To answer your second question, does it provide a solid basis for the implementation of the 3Rs, I would say partially. We are very pleased that it includes explicit reference to the 3Rs and it is important that the 3Rs are implemented, but I think that the proposal and some of the suggestions in the proposal to try and accelerate development of the 3Rs are rather disappointing and miss the point, actually.

Q275 ***Chairman:*** Say more.
Dr Robinson: I completely agree with the principle that you should not be allowed to use an animal if there is an alternative and that you should minimise any suffering and minimise the numbers of animals used and you can see how legislation can provide for that framework. I think it is very difficult to see how the legislation, and particularly some of the suggestions for national reference laboratories for example, can accelerate the development of the 3Rs. What we want to see is the 3Rs' existing knowledge being implemented and I think that the proposal will provide for that, as the UK system does, but if you really want to see advances and to see a replacement, reduction and refinement, then I think that the Directive does not include that. I think that it is very difficult to see how you could include that in a piece of legislation because what you want to do is to engage the scientific community across the board, to get them to understand that the 3Rs are an important research objective and a desirable output and that we need the best minds involved. It is not clear to me that you could do that effectively through the proposals that are included.

Q276 ***Chairman:*** Could you do it if the Directive were crafted differently or is it something that you really cannot achieve through a Directive in any case?
Dr Robinson: My personal view is that it would be very difficult to achieve through a Directive. I think what the NC3Rs has done—and the NC3Rs, as I have said, is not part of the regulatory framework but we have delivered change in the 3Rs very quickly actually over the last five years—is to change the mindset of many scientists in their view of the 3Rs and I think that has come because we are working not within the regulatory framework but because we are saying that this is about good science, it is about doing the best science and it is about maximising the knowledge and expertise to deliver benefits for animals in science. I do not think that you need regulations to deliver that.
Chairman: Let us move on to national reference laboratories.

Q277 ***Earl of Arran:*** National reference laboratories which you have touched on already. There are four questions but I will deal with two at a time, if I may. The first is, what do you think are the benefits of national reference laboratories for alternative methods? Secondly, as you are probably well aware, the RSPCA have said that they would like to see an expansion in the role of the ECVAM. What are your views on that, please?
Dr Robinson: In terms of the role of the national reference laboratories, the wording suggests that this will very much focus on the use of animals in regulatory toxicology, the safety testing of pharmaceuticals and chemicals. That accounts for a small proportion; an important proportion of animal use but a small proportion. I think that it will be a retrograde step in that it will focus on one area of animal use when really what you need to do is focus on all areas of animal use if you are going to make progress in terms of the 3Rs. That would be my first concern. My second concern is that really there is wide understanding within the scientific and

regulatory community that, if we are to find alternatives for some of the animal tests that are currently required, then we need to have lots of different approaches. There is not going to be a one fit approach. We are going to need to exploit tissue engineering, systems biology and so on. My concern would be that you could not have that breadth of experience in one laboratory. I think that it would end up being a white elephant. I think that what you need to be able to do is access the best labs that have the best technologies and have the expertise in those technologies and not have a lab where you have scientists waiting around to validate alternatives. I just do not think that it would work in practice. As regards your second question, I think that ECVAM has an important role to play in terms of validation of regulatory tests and ensuring that, once they are validated, they are put into the regulatory framework. If you look at the current European environment, you have the Cosmetics Directive that is banning the use of animals in safety testing and demanding as a result the development of alternatives. That is one environment that is really putting pressure on the development of alternatives. You also have the REACH legislation which covers chemicals that is going to have a significant impact on animal use, increasing animal use. Conservative estimates are that over 10 million animals will be used over the next few years to accommodate that legislation. I think to give ECVAM more to do at a time when it really should be focusing on its core goals has the potential to dilute its role and I think that that would be unfortunate.

Q278 ***Earl of Arran:*** You mentioned in your answer to the first question about selecting the best labs. Would it not be rather invidious to do that? How would you set about that?

Dr Robinson: I think that you do it by peer review. Some of the techniques that you would be looking for would be so specialist that you could effectively select labs. I think it is a role that NC3Rs could fulfil; we could certainly help identify the best labs for particular purposes and that is something with which we would be very happy to help. Often these validation studies require more than one lab, so I do not anticipate that it would be a problem.

Q279 ***Earl of Arran:*** Thank you for that and I am going to move on to two more questions. Firstly, the National Animal Welfare and Ethics Committees want to share best practice. What is your view of that proposal? Finally, have you alternative or additional suggestions for ways of encouraging Member States to "contribute to the development and validation of alternative approaches"?

Dr Robinson: I think that the issue of the National Animal Welfare and Ethics Committee is trickier to answer in a way. What is being proposed is a committee with a very broad remit which would require a broad expertise to deliver what it would be required to do. I think that some of what is being proposed is already fulfilled by our own Animals Procedures Committee; I think that that Committee delivers what it does very well. Some of what is being proposed is actually delivered by NC3Rs. I do not think that we should be changing the UK model to accommodate having this new committee. In terms of delivery of the 3Rs, as I have indicated, I think it is very difficult to see how a single committee charged with such a broad range of things without dedicated staff and a significant budget could really help accelerate best practice. So, I would be concerned if we were required to have one in the UK as is currently prescribed in the proposal.

Chairman: Let us move on to data-sharing.

Q280 ***Lord Palmer:*** As things stand at the moment, we understand that the proposal will require Member States to share research data in order to avoid unnecessary duplication. What are your views on the scope for greater data-sharing? Do you think that more data could and should be shared in order to promote the 3Rs even further?

Dr Robinson: Yes. My experience is that data-sharing is very important. The NC3Rs did a survey of scientists using animals in the UK several years ago and one of the questions that we asked was, what most important thing could be done to help reduce animal use? Data-sharing came up pretty high in that list. Our experience through the work that we do in NC3Rs is that data-sharing is hugely effective. Just to give you an example, we have a project that we have led for the last couple of years involving 18 pharmaceutical companies and what we have done is shared data on one particular test—it is called acute toxicity and that test is particularly unpleasant, it can involve the death of the animals—and, by sharing data, what we have been able to show across the industry is that you actually do not need to do that test to develop medicine safely. As a result of the data-sharing and the NC3Rs' industry work, the international regulations are being changed to remove the need to do these acute toxicity tests for pharmaceuticals. I think that a lot can be gained by data-sharing. Whether the proposal as it stands will help that I am less clear. I think that it is better for people to volunteer data for projects with which they are involved rather than be forced to do it. I think that there are issues about confidentiality.

Q281 ***Lord Palmer:*** This is obviously very important.

Dr Robinson: Yes. People are much more willing if they feel that they are part of the process and that they have something to gain by it and, with a blanket requirement for data-sharing, I find it very difficult to see how that information could usefully be used for 3Rs' benefit. I think that you have to take a much more targeted approach to data-sharing and ask what data do we need to allow animal use to be reduced or refined or replaced, and certainly that is the approach that we have taken and it works very successfully if you can provide a safe environment for data-sharing. We have done this extensively with the pharmaceutical industry and it works well. I think that the proposal as it is written will turn people off data-sharing.

Lord Palmer: That is very interesting. Thank you.

Q282 ***Viscount Ullswater:*** Dr Robinson, it seems from the evidence that we have heard that sometimes there has to be retesting of drugs which are made in one country and then used in another. It is sort of batch testing; I am not sure that I have even got the right wording. That seems to be a use of a number of animals, whereas could the data that is produced in one country not be sufficient to be recognised in scientific terms for the use of the drug or the chemical in another country without having it retested on animals?

Dr Robinson: Yes. I think that you have raised a very good point and you did indeed use the right term, it is batch testing. I think that the problem with the proposal is that it talks broadly about data-sharing and I think that data-sharing can be very useful in some scenarios. There are cases, for example vaccine batch testing, where animal studies will be repeated even though there is data from another country and I think that that is unacceptable. I think that if the data is available, then there should be processes in place for data-sharing of that type of thing. Within European legislation, for example within the REACH legislation, there is the provision for data-sharing for companies that have common chemicals and even reimbursement for data-sharing. I think that provision does exist and I think that it would be unacceptable for repeat testing of things where there is already data available. I think that the situation is different in academia. I think that it is quite hard to see cases where animal studies are repeated over and above what you would expect as part of the normal scientific process.

Q283 ***Viscount Ullswater:*** What are you, as the National Centre, doing about pushing that forward and making certain that the use of animals in batch testing, or whatever the word is, is eliminated?

Dr Robinson: We are not specifically doing anything on the batch testing issue. It is something that we could look at and one of the reasons why we are not doing something is because other organisations like the RSPCA are doing a lot of very good work in this area and we do not want to duplicate effort ourselves in that area. In terms of the REACH legislation, we do have an active programme looking at how you can avoid animal use and certainly prevent repeat studies and redundant studies taking place.

Q284 ***Viscount Brookeborough:*** Do you have any estimate of what duplication is taking place in the initial stages of research into something? Before research takes place it is authorised and therefore there could be a number of authorisations which come up in exactly the same field. Is there any chance of reducing duplication at that stage or to what extent does it occur?

Dr Robinson: I have to say from my experience—and I am involved on a number of ethical review processes for example that look at project licences in their early stage and several of the committees I am on have similar research fields—that I have in the last five years never seen anything that looks like duplication. Scientists are funded to do different things. You do not get funding for example from a research council if you are trying to do something that somebody else is already doing. I actually have not seen any real evidence of duplication. I know that it is something that does raise concerns with some organisations but I find that actually, as a general principle, there really does not appear to be any tangible evidence certainly that I am aware of.

Q285 ***Viscount Brookeborough:*** So, the part of the Directive that refers to reducing duplication you think is not really based on very much evidence?

Dr Robinson: It does not seem to be. I think that there clearly is duplication with the vaccine batch testing but I think to make a sweeping statement that there is duplication would be grossly unfair from many areas of animal use.

Chairman: We will have to move on and turn to Lord Cameron on human primates.

Q286 ***Lord Cameron of Dillington:*** Your evidence suggests that the use of non-human primates is of concern to you. In fact, I think one could probably say that it is a concern to everyone in different ways on different sides of the fence. The proposal is to limit research to research related to life-threatening and debilitating conditions. Some people have put to us that that is too restrictive, and I am wondering what your views are.

Dr Robinson: I think that the use of primates is clearly a very difficult and emotive issue and I think it is something that both Mark and I feel very strongly about and we have a large programme of activities in NC3Rs looking at how you can minimise primate

use. I think that the wording "debilitating and life-threatening" really is not helpful. It seems to be an area that is causing a lot of concern on all sides, if you like. Rather than words that restrict and in many ways are very subjective, we feel that it is much better to have a framework that takes account of whether this is an important question to ask if you want to use primates. Is the science robust and has it been rigorously reviewed? Has there been a full ethical evaluation? Is there an alternative to using the primate? Is using the primate really going to give added value over and above the other available approaches? Can we be guaranteed that the welfare of the animals will be of the highest standard? Will the results be retrospectively evaluated to ensure that the goals have been achieved and the purported benefits of using the primates have actually been delivered? I think that is a much more reasonable framework rather than saying life-threatening or debilitating because that means different things to different people.

Q287 ***Lord Cameron of Dillington:*** It is slightly longer in the text from the sound of it.
Dr Robinson: Well, yes, but I think it would be fairer.

Q288 ***Lord Cameron of Dillington:*** My second question is on the use of F2 animals and the proposal to set a date by which they become compulsory. What is your view on this?
Dr Prescott: We would support the need for a feasibility study to look at not just the animal welfare issues involved but also the scientific issues and the potential impact upon supply. So, all of the issues involved and I think that it is quite a complex picture. Whilst there seems to be quite a lot of support amongst many of the stakeholders for an eventual move to F2 to minimise the capture of animals from the wild to support the breeding colonies, I think the contentious issue is how realistic are the timescales that are proposed. I think that without a proper rigorous feasibility study, it is just not possible to set timescales.

Q289 ***Chairman:*** I notice that with marmosets the timescale that is indicated at the moment is something like 18 months. That should mean that we already know that it is possible to do. Do we?
Dr Prescott: Yes, we do. The marmosets that are used certainly within the UK and probably within the European Union are from quite long established closed captive colonies, so there is no drawing of marmosets from the wild to feed those captive colonies. So, the animals that are being used in research will be F2 and perhaps generations beyond F2. That is partly possible because we use smaller numbers of marmosets and we have had the colonies available historically and have bred animals from those, but also because the generation time for the marmosets is much shorter than it is for the macaques that we use in research. Also, marmosets typically in captivity would have twins or even triplets or quadruplets whereas the macaques tend to have just singletons. So, it is much easier to breed sufficient F2 animals more quickly and they are already available and I think that is why they suggested that 18 months is the timescale in the proposal for marmosets.

Q290 ***Chairman:*** It is all right if we say that that would satisfy the European market if the effect of Europe going down this route was that globally it became an F2 requirement that practice followed. Do you think that market could be satisfied?
Dr Prescott: I do not think that it would be an issue for marmosets. I think probably the colonies in the States and elsewhere in the world that use marmosets also have F2 animals available. It is more of concern with the macaques I think because, if we move towards only using F2 animals or macaques within Europe, at the moment I think there is a possibility that it would make the UK less competitive and make it a bit more difficult to obtain animals for the EU. Perhaps this would mean that researchers within the EU would be at a disadvantage compared with the rest of the world.

Q291 ***Chairman:*** The macaques' timetable is quite far out, is it not?
Dr Prescott: If I remember correctly, I think they are suggesting 10 years.
Chairman: Let us move on to care and accommodation standards.

Q292 ***Baroness Jones of Whitchurch:*** With care and accommodation, we have heard people from the pharmaceutical industry saying that what we have already for example in the UK is fine and that there is no need to go beyond that and the scientific evidence is not there to justify going beyond that. On the other hand, the animal welfare institutions are saying that of course any improvement must be good and also the science has justified further improvement. I wondered where you stood on that division. Which side are you on? Can it be justified? Is the science there to justify it? What would be the implications for further improvements in the UK scientific industry?
Dr Prescott: I think that I would like to make a number of points. Firstly, clearly if animals are going to be used in research, then they ought to be afforded the high standards of care and accommodation and that is important not just for animal welfare reasons but also because there is an increasingly accepted view that good welfare and good science go hand in hand. So, good welfare quite possibly could improve the quality of the science that is done with animals.

We very much support that view and we are very pleased to see Appendix A transposed into the Directive proposal as Annex IV, although we are concerned that some of the explanatory text that was in Appendix A has been lost in that transposition. The explanatory text was useful because it put the space allocations into context and it contained good recommendations for refinement of laboratory animal use and care. I recognise that a number of stakeholders have concerns about the scientific evidence that was used to support the recommendations in the Appendix and Annex. Having been involved, I have to say that the available scientific evidence at the time was used. Having said that, there were areas where there just was not scientific evidence to support specific space allocations for specific species and, in that instance, it was necessary for the expert working groups to rely on expert opinion and good contemporary practice. That approach is quite widespread and defensible and the background information which supports the space allocations is available on the Council of Europe website, so the process was transparent. As well as taking account of the available scientific evidence, there was also a degree of compromise within the expert working group, amongst the different stakeholders. We are quite comfortable with the proposals as they stand and would support them as mandatory minima for the care and accommodation of animals across Europe. We do recognise that some establishments and sectors may have difficulty in meeting some of those standards and I think that it would be appropriate for them to be given the time and the support in order to achieve those standards. From our experience visiting laboratories and working with the UK scientific community, we would say that very many establishments already apply the standards that are in the new proposal because either there are no or small differences between the proposal and existing Home Office codes of practice or because the establishments have known about the development of the Appendix, which took some seven years, and have already begun to put new standards in place so that they can meet the requirements that come out of Europe.

Q293 ***Baroness Jones of Whitchurch:*** What the pharmaceutical industry was saying to us was that we already have good care standards in the UK and, the more you drive them up, the more you are driving the whole sector into Asia and less regulated places. So actually it is going to have a perverse effect and there will be more research done in even worse conditions as a result.
Dr Robinson: My experience, looking around the UK pharmaceutical industry, is that they have very high standards and they all say that, if they are putting work overseas, it would be done to a comparable standard in the UK. So, I am not sure that I really understand the argument that having higher standards in the UK drives them to go elsewhere because they were very clear certainly in our discussions with them that the standards they expect overseas are what would be comparable with the UK. It is quite difficult to understand, I think.
Dr Prescott: I think perhaps the reasons for moving overseas might be other drivers rather than the high standards of welfare which many of them already meet. So, it does not quite seem to fit.

Q294 ***Baroness Jones of Whitchurch:*** It is not about the care side of it?
Dr Robinson: I do not think that that is the only factor that makes people choose where they invest and I think what is interesting is that, if you look at the UK, it has a very strong base of contract research organisations and many companies worldwide will use the UK CROs because of the high standards that they provide in terms of welfare.

Q295 ***Viscount Brookeborough:*** To what extent do you think bureaucracy plays a role, and perhaps the length of time that it takes for authorisation compared with other countries, even though the standards that may be used in China may be identical but the length of time for authorisation may be much shorter?
Dr Robinson: I think that that is a good point. I am involved with five ethical review processes and I am also on the committee that the Government established to look at better regulation of the Animal (Scientific Procedures) Act. I think that without doubt there are occasions where the process is excessively bureaucratic and that can introduce delays. However, an enormous amount of work has been put into reducing the level of paperwork and the time it takes to get a licence and I think that it would be unfair if there were a view that six months was a norm for getting a licence from the start of the process through to getting it.

Q296 ***Viscount Brookeborough:*** If you do not know how long it is going to take before you start, then you have to assume that it may be six months.
Dr Robinson: I think that it is a lot less than that. From memory, 30 days is usually the time. I think that the process is complicated but sometimes the delays are at the end with the scientist and the bits that they are required to do. So, I do not think that we can necessarily blame the regulatory framework. When it works well, it works very well. There will always be cases where it is complicated and that is unfortunate but I think that, on the whole, the bureaucracy is reducing. Certainly if you talk to people from other countries, they will say, "Actually,

it is pretty similar here" but we never get to hear about that really.

Q297 ***Chairman:*** I would like to check a couple of things. Dr Prescott, you said that some stakeholders may have difficulty in meeting the requirements and should be given time. How long should they have from the adoption of the Directive?
Dr Prescott: I do not think that I can answer that question. I am aware that the laboratory animal breeders are concerned about the space allocations for rodents and rabbits for example, and the important point is that there is a sensible and realistic transition period should the Directive come to be translated into early UK legislation such that people have a reasonable time in order to get up to standard to meet those requirements for accommodation and care. I do not have the specialist knowledge to put a figure on it, I am afraid.

Q298 ***Chairman:*** The other point is that I do understand—and I am speaking from a position of total ignorance—that with the use of rodents in research on diabetes, you may well start with an animal that is relatively large and there is very quick and dramatic weight loss. Is there any way of recognising that?
Dr Robinson: The regulations should always take account of welfare issues and scientific justification and I think that we can have a set of standards that provide the legal minima, the benchmark if you like, but there will always be circumstances where there should be flexibility.

Q299 ***Chairman:*** It is difficult to catch that in a Directive, is it not? At the moment, it is all done on body weight and floor area required for body weight and it does not start at the middle or at the end, if you know what I mean.
Dr Robinson: Yes. I think that it does require some pragmatism involving for example the vet and so on and I think that flexibility is absolutely essential. For some studies, it would be entirely inappropriate to give animals the full amount of space for studies that affected their movement for example. So, it does need to have some pragmatism in there but I take your point that it is quite hard to have the wording.

Q300 ***Lord Brooke of Alverthorpe:*** Are there any other aspects of the Directive proposal, on which you wish to offer views, particularly in relation to the implementation of the 3Rs?
Dr Robinson: I think just to reiterate that it is important that the 3Rs are included and we are very pleased about that. The ideas in the proposal around how to accelerate the development of the 3Rs really require a bit more thinking and it is much better to have an engagement with the scientific community and that can be done effectively without regulation.

Q301 ***Lord Brooke of Alverthorpe:*** In opening, you said that you felt that your body had been successful since it was established. How do you judge its success?
Dr Robinson: I think that you have to look at outputs and outcomes. I think it is early days; this is our fifth year. If you look at the research that we are funding, the research is starting to deliver in terms of publication, so that is more on output, and publications in good journals, but we are also starting to see studies where the number of animals are reduced as a result of the research.

Q302 ***Lord Brooke of Alverthorpe:*** Have they not gone up for one period?
Dr Robinson: If you look at the statistics that the Home Office provide, they are one benchmark of the use of animals in science and I do not think that they represent a particularly good benchmark of the efforts that have been put into the 3Rs. I think more what they reflect are regulatory changes, changes in science and changes in research investment. It is very hard to tease out from the numbers the impact on reduction and refinement and replacement. I think that you have to look in specific scientific disciplines within particular areas of research and we are certainly seeing in the types of research that we are funding that these numbers are going down. It is a slow process unfortunately.

Q303 ***Lord Brooke of Alverthorpe:*** If you do not mind me saying so, as an outsider, I find it very difficult looking to see who ultimately is responsible for accountability on applications to the 3Rs and whether targets are set or not set. Alternatively, is it the Home Office or is it the Animal Procedures Committee? Everybody seems to have a very similar view but it is very difficult when you look at the different sets of evidence which has come before us to identify who ultimately is responsible for the outputs, the success or failure.
Dr Robinson: I think in terms of uptake of the 3Rs, scientists who are using animals are responsible for ensuring that they use animals when there are no alternatives and that they use the minimum numbers of animals and the least amount of suffering. I think it is the scientists who have the licences who are responsible and then the Home Office for ensuring that that is actually enforced. I think in terms of accelerating progress and making new advances in the 3Rs, that is the responsibility of the whole scientific community because that is where the technology and the opportunity lies. I think that it is much more difficult to assign responsibility to individuals or bodies in terms of accelerating

development. In terms of implementation, I think that it is clear.

Q304 ***Lord Brooke of Alverthorpe:*** So, in a time of economic turbulence, if we operate on that basis, there could be a reduction in investment.
Dr Robinson: Quite possibly.

Q305 ***Lord Brooke of Alverthorpe:*** This could be an area in which companies perhaps have to pull back.
Dr Robinson: Yes, quite possibly. Animal studies are incredibly expensive to do and often the alternatives are cheaper and can give better results in some cases. I think that there is an economic as well as a scientific incentive.

Q306 ***Lord Brooke of Alverthorpe:*** So you do not think that there is any need within a Directive to try to set stronger targets for everyone to aim for regardless of economic circumstances that may be encountered?
Dr Robinson: I think that targets sound appealing when you first think about it. I understand that targets are set in many areas. I have been involved in an initiative with the Boyd Group which is an organisation that brings together all sides of the debate on the use of animals to try and reach a position of compromise and one of the things that we have discussed over the last three or four years is, can you set targets? How would they work? What would they achieve? I think it is fair to say that those discussions have gone round and round in circles and have done nothing but really antagonise people at times. I think that has been unfortunately a waste of time; we should have been thinking about putting effort in the last four years on specific projects. I think that just the concept of targets is not always helpful and, in an environment where many scientists have felt persecuted by animal rights extremists for a number of years, I think that the appetite for targets would be low and that it would be difficult to provide incentives.

Q307 ***Lord Brooke of Alverthorpe:*** Are there any additional items that you feel ought to go into the Directive which presently do not appear there?
Dr Robinson: I cannot think of anything, no. I think that Member States should be encouraged to have an NC3Rs-like structure but I am not sure that the Directive is the place to ensure that.

Q308 ***Chairman:*** May I come back to something which was mentioned earlier. Do you have any fears and concerns that one possible result of this Directive may be to lead to the leakage of research to regimes where the level of animal welfare is much lower?
Dr Robinson: I think that is one possibility. The UK is the best place to do animal research. We can guarantee the standards and the scrutiny. I think that it would be naïve to think that research is not going to go overseas for lots of different reasons, not only the Directive, and that that presents opportunities and risks, and risks to animal welfare, and I think that the real concern about the Directive is that it will drive research overseas when we are not ready to address those risks.

Q309 ***Baroness Jones of Whitchurch:*** I have a very simple question following on from your answer to Lord Brooke. Is there a 3Rs movement across the Member States or is it just here? Obviously, you are doing sterling work in the UK. Do you have equivalence in some of the research sectors across Europe or is it just a one-off, that the UK is more for animal welfare than anyone else?
Dr Robinson: Other countries do have 3Rs organisations. The Dutch for example have one and the Germans have a centre. They all tend to work in a slightly different way but I think it is important that you are allowed to meet your national and local needs. So, they work in different ways and have different budgets and I think it is fair to say that NC3Rs has a larger budget than most of the other 3Rs organisations. The 3Rs is a growing movement across Europe and I think that that is important not only for animals but thinking about how you do the best science.

Q310 ***Lord Palmer:*** Are you finding it difficult to recruit scientists up to the grade to help you in your work et cetera and do you think that this is going to be a problem in the future?
Dr Robinson: Finding scientists up to the grade?

Q311 ***Lord Palmer:*** Yes, to help you in your work.
Dr Robinson: I think that we are having the opposite problem. We are overwhelmed by high-quality science and high-quality scientists and trying to keep up with demand, though I guess it is a good position to be in. For example, in terms of the grants that we want to award, we always have more high-quality grants than we can afford at the moment. What we have seen is certainly a 50% increase in the grant applications that we have received this year. We are just about to announce our next round of grant awards. We had 72 applications and some excellent quality work. We use the MRC scoring, so we only fund work that is of an excellent standard.
Chairman: That is it. Thank you very much, indeed. It was a very comprehensive coverage of the area. Thank you.

WEDNESDAY 1 JULY 2009

Present	Arran, E	Jones of Whitchurch, B
	Brooke of Alverthorpe, L	Livsey of Talgarth, L
	Brookeborough, V	Palmer, L
	Caithness, E	Sewel, L (Chairman)
	Cameron of Dillington, L	Ullswater, V

Memorandum by The Dr Hadwen Trust for Humane Research

1. The Dr Hadwen Trust for Humane Research is the UK's leading medical research charity funding and promoting exclusively non-animal techniques to replace animal experiments. We believe that excellence in medical research and safety testing can and should be pursued without animal experiments. We have been working extensively on the revision of Directive 86/609/EEC and in 2008 we published an expert report on the opportunities provided by the revision to advance animal protection, increase transparency and replace animal experiments.[1]

Summary

2. This submission is longer than the six pages requested because we felt it necessary to discuss elements of the draft Directive in detail. We hope the additional material is of use.

3. We have also provided as e-mail attachments two longer publications in case these are of interest ("*Towards a European Science Without Animal Experiments*", and "*Replacing Primates in Medical Research*"), and an Appendix providing examples of current research with potential to replace experiments on primates and advance medical progress in order to alleviate human suffering.[2]

Q1 *Objectives of the Directive*

4. We believe the draft Directive is a proportionate response to current distortions of the internal market in terms of protection of animals, transparency, accountability and enforcement, and in advancement of the 3Rs (Replacement, Reduction and Refinement).

5. We hope that animal welfare and scientific objectives will also be discussed in addition to those involving harmonisation of the European Union (EU) single market. This is in accordance with the Commission emphasis in its explanatory memorandum: "*The current proposal aims at ensuring a level playing field, throughout the EU, for industry and the research community, at the same time strengthening the protection of animals . . .*"[3]

6. In addition, the objective of improving animal welfare is consistent with the Animal Welfare Protocol annexed to the Treaty: "*Member States shall pay full regard to the welfare requirements of animals, while respecting the legislative or administrative provisions*".[4]

7. Improvements to animal welfare will be met by ensuring minimum standards are applied to animal husbandry and to the scientific use of animals. These objectives are also aligned with the Lisbon Strategy calling for the internal market to be further harmonised, and high-quality research and development to be fostered.

8. The objectives also support the implementation of the 6th Environment Action Programme which foresees in Article 7.2a and b that the development and validation of alternative testing methods should be reinforced.

9. The draft Directive identifies implementation of the 3Rs more consistently throughout the EU as being likely to produce scientific benefits. These will result, in part, from more rigorous authorisation, ethical evaluation and retrospective review. Furthering the replacement of animal procedures is expected to have considerable scientific and medical benefits (see Q8), in addition to the economic and animal welfare benefits already mentioned.

[1] Langley G & McIvor E (2008). Towards a European science without animal experiments: Opportunities for the replacement of animal experiments provided through revision of Directive 86/609/EEC. PDF attached to submission email. Publ by & available from the Dr Hadwen Trust.
[2] These publications are not reprinted in this Report. www.drhadwentrust.org/
[3] Commission of the European Communities (2008). Proposal for a Directive of the European Parliament and of the Council on the protection of animals used for scientific purposes. COM(2008) 543 final.
[4] http://eur-lex.europa.eu/en/treaties/dat/11997D/htm/11997D.html#0110010013

10. In animal welfare terms, the existing legislation is outdated in many areas: it is not in line with current public opinion, is insufficiently rigorous in terms of application of the 3Rs and lags behind scientific knowledge of the sentiency of animal species and life stages (see Q4). Differences in levels of training and qualifications across Member States (MSs) lead to variation in standards of animal protection as well as differences in the costs of developing and conducting research projects.

11. One of the leading principles of the 3Rs is to avoid unnecessary testing on animals. However, due to the different laws and administrative procedures in authorisation and inspection arrangements in the MSs, it cannot be guaranteed that duplication of testing will be avoided. Currently there is no harmonised EU approach to ensure an effective exchange of relevant information and data regarding animal use in scientific procedures.

12. Revised EU legislation is one of the instruments by which replacement research can be fostered (see Q8). The Dr Hadwen Trust believes that encouraging research into non-animal approaches and improving the conditions for innovation and introduction of new technologies will put Britain and the EU at the forefront of scientific research globally.

13. Such benefits were indeed recognised by the House of Lords Select Committee on Animals in Scientific Procedures, who wrote: "*. . . all sides of the debate on animal procedures say that animals are highly imperfect models. It will be for the benefit of science, and ultimately of human health, if better methods of research and testing could be developed*" and "*The development of scientifically valid non-animal systems of research and testing is important, not just to improve animal welfare, but to provide substantial benefits for human health*".[5]

14. In response to these comments the British government agreed and added: "*. . . alternative methods are often, in reality, 'advanced methods' broadening the scope and overcoming some of the limitations of existing animal models" and "Replacement methods, such as in vitro screening and computer modelling, can be more reliable, quicker, more efficient and cost effective than animal models*".[6]

15. In order to avoid distortions of the single market, minimum standards of housing and care of animals, accepted humane methods of killing, and rules relating to authorisation and ethical review (including choice of species and equipment) are necessary. Without such minimum standards, the cost of using animals in procedures will continue to vary widely between MSs. This would be detrimental to the UK science base as well as to individual researchers, and could restrict collaboration of scientists working in different MSs and the free movement of labour.

Q2 *International Competition*

16. We believe that better animal protection in the EU should be seen as having a positive impact on international competitiveness in research and testing, not least because poor welfare standards are recognised as having a detrimental impact on data quality and reliability. For example, the Federation of European Laboratory Animal Science Associations (FELASA) has said:[7] "*Pain and distress generally increase variability in experimental results, because of the various neurotransmitter and hormonal responses they elicit. Consequently, an animal in pain or distress is a poor research subject, except when pain itself is investigated*".

17. In this context, we do not believe that companies or academic researchers will want to re-locate their animal facilities to countries applying lower welfare standards. This is to some extent demonstrated already by the high proportion of EU animal procedures being carried out in the UK and Germany, where rigorous regulation (which is in most respects more rigorous than that described in the Commission's proposal) has been in place for some time.

18. Whilst there are inevitable cost implications to improving animal protection, these are proportionate in the Commission's draft Directive, and higher standards will also better satisfy the EU's over-arching duty and desire to minimise animal suffering.

19. Other positive impacts on EU competitiveness will result from a greater emphasis on developing and applying alternative methods. These impacts include increased scientific innovation in the EU, and world-leading expertise in cutting-edge, non-animal research and testing techniques. This is acknowledged by the Commission in its Explanatory Memorandum: "*These costs should be mirrored against the benefits to animal welfare, innovation and science as well as society in terms of increased public accountability and transparency*" (page 8).

[5] House of Lords Select Committee on Animals in Scientific Procedures, vol 1—Report, 2002, HL Paper 150-I, p 39 and p 26.

[6] The Government Reply to the Report of the House of Lords Select Committee on Animals in Scientific Procedures, Session 2001–2002. Presented to Parliament by the Secretary of State for the Home Department, January 2003, p 4 and p 7. Cm. 5729.

[7] FELASA (1992). Pain and Distress in Laboratory Rodents and Lagomorphs. Report of the Federation of European Laboratory Animal Science Associations (FELASA) Working Group on Pain and Distress.

Q3 *Proposed requirement to restrict research on non-human primates*

20. The advanced cognitive skills of non-human primates add significantly to the case against using them in laboratories, and their complex behavioural and social needs make it impossible to capture or breed and transport them to and keep them in laboratories, without compromising their physical and psychological health.[8] This also seriously limits the value of any results obtained from experiments on primates.

21. We would like a prohibition on all primate experiments, and we certainly support the ban on great ape use in the draft Directive (Article 8.2). We do not believe there should be a safeguard clause (Article 50), on ethical grounds. In practical terms, great apes have not been used at all in the EU for a few years. Some MSs, including Austria, the Netherlands and Sweden, have already restricted experiments on great apes. Britain implemented an administrative ban 12 years ago and no exceptions have been permitted. Non-EU countries including New Zealand and Australia also have stringent legislative restrictions. In Switzerland, a great ape prohibition has been proposed, and a bill to ban great ape experiments is being debated in the USA.

22. There is overwhelming public support for better protection of primates in research and testing.[9, 10] The absolute minimum protection that the public expects is a restriction of primate research to only that addressing debilitating or life-threatening diseases and we believe that Article 8.1(a) of the draft Directive, which would prohibit the use of primates for curiosity-driven research without a medical application, represents an appropriate and reasonable first step towards further reducing and ultimately replacing all primate use.

23. There are many modern techniques, including new and existing technologies, which were not available in 1986 when the current Directive came into force. These can replace and in some cases already *have* replaced primate experiments with non-animal methods (see Appendix for descriptive examples of this research).

24. The Commission acknowledges that replacing animals must be the ultimate goal. The proposed restrictions on primate use contained in Article 8.1(a) of the draft Directive would have a modest but highly significant impact on improving animal welfare, in addition to ensuring that public concerns over the ethics of primate research are taken seriously. The draft Directive has further potential for a positive impact on research into human health, since funds currently spent on non-essential primate research could be redirected to non-animal medical studies.

25. Examples of experiments that would no longer be permitted under the draft Directive include trivial and repetitive eye preference tests with no practical application to human health, that are being conducted on Old World monkeys caged in French laboratories, in collaboration with researchers from the UK.[11] Hand and ear preference tests conducted on lemurs kept in German laboratories[12] would also stop. These experiments have no practical application: they are basic biological studies such as that which would be prohibited under the draft Directive, making a reasonable effort to save some primates from being bred, supplied and kept in laboratories. The restriction would have no impact on human health research, but could instead free up funding resources to conduct non-animal studies relevant to human health.

26. Other non-human primate studies which may be classified as fundamental research, such as studies on memory and learning, are often indirectly linked to disorders such as Alzheimer's disease or developmental disorders. These would not be affected by the proposed restrictions so concerns that the new Directive would restrict research relevant to life-threatening or debilitating human disease are unfounded.

27. Greater scrutiny of all primate use would encourage funders and researchers working in these areas to apply existing, and develop new, non-animal techniques that are more relevant to patients than primate studies. These techniques include human imaging with patients and healthy volunteers, cell and molecular studies, and the design of *ex vivo* models[13] (see also Q8 and Appendix).

[8] Langley G (2006). Next of Kin: A Report on the Use of Primates in Experiments. London: BUAV. www.buav.org

[9] 81% of people surveyed agree or strongly agree that the new law should prohibit all experiments causing pain or suffering to primates. 79% agree or strongly agree it should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions. YouGov poll in six EU Member States, March 2009.

[10] 86% of people surveyed in the EU thought it very important to improve the current level of protection for primates; 81% thought it unacceptable to use primates in experiments. European Commission citizens survey, 2006.

[11] 14 monkeys were each presented 100 times with a seed hidden in a tube and researchers recorded which eye the monkeys preferred to use when looking at it. The researchers then deduced whether the two sides of a monkey's brain show lateralisation or "sidedness". This experiment will not save any human or animal lives. It aimed to answer an evolutionary question: at what point in primate evolution did lateralisation occur? *Reference:* Chapelain A S and Blois-Heulin C (2009). Lateralization for visual processes: eye preference in Campbell's monkeys (*Cercopithecus c. campbelli*). Animal Cognition 12:11–19.

[12] Researchers studied whether lemurs are right- or left-handed and with which ear they prefer to listen to sounds. Again, this was intended to indicate whether there is lateralisation in lemurs' brain. There is no practical application for this research. *Reference:* Scheumann M and Zimmermann E (2008). Sex-specific asymmetries in communication sound perception are not related to hand preference in an early primate. BMC Biology 6:3.

[13] Replacing Primates in Medical Research—an expert report by the Dr Hadwen Trust, FRAME & St Andrew Animal Fund. October 2008. PDF is attached to submission email and is available from www.scienceroom.org/reports-submissions

28. We strongly support the Commission's wish to end the capture of wild primates for breeding for laboratory use (Article 10.1). The stresses of capture, caging and transport for wild animals cannot be overstated. The supply problem is mainly with Old World monkeys and the Commission is right to propose a strategy to ensure that only F2 + animals are supplied to laboratories by the deadlines given in Annex III of the draft Directive. Britain has had an administrative ban on the use of wild-caught primates since 1995. Further, it has only allowed the use of primates from overseas centres that can supply purpose-bred animals to acceptable welfare standards.[14] It is appropriate to extend this to include phasing out the use of F1 generation primates.

Q4 *Extension of the Scope of the Directive (Article 2)*

29. We believe that the proposed extensions to the scope of the new Directive to include, in recognition of their sentience, certain invertebrate species (cyclostomes, decapod crustaceans and cephalopods) and life stages before birth or hatching of fetal or embryonic forms, is justified. The European Food Safety Authority (EFSA) Opinion of 2005 recommended extending the scope of the Directive to those invertebrates where sentience is scientifically supported.[15]

30. Cyclostomes (lampreys and hagfish) have a pain system similar to that of other fish and brains that do not differ much from those of some other fish. There is evidence that cephalopods (octopus, squid and cuttlefish) have adrenal and pain systems, a relatively complex brain similar to many vertebrates, significant cognitive abilities including good learning ability and memory retention, social grouping and relationship tendencies. The largest decapod crustaceans are complex in behaviour and have some degree of awareness, with considerable learning abilities. As a consequence of this evidence, EFSA concluded that cyclostomes, all cephalopods, and decapod crustaceans fall into the same category of animals as those that are presently protected.

31. There is a significant risk that a mammalian fetus, or the fetus or embryo of an oviparous animal such as a bird, reptile, amphibian, fish or cephalopod, can experience suffering and be subjected to poor welfare when a procedure is carried out on it within or after removal from the uterus or egg. Indeed, there is considerable evidence that precocial oviparous species, some of which are breathing at the time of hatching, are aware before hatching occurs.

32. EFSA determined that in these cases animals should be included in the list of protected animals. EFSA has stated that most vertebrate animals can be affected by poor welfare at the beginning of the last third of development within the egg or mother. Procedures using a fetus or embryo susceptible to suffering should be subject to the same authorisation and project requirements as those applied to procedures involving adult vertebrate and invertebrate animals.

33. At least 70% of MSs do not include these species and life stages in their legislation. The different levels of animal protection applied in the MSs result in current scientific knowledge not being applied consistently. In addition, the objectives and basic tenets set out in the Protocol to the EC Treaty, which formally recognises the welfare of animals as an element to be taken into account in Community policy-making, are severely undermined.

Authorisation of Persons, Requirements for Establishments, Inspections and Project Requirements (Articles 20–43)

Q5 *Proportionality*

34. The administrative demands that the draft Directive would impose are proportionate to its objectives because, as outlined above, there is an urgent need to harmonise costs associated with the conduct of animal procedures, and to improve animal welfare. The mechanisms by which procedures and projects are authorised, and the controls on persons, establishments, inspections and project requirements, combine to create the core regulatory instruments that are needed in order to harmonise costs and establish minimum welfare standards.

35. Weakening any one of the individual elements of authorisation as proposed by the Commission would risk perpetuating the current unsatisfactory regulatory environment. Strengthening the minimum standards set would lead to a more rigorously controlled regulatory regime, which would have additional benefits in terms of harmonising the internal market and improving animal welfare.

[14] Government Response by Joan Ryan, MP, Parliamentary Under-Secretary of State for the Home Department, to the Report by the Animal Procedures Committee on the acceptance of overseas centres supplying non-human primates to UK laboratories: a report by the primates sub-committee of the Animals Procedures Committee. March 2007. www.apc.gov.uk

[15] Opinion of the Scientific Panel on Animal Health & Welfare on a request from the Commission related to "Aspects of the biology and welfare of animals used for experimental and other scientific purposes", EFSA-Q-2004-105. 2005. http://ec.europa.eu/environment/chemicals/lab_animals/scientific_en.htm

Q6 *Further consideration and/or amendment*

36. Requirements relating to the *education and training* of persons authorised to perform functions listed in Article 20 are most welcome, as these will help to ensure that animal welfare standards are uniformly and rigorously applied. Establishment of EU standards of education and training along with requirements for personnel to meet those standards, would be more appropriate, as under the current proposal, levels of training could differ widely between MSs.

37. In addition, requirements relating to persons carrying out the functions described should include specific training in application of the 3Rs. This should be tailored so that the level of information provided would be appropriate to the functions being performed, and would be provided by the national facilities described in Article 46. Co-ordination of training would be provided through the EU level contribution described in Article 45. (Both Articles 45 and 46 should be amended to include these functions, and we suggest that improvements similar to those proposed by the European Parliament on 5 May 2009[16] should be considered.)

38. It is important for competent authorities to *inspect establishments* to ensure compliance with the Directive, whether these are premises used for breeding, supplying or using animals in procedures. Ensuring that establishments are compliant with the Directive is also an effective means of ensuring that the 3Rs are applied correctly and consistently when animals are not being used in projects (where compliance with the 3Rs is a condition of project authorisation).

39. Without an overall compliance requirement such as that in Articles 21–23, there would be no guarantee that sufficient attention is paid to application of the 3Rs during all life stages of protected animals.

40. It is appropriate that national inspections should be carried out at least twice a year, but we believe that both inspections should be unannounced. An additional arranged visit by the inspector to the establishment should also be made, but this should not be listed as an inspection. We do not believe that genuine "inspections" can be carried out when the establishment has had prior notice of the visit.

41. We welcome the ability of MSs to vary the frequency and extent of inspections according to the compliance record of the establishment and to the number and types of projects carried out, but not to reduce the number of inspections to a frequency below the minimum proposed.

42. We do not believe that the requirements relating to controls of national inspections are adequate (Article 34), and believe that an EU inspectorate should be established. The EU inspectorate would ensure that severity classifications are uniformly and correctly applied, and would allow for sharing of best-practice.

43. We believe that records of inspections should be made publicly available, with confidential information (names of personnel etc.) excluded, and that inspectors should be specifically trained in application of the 3Rs.

44. Establishments should also maintain contact with the NCAMs (see Q8) and mechanisms should be in place to ensure that they are able to receive regular information regarding best practice in applying the 3Rs. A new paragraph should be added to Article 24 requiring that user establishments designate a *person responsible for receiving information on developments in application of the 3Rs* from the NCAM, and disseminating that within the establishment.

45. We would like to see *all procedures being authorised*, and we do not support Article 41.4 which allows group authorisation of multiple projects when those projects are "required by law". It is not clear how ethical evaluation would be rigorously applied to individual projects which are deemed to be constituent elements of "multiple projects" as described in Article 41.4, but we wish to emphasise that no procedures should be exempt from ethical review and specific authorisation.

46. The authorisation of regulatory tests should, in particular, be responsive to new technological developments allowing for innovative approaches in application of the 3Rs; to a harm/benefit assessment that takes into account the intended use of substances being tested, and the presence of relevant existing test data. Improving prospective evaluations of the likely benefits of proposed experiments on animals would help to build EU-wide knowledge of limitations to the validity and relevance of animal use.

47. Article 43.1 of the draft Directive should be amended to prevent a delay in authorisation of projects classified as "up to mild" leading to a decision that the authorisation can be deemed to have been granted. It would be detrimental to animal welfare, as well as to UK competitiveness, if this lighter regulation of projects

[16] European Parliament legislative resolution of 5 May 2009 on the proposal for a directive of the European Parliament and of the Council on the protection of animals used for scientific purposes (COM(2008)0543—C6-0391/2008—2008/0211(COD)) www.europarl.europa.eu/sides/getDoc.do?type=TA&reference=P6-TA-2009-0343&language=EN&ring=A6-2009-0240

classified as "up to mild" were to become part of the new legislation: the UK already requires authorisation of all projects, and ethical review should be applied to all project applications in order to support implementation of the 3Rs.

48. We support *retrospective assessment of all* projects by competent authorities and would like to see Articles 38.1 and 38.4 amended accordingly. Retrospective assessment would allow earlier identification of animal tests and models that are performing poorly. It would enable better judgements to be made in project authorisations and also, importantly, would allow *resources* to be diverted away from failing animal models towards more relevant and reliable models (which are highly likely to be non-animal approaches).

49. In Britain, Ethical Review Processes have been responsible for ongoing and retrospective project assessments for nearly 10 years and there is a large body of useful experience to draw on. As the Home Office said, retrospective reviews allow an analysis of whether "*original assumptions . . . were correct when the request for authority was originally considered, and to consider if additional 3R strategies can be identified and incorporated*".[17]

50. Better implementation of the 3Rs enabled by retrospective assessment will also improve the quality of EU science. For example, reducing animal stress (eg by refinement) improves data reliability and introducing advanced replacement techniques is also advantageous, enhancing scientific method innovation and contributing to medical progress (see Q8).

51. A report by the Laboratory Animals Science Association (LASA) five years after the introduction of retrospective assessments in Britain confirmed these points. LASA stated[18] that as well as enhancing the "culture of care" in laboratories, retrospective assessments had already had important scientific benefits, including:

> "*a study of receptors in different species led to abandoning irrelevant animal models; the implementation of better techniques causing less stress or the use of fewer animals; an increase in the level of in vitro work undertaken in a project*."

52. In 2007 LASA added[19] that retrospective assessments offer opportunities to ask key *scientific* questions such as: Is the animal model still the most appropriate for this type of study? Are there any recent developments in science or technology which should influence the study? Are there non-animal methods? Are animal numbers statistically appropriate (not enough/too many) in the light of the results to date?

53. In addition to the above points relating to possible amendment of the draft Directive, we wish to signal the need for more regular review of legal requirements relating to the use of animals in scientific procedures. We see this as central to future regulation, and believe that it is right to review regularly and examine the impact of developments in technological, scientific and animal welfare knowledge, and progress towards replacing animal use. We would like to see the Commission and MSs giving priority to the reduction and elimination of procedures causing the greatest pain, suffering and distress to animals, and to reduction and elimination of those experiments which do not have a direct medical application.

54. In view of the particular concern relating to procedures causing a high degree of pain, distress or suffering to animals, we wish also to note our support for the intention of Article 15.2 of the draft Directive, which indicates acknowledgement that an "upper limit" of permissible pain and distress should be established by proposing a prohibition of procedures classified as severe if the pain, suffering or distress is likely to be prolonged. This reflects current practice in the UK, outlined in Section 10(2A) of the Animals (Scientific Procedures) Act, which states that: "The Secretary of State will not licence any procedure likely to cause severe

[17] Animals (Scientific Procedures) Inspectorate (2001). Review of the "Ethical Review Process" in Establishments Designated under the Animals (Scientific Procedures) Act 1986. Para 121: "Retrospective review seeks to look back on the animal welfare costs encountered and benefits realised. This permits assessment of the extent to which the original assumptions, including the severity limit of protocols, were correct when the request for authority was originally considered, and to consider if additional 3R strategies can be identified and incorporated. This information is of value to licensees and the ERP in planning future work and, as ERP records are available to the Inspectorate, it may also influence future Home Office assessments."

[18] LASA Ethics and Training Group (2004). Guidance Notes on Retrospective Review: A discussion document. Publ LASA, UK.

[19] Jennings M, Howard B & Berdoy M (2007). The Value of Looking Back: Improving Science and Welfare through Retrospective Review. Publ LASA. www.rspca.org.uk

pain or distress that cannot be alleviated" (Home Office, 2000). We would prefer to see the complete prohibition of pain, distress or suffering that is more than transient in duration, as a first step towards the elimination of all painful procedures.

Q7 *Care and Accommodation (Article 32)*

55. The Dr Hadwen Trust for Humane Research supports the inclusion of the full requirements for care and accommodation as revised recently by the Council of Europe Convention ETS123, instead of the existing Annex IV. These standards are already in place as European Commission guidelines, and are already applied as a legal requirement in at least one EU MS. It is extremely important that the full standards are applied as legal requirements in the new EU legislation, so that those MSs in which they are already applied are not economically disadvantaged.

Q8 *Alternative Methods*

56. The provisions contained in Articles 45 and 46 are very welcome. The establishment of National Reference Laboratories (in the draft Directive) or NCAMs (as suggested in the text adopted by the EU Parliament, see above) tasked with taking part in pre-validation and validation studies is a very positive step.

57. However, there are limitations to the model in the draft Directive which have been well addressed in the text recently adopted by the European Parliament. Therefore the Dr Hadwen Trust strongly supports amendments 138–145 to Articles 45 and 46 in the text adopted by the European Parliament.[20]

58. In particular, amendment 139 proposes extending the EU level "contribution" (as mentioned in Article 45) to encompass an EU Centre co-ordinating and promoting the development and use of alternatives to animal procedures, including in applied and basic biomedical research, veterinary research and regulatory testing.

59. According to this amendment, the EU Centre would have these functions:

- *co-ordinating* research to develop, pre-validate and validate alternatives conducted by the national laboratories (described in Article 46);
- *conducting* its own research and *commissioning* research to facilitate the 3Rs;
- *creating and implementing strategies* for the 3Rs;
- making available *information* on alternatives through regular reporting to the public, to stakeholders and to MS authorities;
- providing *databases* to facilitate the exchange of information on the 3Rs and on unpublished information to prevent duplication; and
- facilitating the *scientific endorsement and regulatory acceptance* of alternatives to animal testing for regulatory purposes.

60. Equally important is Amendment 140 proposing that MSs shall nominate National Centres for Alternative Methods to support not only the development, but also the validation and promotion of alternatives to animal tests used for regulatory purposes; and facilities to develop and promote the use of alternatives to animal procedures undertaken for other purposes, such as basic and applied biomedical and veterinary research.

61. An essential function of the NCAMs would be to conduct and commission replacement research, as the German Centre for Documentation and Evaluation of Alternatives to Animal Experiments (ZEBET), established in 1989, has done for many years.[21] The British NC3Rs also funds research into the 3Rs. ZEBET additionally assesses and recommends alternatives for recognition, both nationally and internationally.

62. Amendments 143 and 144 extend the roles of the NCAMs to provide scientific and technical assistance and training in the 3Rs, not only to the relevant authorities but also to user establishments. For increased transparency, amendment 145 sees the NCAMs also communicating developments on alternative methods and informing the public of positive and negative outcomes. ZEBET and the NC3Rs both disseminate useful information, and the former manages a freely accessible internet database of alternative techniques.

63. We would also like to see user establishments maintaining contact with the NCAMs and mechanisms should be in place to ensure that they are able to receive regular information regarding best practice in applying the 3Rs. A new paragraph should be added to Article 24 requiring that user establishments designate a person

[20] European Parliament legislative resolution of 5 May 2009 on the proposal for a directive of the European Parliament and of the Council on the protection of animals used for scientific purposes (COM(2008)0543—C6-0391/2008—2008/0211(COD)) www.europarl.europa.eu/sides/getDoc.do?type=TA&reference=P6-TA-2009-0343&language=EN&ring=A6-2009-0240

[21] See website: www.bfr.bund.de/cd/1591

responsible for receiving information on developments in application of the 3Rs from the NCAM, and disseminating that within the establishment.

64. People authorised to conduct animal procedures should also have specific training in the application of the 3Rs. A brief introduction to the 3Rs is currently offered in Britain to new licensees, but is sorely inadequate. Training can be tailored to the functions being performed, as long as it meets a certain minimum level. The training would be provided by the NCAMs and co-ordinated by the EU Centre (discussed above).

65. The British government[22] and the European Commission[23] have accepted the potential of non-animal methods to *improve science* and *yield quicker and more cost-effective results*. Several scientific reviews have shown that many animal "models" used to study human illnesses are unreliable. Examples include multiple sclerosis, stroke, rheumatoid arthritis, Parkinson's disease, Alzheimer's disease and cancers of the lung, brain and bowel. For example, an extensive study examined 221 experiments using over 7,100 animals in research into six different treatments for five human illnesses.[24] They found that half the animal experiments failed to correctly predict human responses to treatment.

66. Medical research on animals relies on conditions that are dissimilar to human illnesses, artificially induced in non-human species. In safety testing, most animal tests have not undergone formal validation and there are serious and unsolved inherent problems.[25] To secure the health of citizens, the quality and relevance to humans of research and testing must be improved.

67. It is now widely accepted that advanced, non-animal, human-based techniques overcome many of the limitations of outdated animal experiments.[26] Test-tube safety methods are more precise, versatile and reproducible than testing drugs and chemicals on animals. For example, every batch of insulin used to be tested for safety by the mouse convulsion method, using 600 mice each time. When the non-animal technique replaced the mouse test, faster and more precise results became available.[27]

68. When chemicals were tested for skin irritation using rabbits, the test took 14 days to complete. In comparison, the new test-tube methods that now replace rabbits take only 42 hours.[28]

69. New human cell-based techniques to ensure the purity of injectable drugs were recently validated by ECVAM (the European Centre for the Validation of Alternative Methods). The methods greatly enhance patient safety and are replacing up to 200,000 rabbit tests each year.[29] They are also a major commercial success with a worldwide market of €200 million, according to the Commission's Vice-President, Günter Verheugen, who said: ". . . *research in the development of alternatives is not only beneficial for animal welfare but also encourages the development of new markets for these methods*."

70. Ensuring that legislation provides an impetus for further development of these world-class skills in modern, non-animal technologies, will facilitate an essential competitive edge for Britain and the EU in the fast-moving world of science, whilst advancing medical progress and meeting citizens' concerns about animal experimentation.

Q9 *Subsidiarity and Legal Base*

71. In order to ensure harmonisation of the internal market, action at EU level is necessary in this case. EU funded research is frequently conducted across national boundaries, and markets pertaining to the use of animals in procedures are not confined to single EU MSs. Companies based in one country may contract companies based in other countries to carry out animal procedures on their behalf, and costs associated with the purchase of animals and their care, as well as the training of staff and other welfare-related elements of animal use are likely to produce a wide variation in costs across the various MSs (as is currently the case [1]).[30] Because of the potential for wide variations in both the cost of animal procedures and standards of animal welfare, EU legislation should in this case be highly prescriptive and should endeavour to impose both high

[22] The Government Reply to the Report of the House of Lords Select Committee on Animals in Scientific Procedures, Session 2001–2002. Presented to Parliament by the Secretary of State for the Home Department, January 2003, p 4 and p 7. Cm. 5729.

[23] Commission of the European Communities Commission Working Document on a Community Action Plan on the Protection and Welfare of Animals 2006–2010. Strategic basis for the proposed action. SEC(2006)65. COM(2006) 14 final. Brussels 23.01.06.

[24] Perel P, Roberts I, Sena E *et al* (2007). Comparison of treatment effects between animal experiments and clinical trials: systematic review. Br Med J 334:197. The five illnesses were: head injury, haemorrhage, acute ischaemic stroke, neonatal respiratory distress syndrome and osteoporosis.

[25] The inherent problems include: species differences, dosing discrepancies (between tests and real human exposures), and scaling up results from small, short-lived animals (mainly rodents) to larger, long-lived humans.

[26] US National Research Council Committee on Toxicity Testing and Assessment of Environmental Agents (2007). Toxicity Testing in the Twenty-First Century: A Vision and a Strategy.

[27] Anon. (1985). Reduction of the use of animals in the development and control of biological products. Lancet 2:900–902.

[28] See, for example: European Centre for the Validation of Alternative Methods (ECVAM)—ESAC Statement on the scientific validity of in-vitro tests for skin irritation testing. 5 November 2008. http://ecvam.jrc.it

[29] Europa release. Fewer tests on animals and safer drugs: New EU tests save 200,000 rabbits per year. Reference IP/03/662. 12 May 2003.

[30] [1] Commission Staff Working Paper accompanying the Proposal for a Directive of the European Parliament and of the Council on the protection of animals used for scientific purposes.

welfare standards and mechanisms to ensure appropriate and harmonised standards of transparency, accountability and inspection/enforcement. The Dr Hadwen Trust for Humane Research believes that in many cases the draft Directive is not prescriptive enough (see suggested amendments above) and we support the introduction of comprehensive and detailed regulatory requirements set at EU level, while also acknowledging that the proposed legislation should take the form of a Directive so that individual MSs can impose higher standards of animal welfare where appropriate.

21 May 2009

APPENDIX

REPLACING PRIMATE EXPERIMENTS WITH NON-ANIMAL METHODS

Here we provide information about existing research addressing the replacement of primate experiments with non-animal alternatives; and we mention promising areas of research which need funding.

We focus on areas of medical research using primates where investment in non-animal replacement techniques is most urgent, particularly in terms of exciting new replacement technologies and the potential scientific and medical value of investing in these.

These case studies are intended to illustrate our contention that much has already been achieved with replacement techniques and that there are many further opportunities to exploit and adapt exciting new technologies for this purpose.

A. Neurological Research

A1. *Cognitive research: Human attention studied with advanced transcranial magnetic stimulation techniques*

The Dr Hadwen Trust is currently funding Dr Amanda Ellison at Durham University in England to improve a technique called Transcranial Magnetic Stimulation (TMS) in research with human volunteers.

Dr Ellison is applying a dual-site TMS paradigm, not widely used in the neuroscience community due to the requirement for rigorous control. However, she has successfully used the method in the recent past [1] and is now applying it to the question of how two distinct human brain areas, known to be involved in attentional control, interact together.

To date, these kinds of issues have often been studied in primate experiments via deactivation or microstimulation of one area and recording from another. Such experiments require between two and five primates (most commonly rhesus macaque monkeys) on which surgery must be performed, either to lesion the region of interest or to screw a head fixation device to the skull in order to expose on an area of the brain for stereotactically precise recording/stimulation, or for a combination of both. A scleral search coil may also be fitted around the eye [see for example refs 2–11].

In addition to the usual pre-operative training routines administered to the animals, the procedure is persistently invasive. Although the brain has no pain receptors and so microstimulation or recording from electrodes implanted in the brain to test the region's involvement in the particular task is "painless", having a head socket in situ over a hole in the skull is inevitably unpleasant and uncomfortable for a monkey and liable to cause irritation. The monkeys are sacrificed at the end of the experiments and the brain removed for histological procedures. Such studies also often require additional control animals.

The major scientific disadvantage of the primate experiments is that any inference made about human brain function from animal studies is necessarily indirect and speculative.

Dr Ellison's approach with the new TMS paradigm in human volunteers can help show exactly how brain areas are contributing to the function in question and when they are active. There is then the possibility of devising neuro-rehabilitative methods to recover functions lost by patients after brain damage such as results from cerebrovascular disease.

The experiments address issues relating to the orientation of attention in space while avoiding all use of primates. Dual-site TMS is being used to investigate the co-involvement of the frontal eye fields and posterior parietal cortex in spatial attentional tasks in human volunteers, experiments that previously would have had to be carried out using primates. The time course of the interactions will be delineated, a question only otherwise answerable through invasive surgical interventions in animal experiments.

References

1. Ellison, A, Lane, A R, Schenk, T (2007) The interaction of brain regions during visual search processing as revealed by transcranial magnetic stimulation. Cereb Cortex, 17:2579–2584.

2. Moore, T & Armstrong, K M (2003) Selective gating of visual signals by microstimulation of frontal cortex. Nature, 23:370–373.

3. Moore, T & Fallah, M (2004) Microstimulation of the frontal eye field and its effects on covert spatial attention. J Neurophysiol 91:152–162.

4. Reynolds, J H & Chelazzi, L (2004) Attentional modulation of visual processing. Ann Rev Neurosci, 27: 611–647.

5. Juan, C-H, Shorter-Jacobi, S M, Schall, J D (2004) Dissociation of spatial attention and saccade preparation. Proc Natl Acad Sci USA, 101:15541–15544.

6. Schiller, P H & Tehovnik, E J (2005) Neural mechanisms underlying target selection with saccadic eye movements. Prog Brain Res 149: 157–71.

7. Armstrong, K M, Fitzgeralds, J K & Moore, T (2006) Changes in receptive fields with microstimulation of frontal cortex. Neuron 50:791–8.

8. Armstrong, K M & Moore, Y (2007) Rapid enhancement of visual cortical response discriminability by microstimulation of the frontal eye field. Proc Natl Acad Sci USA 104:9499–9504.

9. Mushiake, H, Fujii, N & Tanji, J (1999) Microstimulation of the lateral wall of the intraparietal sulcus compared with the frontal eye field during ocularmotor tasks. J Neurophysiol 81:1443–1448.

10. Cutrell, E B & Marracco, R T (2002) Electrical microstimulation of primate posterior cortex initiates orienting and alerting components of covert attention. Exp Brain Res 144:103–113.

11. Lynch, J C & Tian, J R (2005) Cortico-cortical networks and cortico-subcortical loops for higher control of eye movements. Prog Brain Res 151:461–501.

A2. *Cognitive research: A novel device to create safe, virtual lesions in deeper areas of the human brain than is possible with transcranial magnetic stimulation*

Primate lesion research is currently used extensively to explore cognitive function. It is argued that this research is necessary because chance lesions in humans are rarely sufficiently focused, and seldom occur in deep brain structures. Using transcranial magnetic stimulation (TMS) in human volunteers is a powerful technique but is insufficiently focused for use with deeper brain centres [1].

Because much cognition is mediated by deep brain structures, research to date has depended heavily on focused lesion studies in primates. However, even given the greater ability to focus lesions in animals, modeling the neural bases of cognition from such lesions is limited in terms of what cognitive processes can be measured and the uncertainties of inter-species extrapolations.

However, some researchers are planning to develop an entirely new, safe device (based on radio frequency pulse stimulation) able to temporarily disrupt organized electrical activity in focal regions anywhere in the human brain. This would provide human data on the role of different deep brain structures in cognition.

The first stage would be to establish proof of principle for the device using simulation and a realistic human head and brain phantom. After optimisation, the work could move to human volunteers using structural and functional magnetic resonance imaging to see if pulse stimulation can be sufficiently focused on targeted deep brain structures.

This kind of creative work is in need of funding to enable pilot studies and further development to proceed. It is simply one example of many potential novel ideas for safe human brain research that could replace primate experiments and provide gold standard data.

Reference

1. Roth, Y, Amir, A, Levkovitz, Y & Zangen, A (2007) Three-dimensional distribution of the electric field induced in the brain by transcranial magnetic stimulation using figure-8 and deep H-coils. Journal of Clinical Neurophysiology 24:31–38.

A3. *Human neurochemistry and therapeutics: Combining non-invasive techniques to study the effect of drugs on the human brain as an alternative to animal experiments*

This research project is currently being funded by the Dr Hadwen Trust and conducted by Dr G Barnes, Dr A Hillebrand, Dr P Furlong and Dr S Hall at Aston University.

The main focus is the development and application of non-invasive functional imaging techniques in the study of cortical structure and function. The work encompasses fundamental neuroscience and clinical research aimed at understanding and improving treatment of a range of neurological illnesses which are very often studied in primates.

Many mental conditions, such as depression, are difficult to characterise in other species. Despite this, many animals including primates continue to be used in research into human mental illness.

To understand and ultimately combat diseases such as schizophrenia, dementia, depression and developmental disorders such as autism, we need to study human beings. There is now a range of functional neuroimaging techniques that allows non-invasive measurements from the intact human brain.

The long-term goal of this project is to provide models of human neurochemistry linked to the electrical behaviour in the cerebral cortex. The ability to directly and accurately measure the electrical profile of drug-induced change in the human brain would have a wide spectrum of applications, relating to the understanding of normal brain function, treatment of neurological disorders and the targeted design of new drugs.

The Aston research is investigating the use of two non-invasive imaging techniques: magnetoencephalography (MEG) and magnetic resonance spectroscopy (MRS). Combining these two techniques permits more detailed information to be collected than is possible with either method singly.

MEG uses highly sensitive magnetic field sensors to determine neuronal electrical activity on a millisecond by millisecond basis. It provides high spatial and temporal resolution images of the electrical behaviour of the cortex, but no chemical or anatomical information. The Aston group has demonstrated that non-invasive MEG studies can effectively replace certain invasive experiments on primates [1].

MRS uses high-strength magnetic fields to determine the chemical composition of regions of the brain, based on the resonant frequency of particular atoms, such as hydrogen. It can show the distribution of targeted neurotransmitters and various metabolites across the brain [2].

MEG has proved to be extremely successful at identifying the cortical areas affected by the modulation of GABA receptors and at monitoring changes in activity over time following the administration of diazepam, used as a pharmacological tool. Comparative data were collected with targeted pharmacological MRS during diazepam uptake, to provide anatomically relevant chemical measures.

This combination of MEG and MRS into a pharmaco-imaging method is a novel approach [3] that possesses great potential for drug development and the replacement of primate experiments. Work is continuing to further develop and optimise this pharmaco-imaging method, and to investigate painkillers and the drug zolpidem used in the treatment of brain injury.

References

1. Hall S D, Holliday I E, Hillebrand A *et al* (2005) The Missing Link: analogous human and primate cortical gamma oscillations. Neuroimage 26:13–17.

2. Ugurbil K, Adriany G, Andersen P *et al* (2000) Magnetic resonance studies of brain function and neurochemisty. Ann Rev Biomed Eng 2:633–660.

3. Hall S D & Adjamian P (2006) The Chemistry of Cognition. In: Gazzaniga M S, Senior C & Russel T (eds), Methods in Mind. Cambridge USA: MIT Press.

A4. *Multiple sclerosis: Functional analysis of the T-cell immune response in multiple sclerosis by gene silencing*

Professor Daniel Altmann at Imperial College London has a research grant from the Dr Hadwen Trust for a pilot study to apply gene silencing techniques to human cell lines established from multiple sclerosis patients. The aim is to characterise key changes in the control of immune function *in vitro* with the longer term goal of developing an *in vitro* model system for studying key candidate immune system genes.

There have been more than 10,000 publications on the induction of an animal surrogate for multiple sclerosis, called experimental allergic encephalomyelitis, in rodents, rabbits and monkeys, including macaque monkeys [1, 2]. Animals suffer inflammation and damage to the nervous system that may result in paralysis, in experiments that can cause distress and suffering. Pre-clinical primate experiments are largely confined to the Netherlands and the USA [3].

It is essential to reappraise whether valuable, functional data about the immunology of multiple sclerosis can better be obtained from studies of human patient T-cell responses. The advantage of this is that, in what is a rather heterogeneous and poorly understood disease, one avoids any of the prior assumptions as to mechanisms that necessarily constrain the animal models.

Recent advances in molecular understanding and immunological reagents mean that one can now gain considerable insight into MS-related T cell immune processes from *ex vivo* analysis [4, 5]. This can encompass analysis of specificity, tetramer binding, clonality, cytokine profile, markers of *in vivo* replicative history and expression of cell-surface antigens to allow sub-setting of responding human cells into recent memory, chronically stimulated, effector memory and senescent effector T cells. Furthermore, it is increasingly possible to evaluate the role of particular molecules in culture through the use of siRNA knockdown approaches [6].

A shift to human *in vitro* studies for studying multiple sclerosis disease mechanisms also offers a major advantage in research costs.

References

1. Rivers T M, Sprunt D H, Berry G P (1933) Observations on attempts to produce acute disseminated encephalomyelitis in monkeys. J Exp Med 58:39–53.

2. Gold R, Linington C, Lassmann H (2006) Understanding pathogenesis and therapy of multiple sclerosis via animal models: 70 years of merits and culprits in experimental autoimmune encephalomyelitis research. Brain. 129:1953–1971.

3. 't Hart B A, Bauer J, Brok H P and Amor S (2005) Non-human primate models of experimental autoimmune encephalomyelitis: Variations on a theme. J Neuroimmunol. 168:1–12.

4. Davies S, Nicholson T, Laura M, Giovannoni G and Altmann D M (2005) Spread of T lymphocyte responses to myelin epitopes with duration of multiple sclerosis. J Neuropath Exp Neurol 64:371.

5. Bielekova B, Sung M, Kadom N, Simon R, McFarland H, Martin R (2004) Expansion and Functional Relevance of High-Avidity Myelin-Specific CD4+ T Cells in Multiple Sclerosis. J Immunol 172:3893–3904.

6. Hafler D A (2004) Multiple sclerosis. J Clin Invest 113:788–794.

A5. *Human brain networks: Computational frameworks to analyse human brain networks and their breakdown in disease using diffusion tensor imaging*

Dr Heidi Johansen-Berg and Dr Tim Behrens from Oxford University have a grant from the Dr Hadwen Trust to develop computational approaches for analysing human brain networks and their breakdown in disease.

There are several neurological and psychiatric disorders in which connections between deep brain structures and cortical regions are damaged or disrupted. They include schizophrenia, chronic pain, and movement disorders such as Parkinson's disease. Detailed knowledge of human subcortical-cortical brain circuitry is therefore crucial to understanding and treating these disorders.

At present much knowledge of brain connectivity comes from inferences based on invasive tracer studies in animals, including rodents, cats and monkeys. Recent developments in the field of non-invasive diffusion tensor magnetic resonance imaging (DTMRI) allow tracing of fibre pathways in the living human brain. DTMRI can provide images that allow these pathways to be visualised in living human brains [1–3]. This opens up many new possibilities for testing how the pathways develop and age, and how they are disrupted in disease.

Using funding from the Dr Hadwen Trust, Dr Johansen-Berg and Dr Behrens are using DTMRI to scan healthy people and those with disorders such as stroke, multiple sclerosis, schizophrenia and pain disorders [4]. The research will provide a general framework in which to test hypotheses about breakdowns in subcortical-cortical network connectivity in brain disorders, with a focus on chronic pain.

DTMRI provides exciting and important new developments for the study of the healthy brain, as it enables the identification of specialised brain regions in living people [5–7]. For example, our grant-holders have recently identified, for the first time, sub-regions within the human premotor cortex, based on their patterns of connections with other areas. Previously, this region could only be reliably identified by microscopically examining slices of post-mortem brain.

The ability to identify the region in living people means that both the structure and function of this area can be studied in humans at the same time. This approach will also help tackling clinical challenges. For example, identifying brain regions in living subjects may be useful for accurately targeting these structures for medical interventions, such as brain surgery for Parkinson's disease or brain stimulation for stroke.

This technique has enormous potential to replace invasive tracer studies in animals, especially primates, as well as enhancing the quality of evidence concerning brain connectivity.

References

1. Tomassini V, Jbabdi S, Klein JC *et al* (2007) Diffusion-weighted imaging tractography-based parcellation of the human lateral premotor cortex identified dorsal and ventral subregions with anatomical and functional specialisations. J Neurosci 27:1059–1069.

2. Jbabdi S, Woolrich W M W, Andersson J L R *et al* (2007) A Bayesian framework for global tractography. NeuroImage 37:116–129.

3. Behrens T E J, Johansen Berg H, Rushworth M F S *et al* (2007) Probabilistic diffusion tractography with multiple fibre orientations: What can we gain? NeuroImage 34:144–155.

4. Johansen-Berg H & Behrens T E (2006) Just pretty pictures? What diffusion tractography can add in clinical neuroscience. Curr Opin Neurol 19:379–385.

5. Johansen-Berg H, Behrens T E, Robson M D *et al* (2004) Changes in connectivity profiles define functionally distinct regions in human medial frontal cortex. Proc Natl Acad USA 101:13335–13340.

6. Klein J C, Behrens T E, Robson M D *et al* (2007) Connectivity-based parcellation of human cortex using diffusion MRI: Establishing reproducibility, validity and observer independence in BA 44/45 and SMA/pre-SMA. Neuroimage 34:204–211.

7. Behrens T E & Johansen-Berg H (2005) Relating connectional architecture to grey matter function using diffusion imaging. Phil Trans R Soc Lond B Biol Sci 360:903–911.

B. Infectious Diseases Research

B1. *Hepatitis C: Design and construction of novel synthetic receptors to study infectious diseases and replace animals*

Current therapy for chronic hepatitis related to hepatitis C virus (HCV) infection is based on the use of interferon. However, its effect on virus clearance rates is insufficient. Chimpanzees are the only experimental animals susceptible to infection with HCV, although they do not develop the pattern of illness seen in humans.

Studies to develop anti-viral therapy or to understand the life cycle of this virus have been hampered for a long time by the lack of an effective *in vitro* viral culture system. Recently a sub genomic replica of a strain of HCV (JFH-1) isolated from a patient with culminant hepatitis has been found to replicate efficiently in cell culture, leading to an all-important HCV infection system in cultured cells.

In further developments, the full HCV life cycle can now be studied *in vitro* but it has relatively limited use when faced with naturally occurring virus isolates, since it relies on *in vitro* transcribed templates of HCV. The next key step to replacing chimpanzee studies would be a robust cell-based approach for the propagation of *naturally occurring* infectious HCV particles.

Some researchers have pioneered the concept of developing an artificial receptor to facilitate uptake of an infectious virus. In 1996, they created a synthetic receptor for foot and mouth disease virus that permitted infection following binding [1]. This study demonstrated the first production of a totally synthetic cell-surface receptor for a virus.

The approach will be useful for studying virus interactions and, the scientists suggest, for the development of safer vaccines against viral pathogens of animals and humans. They are seeking funding to create a synthetic HCV receptor that will be expressed in human hepatoma cell lines, which would enable studies of the binding, internalisation and replication of naturally occurring HCV strains. If successful the model would be a significant advance, also permitting a robust cost-effective screening of drugs against this chronic disease, without the use of animals.

REFERENCE

1. Rieder E, Berinstein A, Baxt B, Kang A, Mason P W (1996) Propagation of an attenuated virus by design: engineering a novel receptor for a noninfectious foot-and-mouth disease virus. Proc Natl Acad Sci USA 93:10428–10433.

B2. *Hepatitis C: Three-dimensional in vitro liver models*

The Dr Hadwen Trust is currently funding Dr Brian Thomson, a Clinical Associate Professor in the School of Molecular Medical Sciences at Nottingham University, to use tissue engineering to develop three-dimensional *in vitro* models of human liver. These will permit both the long-term growth and preservation of function of primary human hepatocytes *in vitro*. The 3-D spheroids will also include hepatic stellate cells which play a key role in liver response to injury. The inclusion of these cells provides an excellent basis for modelling human liver disease.

Building on his earlier work based on rodent cells [1], Dr Thomson is adapting the approach to develop a 3-D *human* hepatocyte culture for research into human hepatitis viruses. Hepatitis B is currently researched in animals including chimpanzees, and hepatitis C studies still use chimpanzees, tamarins and marmosets [2, 3].

The development of a robust, multicellular culture system which supports viral replication and virion production will enable the replacement of primates and small mammals in many areas of hepatitis virus research including: determination of infectivity for virus and molecular clones; studies of viral kinetics; studies of cytopathicity; and neutralisation studies.

REFERENCES

1. Thomas R J, Bennett A, Thomson B, Shakesheff K M (2006) Hepatic stellate cells on poly(DL-lactic acid) surfaces control the formation of 3D hepatocyte co-culture aggregates in vitro. Eur Cell Mater 11:16–26

2. Dandri M, Volz T K, Lutgehetmann M & Petersen. Animal models for the study of HBV replications and its variants. J Clin Virology 2005, 34 Suppl 1: 54–62.

3. Grakoui A, Hanson H L and Rice C M. Bad time for Bonzo? Experimental models of hepatitis C virus infection, replication and pathogenesis. Hepatology 2001, 33: 489–495.

B3. *Viral encephalitis: Development of a human ex-vivo blood brain barrier model for research*

As a medical research charity, we are currently funding Professor Tom Solomon, at Liverpool University in England, to establish a robust, working *ex vivo* model of the human blood brain barrier (BBB) to examine the putative mechanisms of viral entry into the nervous system.

Currently studies of the pathogenesis of viral encephalitis are very dependent on animal models, including primates. For example, a study of Japanese encephalitis virus using 20 rhesus monkeys inoculated by intranasal virus caused animals to suffer depression, anorexia, tremors, paralysis, coma and death [1].

The Liverpool Brain Infections Group is one of the leading international groups studying viral encephalitis in humans, examining the pathogenesis during disease, and also in human post-mortem material [2–5].

Having established a robust, working ex-vivo model of the human BBB for examining mechanisms of viral entry into the nervous system, the second phase of Professor Solomon's research will focus on Japanese encephalitis virus (JEV), one of the most important causes of viral encephalitis globally. The roles of virus replication and the pro-inflammatory cytokine response on BBB integrity will be explored.

Professor Solomon will also test the hypothesis that the pro-inflammatory cytokine milieu induced by JEV replication is more important in disrupting the BBB than viral replication itself. The longer term objectives are to be able to study treatments for encephalitis in this model system, which will be an important step towards new therapies.

Targeted European support for this kind of research could have an enormous impact on progress in understanding and treating viral encephalitis, whilst sparing some primates from suffering.

REFERENCES

1. Raengsakulrach B, Nisalak A, Gettayacamin M, *et al* (1999) Safety, immunogenicity, and protective efficacy of NYVAC-JEV and ALVAC-JEV recombinant Japanese encephalitis vaccines in rhesus monkeys. Am J Trop Med Hyg 60:343–9.

2. Solomon T. (2004). Current Concepts—Flavivirus encephalitis. N Engl J Med 351: 370–8.

3. Solomon T, Dung N M, Kneen R, *et al* (2002) Seizures and raised intracranial pressure in Vietnamese patients with Japanese encephalitis. Brain 125:1084–93.

4. Winter P M, Dung N M, Loan H T, *et al* (2004) Proinflammatory cytokines and chemokines in humans with Japanese encephalitis. J Infect Dis 190:1618–26.

5. German A C, Myint K S, Mai N T, *et al* (2006) A preliminary neuropathological study of Japanese encephalitis in humans and a mouse model. Trans R Soc Trop Med Hyg 100:1135–45.

B4. *Airways disease: Ex vivo models of infection and therapeutics*

Current models of respiratory viral infection and its effect on airways diseases such as chronic obstructive pulmonary disease, often involve laboratory animals infected with isolates of viral pathogens. These animals experience potentially severe symptoms of acute viral respiratory illness in addition to the invasive sampling procedures necessary to obtain relevant specimens of the lung.

Rodents are commonly used, but primate models have also been developed to enable lower airway sampling during active infection using bronchoscopic techniques; these include macaque monkeys in fatal experiments [1]. Further, novel investigational medicinal products are often assessed in primate models prior to phase one studies.

Some researchers plan to develop an *ex vivo* model of human bronchial tissue grown in explant culture. Once established the model would allow in-depth study of the complex mechanisms of inflammation and repair involved in common respiratory conditions such as asthma and chronic obstructive pulmonary disease, which cannot be adequately studied using existing techniques.

Such a model would facilitate analysis of the effects of respiratory pathogens, such as influenza, on the lung and help determine potential benefits of novel therapeutic agents for both airways disease and acute infection. Establishing an *ex vivo* human model will thus help to replace primate experiments, which are less relevant to human disease.

European support for this area of research could have a significant impact on replacing primate studies and in advancing medical progress for patients with these conditions.

Reference

1. D Kobasa, S M Jones, K Shinya, J. C. Kash *et al* (2007) Aberrant innate immune response in lethal infection of macaques with the 1918 influenza virus. Nature 445:319–323.

C. Reproductive Research

C1. *Uterine function and premature labour: Development of a human tissue model*

The Dr Hadwen Trust is funding Dr Rachel Tribe and Dr Michael Taggart at Kings College London and Manchester University, to develop an *ex vivo* tissue model of human uterine smooth muscle to study uterine function and premature labour.

30% of pregnant women experience a problematic labour, most commonly associated with inappropriate activation of uterine muscle contractile activity. Dr Tribe and Dr Taggart have a distinguished track record of studying these processes *in vitro* [eg 1–5]. Their new work applies the novel techniques of small interfering RNA and short hairpin RNA interference in human biopsy tissue, to knock down targeted genes known to control uterine muscle contractility.

Currently, research into uterine function often involves transgenic mice and primates [6], especially studies of the regulation of human uterine smooth muscle contractility—a very important medical topic. Premature labour, closely dependent on control of uterine muscle contractility, is responsible for 75% neonatal deaths and a significant proportion of morbidity from childhood diseases.

Understanding of the regulation of uterine smooth muscle has progressed slowly. From a scientific point of view the animal models are not representative of human labour. The human pathways that link to signalling in the uterus/feto-placental unit are different than those described in other species.

However human studies have been hampered because it is difficult to access human tissue from women at different stages of pregnancy, especially during premature labour. The aim of the current research, therefore, is to develop a validated *ex vivo* technique (siRNA) for silencing gene and protein expression in human uterine tissue as a more scientifically appropriate alternative to using animals.

The main objective for the period of the project proposal is to develop a validated method for transfecting human uterine smooth muscle (from biopsies) with agents that alter gene expression and contractile function. The validated model will then be used to assess the contribution of specific signalling molecules (such as TRPC1, TRPC3 and caveolin-1) to human uterine contraction. It may also be effective in determining the efficacy of therapies designed to prevent premature labour.

This model may also form the basis of wider studies into smooth muscle function (eg cardiovascular disease and asthma). An *ex vivo* human model for gene silencing or over-expression is likely to be attractive to pharmaceutical companies developing therapies for the treatment of preterm labour.

References

1. Riley M, Baker P N, Tribe R M, Taggart M J (2005) Expression of scaffolding, signalling and contractile filament proteins in human myometrium: effects of pregnancy and labour. J Cell Mol Med 9: 122–134.

2. Bai X, Bugg G J, Greenwood S L, Glazier J D, Sibley C P *et al* (2005) Expression of TASK and TREK, two-pore domain K + channels, in human myometrium. Reproduction. 129:525–30.

3. Dalrymple A, Slater D M, Poston L, Tribe R M (2004) Physiological induction of TrpC Proteins, calcium entry channels, in human myometrium: influence of pregnancy, labor and IL-1b. J Clin Endocrinol Metab 89:1291–1300.

4. Tribe R M, Moriarty P, Dalrymple A *et al* (2003) Interleukin-1b induces calcium transients and enhances basal and store operated calcium entry in human myometrial smooth muscle. Biol Reprod 68:1842–9.

5. Dalrymple A, Slater D M, Beech D *et al* (2002) Molecular identification and localization of Trp homologues, putative calcium channels, in pregnant human uterus. Mol Hum Reprod 8:946–951.

6. Goldsmith L T, Weiss G, Palejwala S *et al* (2004) Relaxin regulation of endometrial structure and function in the rhesus monkey. Proc Natl Acad Sci 101:4685–4689.

Examination of Witnesses

Witnesses: **Dr Gemma Buckland,** Science and Policy Officer, and **Ms Emily McIvor,** Policy Director, Dr Hadwen Trust for Humane Research, examined.

Q312 ***Chairman:*** First of all, thank you very much indeed for finding time to come along and help us with the inquiry. We have obviously read your written evidence and it is good that we can now have an interchange. A couple of formal things that I always have to say. This is a formal evidence-taking session; there will be a note taken. You will get a copy of the transcript which you will be able to correct in terms of any slips and errors that have come in. The other point, as you most likely heard before, is that we are being webcast, so there is a possibility that somebody will be listening into the session. As I have said, we have very little evidence about that. Would you like to start by making an opening statement and then we can go on to questions and answers.

Ms McIvor: Thank you very much for the invitation to present evidence. My name is Emily McIvor and I am Policy Director of the Dr Hadwen Trust for Humane Research. I have worked on the revision of the Directive for many years including as a member of the Commission's Technical Expert Working Group in 2002. I will hand you over to my colleague, Gemma Buckland, and then I will introduce the organisation a little more fully.

Dr Buckland: Good morning. My name is Dr Gemma Buckland and I am the Policy and Science Officer at the Dr Hadwen Trust. My training is in immunology and cell biology and I joined the Trust in 2008.

Ms McIvor: The Dr Hadwen Trust is a medical research charity funding exclusively non-animal techniques. We are ethically opposed to the use of animals in experiments but our approach is very much solutions-based. We see the need for research organisations and researchers to embrace the vision of a world where animal experiments have either been fully replaced or are prohibited. Our emphasis on replacement is one that is rooted firmly in the idea that tackling animal experiments in a purely oppositional way has not been helpful. We really want to find the science that will help us to that world where animal experiments are no longer needed. Our research portfolio includes projects looking at asthma, multiple sclerosis and many other human diseases, and we have a funding mechanism whereby we fund around £700,000 worth of medical research each year, and that is the key emphasis of our organisation. In terms of our interest in the revision of the Directive, that springs from various angles. We are very interested in those mechanisms that will improve animal welfare, we are interested in mechanisms that will increase transparency and above all we want to see the Directive used to really push this agenda of replacing animal experiments. We believe that those mechanisms designed to protect animals and to increase transparency are very often

the very same mechanisms that will ensure full implementation of the 3Rs. We see this as a once in a lifetime opportunity, not only to change the way in which animal experiments are regulated, but to change the whole direction of the way in which animal research is conducted and the attitudes to animal research among the scientific community and among the public.

Q313 ***Chairman:*** Thank you very much. That was a very helpful opening statement. I think that we understand where you are coming from. You say in your submission that the draft Directive is a proportionate response to the deficiencies that you see in the current arrangements. That really invites two questions, does it not? What are the deficiencies in the current arrangements and what do you see as the main advantages of the proposals?
Ms McIvor: In comparing the existing Directive with the legislative proposal, we can see that the aspirations are very similar, but the 86 Directive really set only a framework with those aspirational objectives. They did not provide any mechanisms for ensuring that what could be seen as aspiration in terms of better protecting animals would be enforced in the Member States. We think that it is really long overdue that this review is taking place where the aspiration is filled out with mechanisms to ensure that animals are better protected.

Q314 ***Chairman:*** Can you be specific about the present deficiencies?
Ms McIvor: The main deficiencies would be that, although the 86 Directive set frameworks for ensuring that experiments are authorised or that there may be some kind of a review, the proposal now puts that in very concrete terms, that there will be an ethical review carried out at national level and that there will be authorisation required at national level. The mechanisms that spring from those two centrepieces of the proposal are the ones that have not been present in the existing Directive and those are the ones that we are most pleased to see.

Q315 ***Chairman:*** Let me put the question that I put to the previous witnesses. The European Commission say that the proposals provide a solid basis for a full implementation of the principles of the 3Rs. Do you agree with that assessment and would you expect full implementation of the 3Rs to be achieved in the foreseeable future?
Ms McIvor: I think that the draft proposal makes a very good attempt to encourage implementation of the 3Rs and I want to divide right at the start our view as regards the terms of reference for 3Rs. We see implementation of existing 3Rs' techniques and methods as quite separate from the further development of additional 3Rs' techniques and methods. The Directive includes many mechanisms that would certainly include existing techniques and those come in though ethical review, through authorisation and through retrospective assessment and, as well as seeing those measures implemented, we want to go further and look at what we can do in terms of seeing the Directive as a means to inspire further development of additional 3Rs' techniques and methods.
Chairman: Let us move on to alternative methods.

Q316 ***Lord Livsey of Talgarth:*** The proposal at Article 46 requires Member States to designate a national reference laboratory for the validation of alternative methods replacing, reducing and refining the use of animals. What is your view of this suggestion?
Ms McIvor: We are delighted to see that the proposal includes an article which clearly states that both the Member States and the Commission have a duty to make a contribution. That article at the moment is really quite vague; it says "a contribution", and then it moves on to describe the national reference laboratories. We would firmly agree with the NC3Rs that at the moment it appears from what is written in the proposal that the emphasis is on regulatory testing, and that is something that we would like to see expanded upon. Regulatory testing represents, as you know, only a small number of animal experiments compared to the whole; it is a relatively small percentage, around 8%. It is not ambitious enough really and it does not properly address the needs of science. What it specifically addresses is the political agenda springing from needs created by other legislation, such as the Cosmetics Directive and REACH on chemicals and pesticides legislation. All of those pieces of vertical legislation are pushing companies and regulators in the direction of replacing animals used for regulatory tests and that is why the current focus has been on regulatory testing; but in fact, as we have heard from the NC3Rs, there are so many more opportunities to be taken in terms of replacing animals used in basic or applied medical and veterinary research. We really want to see that agenda expanded. We very much like the model of the NC3Rs. That organisation has been immensely successful. As an aside, in terms of the debate about expertise moving out of the UK or research moving out of the UK, the NC3Rs seems to be a fantastic example of the kind of organisation that can really bring these efforts into the UK and focus UK expertise as a world leader. I think that it is an inspirational story to see what has been achieved. We would like to see something like that achieved in the Member States. Rather than the kind of European Commission model of the national reference laboratory which is based on existing structures working in other scientific fields, we would like to

broaden that and talk about national centres for alternative methods or national centres for the 3Rs which will do a combination of things. They will take a twin-track approach helping to implement the existing 3Rs' techniques because very often researchers and companies find that there may be a technique out there but they cannot find the information or they do not know how to do it. In the case of regulatory testing, training is extremely important because it is often the case that people have to change practice and do something that they have not done before, so training is important. We want to see those laboratories working on implementing existing methods and working then to further develop 3Rs' techniques. So, national centres, yes. National reference laboratories, I would say a little bit limited in ambition.

Q317 ***Lord Livsey of Talgarth:*** From what you have just said, you want the legislation to be more prescriptive as far as the Directive is concerned. Is that going to bring in an extra level of bureaucracy which might force research to go to other places?
Ms McIvor: I would say that it could be seen exactly the other way around, that it is producing an infrastructure that would be extremely useful to the scientific community and that, in that way, it can be used to benefit science strongly. Recently the US Academies of Sciences produced a report *21 Century Toxicology: A Vision and a Strategy*, and, in that, they set out a clear understanding of why animal methods in toxicology are failing; and then they set out a vision where many new emerging technologies would be brought together to entirely replace animals used in regulatory testing. But the scope of that vision is so enormous, it is on a scale with the human genome project, that, in order to properly implement that, we need co-ordinated approaches in laboratories and infrastructure all over the world, not just in Europe, but certainly in terms of implementing a very ambitious vision, having laboratories in each of the Member States able to carry out specific tasks, which would need to be co-ordinated at EU level. I will come to the EU level in a minute as well; having the infrastructure available to take on these really very ambitious tasks is something that has the most enormous potential to benefit industry as well as everybody else and it will help move research on animals into alternative methods.

Q318 ***Lord Livsey of Talgarth:*** May I ask my second question before you respond on a European level. The RSPCA have said that they would like to see the role of the existing European Centre for the Validation of Alternative Methods expanded in order that it could act as a central body co-ordinating the work of the various national laboratories or centres. How do you view this possibility; and perhaps to enlighten people like me who do not know a lot about what is going on, could you describe what the existing European Centre is and how this compares with for example existing UK practice?
Ms McIvor: The European Centre for the Validation of Alternative Methods is a unit within the European Commission's Joint Research Centre and sitting within the Institute for Health and Consumer Protection. In terms of the European Commission's structure, ECVAM is a service provider. It can provide validation studies that seem to be of benefit to the community. They will typically at the moment carry out validation studies and work with other bodies internationally that are responsible for the same thing. At the moment, the great hope is that validation studies will be co-ordinated internationally so that when new methods come on-stream, they will then be closer to international acceptance. Sadly, what sometimes happens now is that ECVAM will validate a method, it will be endorsed by EU experts and ready for EU acceptance. There can be some delays in achieving regulatory acceptance but then, when it moves into the international arena, there would be even more delays because there will be a certain sense of needing to rerun studies that have already been conducted. ECVAM at the moment: firstly service provider; secondly concentration on regulatory testing. In order to expand that remit to include research and activities that would be relevant to other fields of research, ECVAM can be expanded as it is now but another structure within the EU will need to take on the strategy-setting role and we think that the strategy-setting role is really of very crucial importance. What we would like to see is to see maximum use made of the national centres and the national laboratories, we want to see that co-ordinated at EU level—and that could be part of the ECVAM structure or part of the Commission structure—and we want to see a strategy set as well, so that for instance it would be possible to look at areas of research where there may be particular scientific motivation for trying to switch from a failing animal model or where there might be an animal welfare motivation for trying to switch from a very painful and distressing procedure. I do not think that that is going beyond what could be achieved through the revision of the Directive but it will require the Member States to make sure that they put the necessary pressure on the Commission to get that funding and I do not think that we are talking about a vast amount of money. We might even be talking about a handful of people behind desks. The Commission is quite keen at the moment that their proposal should be budget neutral—they do not want to increase spending—but has asked the Member States to increase spending. I am hoping that the Member States will go back to the

Commission and say, "Right, here are your responsibilities and this where you increase spending".

Q319 ***Lord Brooke of Alverthorpe:*** Who funds ECVAM?
Ms McIvor: At the moment, in terms of its infrastructure and its operating budget, it is funded partly through the Commission budget but it also, through working with other organisations, attracts framework programme funding which is the DG research EU funding mechanism. So, it has two sources of funding from within the Commission.
Chairman: Let us move on to data-sharing.

Q320 ***Viscount Brookeborough:*** Before I ask about that, do you actually think it is achievable to achieve your aim of no use whatsoever of animals? Secondly, what would you therefore say to scientists who say that there will always be a level of which for various diseases there has to be something between a test tube and a human being because test tubes cannot react?
Ms McIvor: The use of animals and the uses to which animals are put shift and, in some fields of research, animal use can be seen to be reducing and in others it is increasing. With regard to your question as to whether animal experiments can be entirely replaced, I would answer "yes" and I would also draw your attention to the words of Professor Tim Hammond who gave evidence to you recently when he quite clearly stated that, in the field of biomedical research, yes, he does expect that at some point animal research will be—I do not want to speak for him but you can refer back to what he said. His statement implied a belief in the idea that animal research could be fully replaced. We certainly believe that because we believe that the animal model is inherently flawed. It will always be a model that is used to represent a condition in a human being, so it is always a surrogate. In terms of biomedical research, it is always a surrogate. It would be wrong to assume that that is the best that we can ever achieve and, exploring the technologies that might replace those animal uses is something that is at the moment unmeasured. We cannot say when and we cannot say what science is going to bring us in the future, but we can say that it is very wrong to limit our ambitions in terms of what science can deliver now because what science can deliver now is not going to be the same as what can be delivered tomorrow or in five years or 10 years. I think that it right to be ambitious; it is right to remember that animals are used as a surrogate in biomedical research for human beings; and the strong likelihood is that we will always be able to improve upon that to obtain more human relevant results.

Q321 ***Viscount Brookeborough:*** Now, data-sharing. The proposal requires Member States to share research data to a greater extent, subject to safeguarding confidential information, in order to avoid unnecessary duplication. Do you consider that there is a problem with duplication at the moment and at what level do you see it taking place?
Ms McIvor: That is such a difficult question and, as I think everybody coming before you giving evidence has said, there are so many different kinds of research and different reasons for carrying out animal research for testing. In terms of regulatory testing, I think that data sharing needs to be handled in the vertical legislation, but there also needs to be a very strong steer in the Directive to ensure that where results of a scientifically satisfactory nature can be obtained from another method other than using animals, they should be used. Both the existing Directive and the proposal include words to that effect. So, you could actually say that at the moment any company carrying out repeat testing or duplicate testing is in breach of the existing legislation.

Q322 ***Viscount Brookeborough:*** Are these pharmaceutical companies not economically minded and financially minded, since you seem to say that duplication is not cost effective?
Ms McIvor: Thank you for clarifying that. I am not saying that they do it unthinkingly, I am saying that sometimes they will do it because of some regulatory requirement and you have heard about batch testing and vaccines. The Commission representative I think quoted the figure of 160,000 retests being carried out on an annual basis. That retesting is being carried out because of other legislative requirements but, in the majority of cases, the other vertical legislation has wording to clearly state that animal testing should be carried out according to the provisions set out in Directive 86/609. So, I think that any company being required to retest would actually have very good grounds for going back and saying, "I don't need to retest this because I have another scientifically satisfactory way of obtaining the results sought". If it is scientifically satisfactory to use the results of batch tests carried out for another regulator, then really, under the existing Directive, they should be able to use those results now.

Q323 ***Viscount Brookeborough:*** But if they had world regulation?
Ms McIvor: It is about existing legislation now.

Q324 ***Viscount Brookeborough:*** Presumably within the EU.
Ms McIvor: It is talking about duplication of tests that is happening in the EU now and that we hope under the new Directive would be fully prohibited because retesting is one of those areas that really

should be the easiest one to tackle of all. It should be absolutely easy to say, "We have the result of this test already. We don't need to carry it out again. In order to fully implement the 3Rs, it would be wrong to be required to carry this out again" and I would love to see those pharmaceutical companies challenge any requirement to retest batches where it is not scientifically necessary.

Q325 ***Viscount Brookeborough:*** Who is forcing this requirement on them?
Ms McIvor: I do not know but I think that it comes through the many different pharmaceutical rules and regulations. I can find out and I can send it in as supplementary evidence. I want to identify retesting as the area that has to be tackled first. It is absolutely absurd that retesting is taking place. That is retesting where the person wanting to carry out the test already knows that data exist.

Q326 ***Viscount Brookeborough:*** From within the same jurisdiction?
Ms McIvor: No. I am talking about what is scientifically applicable. I am not talking about different jurisdictions necessarily, I am talking about whether something is scientifically applicable rather than in terms of a legal requirement. Moving on to repeat tests that are carried out when the person applying to carry out the test does not know that data already exists, some of the vertical legislation tries to tackle that but a lot of the transparency requirements that we are hoping will be introduced will tackle that. In terms of publication of project applications or technical summaries, it is important that data holders know what data are out there. There is something else that I want to mention in relation to data sharing which is probably more aspirational than something that is going to be contained in this Directive. When we look overall at the relevant data that exist, the human data obtained from human beings used in clinical trials would be incredibly useful not only in the development of alternative methods because it would be possible to take alternative methods and actually read them against human toxicological data, but also in checking the validity of the animal methods. There are a number of moves being made to try to ensure that human data are used more effectively. The USFDA at the moment has a voluntary scheme whereby companies are bringing forward human data in order to contribute to the 21st century vision that I mentioned earlier in order to improve regulatory testing; and I think that we should not forget that it is not only animal data that are out there that could be useful but human data exists too, and that type of project of course is ideal for those organisations that are working with industries. So, we are not talking there about data that need to be out in the public domain which is what they find most worrying, we are talking about data that could be shared internally within a scientific study between scientists to really push the science ahead and that really would push the science ahead because we have serious problems with animal toxicology and applying that to human beings and it is time that everybody got together to address that. I think that it will happen, but that we need to do what we can to make it happen sooner rather than later.
Chairman: I think that we have to make progress, so let us turn to non-human primates.

Q327 ***Earl of Caithness:*** This is an emotional and difficult subject. I think that you heard the last evidence session. Do you find the existing wording in the Directive confusing as a lot of people have submitted to us that it is and do you think that the proposal of Dr Vicky Robinson that there should be much more of a framework rather than this strange wording in the Directive would be a better way forward?
Ms McIvor: I can see the difficulties, and I think that the restriction that the Commission has attempted to put in place that would stop non-human primates being used in purely speculative basic research with no known medical outcome is a laudable aim, and I think it is one that should be encouraged. There is clearly a need to eliminate the use of primates in research and having a mechanism to do that is going to be hard but, as a very first step, purely speculative research where there is no medical application seems like a good place to start and I would like to see that research prohibited in the terms of the legislative text. I believe that there is very little of such research being carried out and I think that the impact would be minimal.
Dr Buckland: I would like to say that under Article 8.1A they are referring to fundamental research but there is also obviously fundamental medical research and the distinction is not made in the proposal. We certainly know from the research that we have seen in the neurological field that if the research is attributed to a disease, then it can also be quite speculative and marmosets and macaques are often used in Alzheimer's research after brain damage to look at cognition, knowledge and learning and this is attributed to the disease. Yet the research itself is incredibly speculative and we would like to see an end to this.

Q328 ***Earl of Caithness:*** What sort of fundamental research do you envisage being allowed under the Directive which might not be life-threatening or debilitating?
Dr Buckland: We feel that fundamental research can go ahead as long as it is using replacement techniques already available that can be used for non-human primates such as basic biological processes and

looking perhaps at potential treatments can still be carried out without using non-human primates.

Q329 ***Earl of Caithness:*** I have a couple more questions, one following up on Lord Brookeborough's question. Do you have a guesstimate as to when there might be widespread replacement possible? Secondly, could you comment on the dates that are set in the Directive for the various species?
Dr Buckland: Obviously, it is incredibly difficult to put a time to when we will see the widespread replacement of non-human primates. In terms of our organisation, we would like to see this as soon as possible but we understand that this is not going to happen overnight, and we feel that a targeted strategy needs to be in place for this. We do think that deadlines are essential and the deadlines that the Commission has put into place were found from the impact assessment to be achievable and there is also a mechanism within those deadlines for them to be pushed forwards or backwards if so needed. Of course, we can also look at the Cosmetics Directive deadlines that were used and, from this paradigm, we can see that there really does need to be a vision in place in order for progress to be made. Without that vision, then the replacement field will just carry on solely producing results and non-human primates will carry on being used and replacement will not happen as quickly as it could.

Q330 ***Earl of Caithness:*** So, you back the Commission's wording and date for this?
Dr Buckland: We do.
Chairman: We turn to authorisation and inspection.

Q331 ***Viscount Ullswater:*** You say in your evidence submitted to us that you consider the proposal's administrative demands are proportionate to its objectives, but you want to add to these, and I think that this is the only evidence that we have had that wants to add an EU Inspectorate particularly to look at the classification of severity. It looks as if that classification may not even be agreed by the time the Directive is agreed because it may come in later, which must make it rather difficult for you to work at. Why do you think that the Member States are incapable of administering this part of the Directive, and how would you see the EU Inspectorate work?
Ms McIvor: The Commission has identified the need for some level of central control of national inspections and I think that that is a good step but, as was said in the evidence, I do not think it goes far enough. One of the problems that could be envisaged is that the Member State infrastructure is such that severity classifications are adopted at EU level and implemented nationally and the implementation could become quite isolated. I think that assessing the severity of some experiments using written criteria is something that is very hard and I think that is one of the reasons the Commission has taken such a long time and has found it so problematic drawing up the definitions. It is one of those areas where a lot of cross-checking is needed, I think, between establishments and between authorisation bodies even in the Member State to make sure that everybody is exactly doing it in a uniform way. If it takes that kind of checking within Member States, I would say that it is a natural progression to say that it needs that kind of checking at an EU level as well. That is one reason for saying that we would like to see an EU Inspectorate. The other reason is that, with an EU Directive that is quite prescriptive in nature, it would seem to me to be very important to ensure, in order to realise the benefits of the level playing-field inside the internal market, that there does need to be a check to make sure that it is being implemented fairly and properly in all of the Member countries. In coming back to the point about the severity classifications, yes, I think that it is as much of a frustration to us as to all of the other people who have given evidence to you that the classifications have not yet been defined, but I think that, as a result of the activity in the Parliament, there is now a very strong move to make sure that those definitions are decided upon very soon. It is one major piece of action that we have seen taken place that we were not necessarily expecting because we always hated the idea of having to wait so long and I now think that we will not have to wait that long. I think that there is a lot of momentum behind all of the calls from all of the stakeholders for those classifications to be put in place so that decision makers can see exactly what they mean when they are talking about different severity classifications. It really is necessary that they can see what those actually are. Does that answer your question?

Q332 ***Viscount Ullswater:*** It is good to hear your views. I would like to ask a further question and that is that we have heard evidence from the bioscience sector that they are concerned about the level of bureaucracy. I have to say that what I have just heard from you may even add to that bureaucracy because of the imposition of another layer, especially when you are defining particular areas of research which obviously have an interpretation on the severity level. You clearly disagree that the burden of bureaucracy at the moment in the EU might be driving a little bit of science outside because you say that better animal protection in the EU should be seen as having a positive impact. How do you justify that? What evidence do you have for that statement?
Ms McIvor: One of the ways I would justify it is by picking up on statements made by animal research advocacy organisations which clearly talk about the

benefits of robust regulation and, when I see letters sent by researchers complaining about the provisions within the proposal, what I see most often is an assumption that everything in the UK is going to radically change overnight. That really is not the case. In their letters they also very often make it absolutely clear that they want to be regulated. I do not know that anybody sees animal research as an activity that should not be regulated and although I see a lot of people who would lean in the direction of self-regulation, I do not believe that if you actually put them on the spot and said, "Do you want animal research to be only self-regulated?" that they would say "yes". I think that everything accepts that a level of regulation is necessary. This is an activity that it is entirely appropriate to regulate. Having agreed that premise, then I think it is right to look at what the mechanisms are that we need to ensure that this is robustly regulated. I think what the Commission did was to completely unpick all of the existing legislation and all of the existing assumptions and say, "What do we need in order to regulate this activity?" There has to be an authorisation process. "What should the authorisation process be based on?" It should be based on ethical review. That is how those mechanisms have been born and of course what is in the proposal mirrors almost exactly, with some variations, what we currently have in the UK. In terms of the question about whether researchers will relocate, I would say that we know that there is a very strong research base in the UK, we know that there is a very strong CRO contract research organisation base in the UK and we know that there is a strong pharmaceutical base in the UK. Our legislation, which is so similar to the proposal, has been in place since 1986 and they have not relocated yet. Now, it does not mean that they will not and it does not mean that that should not be taken seriously, but I think it does mean that some of the fears have been possibly exaggerated and are not based on evidence. I know that there has been a strong thread in your discussions to find the evidence of the relocation, and I would again make the point that the evidence in the UK is that there has not been substantial relocation and that researchers like working within a robust regulatory environment, even though they do not like to be restricted. They want the regulatory environment to be robust but they do not want firm lines drawn or firm restrictions. I would say that it is absolutely appropriate to have some firm lines drawn and I think it is appropriate because animal research requires that level of attention by regulators. The public is in favour of robust regulation and I also think that it helps because some of those mechanisms produce stronger implementation of the 3Rs and my view is that that can only benefit science as well.

Q333 ***Lord Brooke of Alverthorpe:*** If I may continue on the same theme, firstly you made the statement that the Directive almost directly mirrors the position in the UK, which is not what has been put to us by much of the written evidence and by people who have appeared before us. They say that they have looked at the British system which is the leading one, they have then dissected it and they have produced now an awful monster which will add substantially to the bureaucracy and ultimately to the cost. There is a very big gap between what you are saying and what has been said to us.
Ms McIvor: Yes and I suppose that, within the scope of your inquiry, a line-by-line analysis and comparison might be useful, but what I see in the proposal is the ethical review requirement and the authorisation requirement strongly resembling the UK system. I also see in the Commission's proposals something which I do not like, which is that those experiments classified as up to mild might be notified to the competent authority but not necessarily scrutinised, and that is in the proposal.

Q334 ***Lord Brooke of Alverthorpe:*** Is that a weakening of the present system?
Ms McIvor: Yes, absolutely. In terms of comparing the proposal to what we have in the UK, that would be an enormous weakening and I do not think that it is something that the UK authority would want to have. I think that the UK Minister has made quite a clear statement to say that the Government does not envisage reducing the regulatory requirements. So, there are some areas where the regulatory burden would increase and some of those are invertebrate species for instance, and some areas where, if the proposal were implemented as it is in the UK, the regulatory burden would reduce, and that specific example is one where that would be the case.

Q335 ***Lord Brooke of Alverthorpe:*** Are there any other aspects of the Directive on which you would wish to offer views, particularly in relation to its implications for the implementation of the 3Rs? You have already given us a fair number of steers on areas in which you would like to see use of the Directive if you had the freedom but, specifically coming back to the 3Rs and we heard the evidence from the last session, is there more that you feel could be done there that ought to be in the Directive?
Ms McIvor: Yes, I think there is. I see the prospective ethical evaluation as absolutely essential and I think that the measures listed by the Commission that would be examined during the prospective ethical evaluation are spot on and I am really delighted to see that and that includes the check, is there another method of carrying out this experiment et cetera? It includes that 3Rs check not only in relation to techniques chosen but in relation to species, housing, equipment, all of those elements. That is the mechanism for ensuring that the 3Rs are applied and that is, I think, one of the reasons why the UK, I am

hoping, will back the Commission proposal over the European Parliament report because, in the Parliament First Reading position, there is a scaling back from that centrally conducted ethical review and authorisation for experiments classified as up to mild. That is not the same example I was giving early of the notification. It is a different scaling back. I think that we should certainly apply ethical reviews to all project applications. The other side of the ethical review is the retrospective review and I do see these as definitely being carried out hand in hand. It would be very sad to see the retrospective review whittled away at in the interests of reducing bureaucracy, because the retrospective review provides the opportunity to learn from existing practice and that opportunity to look at the output of projects and to compare it with the prospective ethical review. Were we right in assuming the severity levels? Were we right in assuming that there was not an alternative technique for this? Were we right in assuming that this project, with the objectives that we have listed for it, would produce those objectives? The retrospective review, which sadly the Parliament has reduced now to a level where it would cover only a tiny minority of projects, really is an instrument for implementing the 3Rs and it needs to be brought back in with the full force of a community that wants to promote full implementation of the 3Rs, really robust scrutiny of animal research in order to produce better techniques and to ensure that we learn from past experience.

Q336 ***Chairman:*** I think that is it. Thank you very much, indeed. It has been a very helpful and a very useful session.

Ms McIvor: May I add one thing? In terms of the EU structure for replacing animal experiments, we envisage the creation of an EU centre. I know politically it is difficult; I know that the structures are hard and I know that the structure is leaning towards using ECVAM because it is an existing unit of the JLC. But I think that public opinion as well as the scientific agenda and the animal welfare agenda really are looking for something much better at the EU level, and we are proposing an EU centre for replacement of animal methods and that will incorporate, we hope, the strategic vision. It will ensure that not only are animal experiments replaced where they can be replaced now but we really want to be looking at that new vision of science for the future in a way that includes the scientific community, and I really want to pick up on what NC3Rs said because it is so important that the scientific community is included in that agenda. The debate in the UK is so polarised. It is so sad to see the way the debate is so polarised that scientists who are advocating in favour of animal use and those of us who are advocating for this replacement vision are seen at opposite ends of the spectrum, because in fact the scientific agenda that is driving forward this progress is one that need not be seen within that very polarised frame of reference and it is really time to break that down. I think that what we say about the use and the vision for alternatives in response to the Directive and what happens when the Directive is adopted will set the framework for a future that could be really quite different. I think that that would be really very beneficial. I think that it does not dismiss all of the input and all the work and all of the interest from researchers who use animals, but it takes in all of the interest and the motivation of those scientists who are working in biomedical research who do not use animals; do not forget that the majority of biomedical researchers do not use animals. To try to actually break down those barriers and move forward in a way that says let us improve upon this because we know we can is what this Directive needs to achieve. Thank you.

Chairman: Thank you very much, indeed.

WEDNESDAY 8 JULY 2009

Present	Brooke of Alverthorpe, L	Dundee, E
	Caithness, E.	Livsey of Talgarth, L
	Cameron of Dillington, L (Chairman)	Palmer, L
		Sharp of Guildford, B

Memorandum by the British Union for the Abolition of Vivisection (BUAV)

The BUAV welcome this opportunity of contributing to the committee's inquiry. We will discuss both the Commission's original proposal and the Parliament's amendments to it.

The BUAV is generally regarded as the key organisation in Europe leading the debate against the use of animals used in experiments. We lead an Europe-wide coalition of animal protection groups opposed to animal experiments (ECEAE). We are a funding member of the International Council on Animal Protection at OECD (ICAPO) which has observer status at the Organisation for Economic Development and Co-operation (OECD).

We are also an invited interested party at the European Medicines Agency and the European Chemicals Agency and participate in regular committee meetings at both. We are also a government-appointed member of DEFRA's Chemical Stakeholder Forum. We were members of expert working groups set up by the European Commission (the Commission) which considered options for revision of EC Directive 86/609 (the animal experiments directive) and have participated in working groups looking at implementation of the animal test bans in the cosmetics directive.

Objectives of the Directive

The existing rules on the protection of animals used in experiments and other scientific purposes were adopted in 1986. Despite the fast development of techniques of experimentation, the increased understanding of the capacity of animals to feel pain and the obvious need to take into account ethical concerns on the use of animals in laboratories, the existing rules have not been updated since their adoption.

We believe it needs to be clearly stated at the outset of the revised directive that it should reflect current evolving public opinion and that science should move away from its current unhealthy dependence on animals into humane, often more reliable and often cheaper non-animal methods as soon as possible.

In harmonisation terms, the draft Directive is a proportionate though not entirely satisfactory response to the different approaches which currently exist in the EU.

For further information, please see paragraphs 24 to 26 in the BUAV's main submission.

International Competition

There is no doubt that the revision of the current legislation on the protection of animals used in experiments is the best opportunity for the EU to take the lead and raise minimum standards for animal welfare much higher than at present.

There is no evidence—as opposed to claim and threat by the animal research industry—that strengthening the rules on the protection of animals used in experiments would result in displacing research in third countries.

Decisions about where to conduct or source animal testing are influenced by numerous factors, such as fiscal policy, wage differentials, infrastructure and the availability of suitably qualified researchers.

Animal experiments in the UK are highly (though not always well) regulated and yet has one of the highest number of animal experiments in the world.

Paragraphs 27 to 32

The Proposed Requirement to Restrict Research on Non-human Primates (Article 8)

The Commission proposed (in Article 8) that NHPs should only be used where (*inter alia*) the research is "*undertaken with a view to the avoidance, prevention, diagnosis or treatment of life-threatening or debilitating clinical conditions in human beings*". The Parliament has removed this restriction, such that NHPs can now be used for just about any purpose.

The BUAV is clear that non-human primates (NHPs) should not be used in experiments. They suffer hugely, not simply from the experiments themselves but also from the necessarily very confined and unnatural housing and, in many cases, capture and transport as well.

There is a very large and growing body of evidence that NHP experiments are not efficacious.

Paragraphs 33 to 36

Extension of the Scope of the Directive (Article 2)

The BUAV believes that all sentient animals housed and killed within laboratories should be covered by the revised Directive.

The existing Directive does not include the use of animals in harmful experiments when used for basic research (around of third of all use), education and training, breeding (including of GM animals), and animals humanely killed for their tissues.

Any act carried out on an animal such as marking, toe clipping, ear or tail cutting, abortion or sterilisation, even if not as part of an experiment, should be included within the scope of the Directive and subject to authorisation by the member states and approval by a local Ethical Committee.

Currently, an "animal" covered by the scope of the Directive is considered to be a living non-human vertebrate, including free-living larval and/or reproducing larval forms. Therefore, invertebrates and fetuses for which there is evidence of sentiency, are not currently covered.

Paragraphs 37 to 39

Authorisation of Persons, Requirements for Establishments, Inspections and Project Requirements (Articles 20–43)

The Commission's proposals broadly mirror the requirements of ASPA (Animals (Scientific Procedures) Act 1986), under which persons, establishments (breeding, supply and research) and projects have to be authorised by the Home Secretary.

Authorisation of projects

The BUAV supports the Commission proposal requiring authorisation for all projects based on an ethical evaluation by member states.

The Parliament has come up with a wholly unsatisfactory and unworkable compromise, which would exclude millions of animal experiments from authorisation. Amendment 167 stipulates that only projects classified as "moderate" or "severe" (or those involving non-human primates (NHPs)) need authorisation. All other projects need only be notified to the competent authority following local ethical review.

Permissible purposes

The BUAV strongly believes that experiments for household products, alcohol and tobacco products, weapons, psychology testing, food additives, shellfish safety (which involves very painful tests), plants, education and training (where there are ample alternatives), research aimed at the preservation of a species and forensic inquires are particular examples of types of animal experiments which should not, on any footing, be allowed.

We also believe that the revised directive should give the Commission, in consultation with stakeholders and the Parliament, the power to prohibit the import into the EU of particular products which have been developed under standards significantly below those mandated for the EU under the revised directive, or in circumstances which would not be permitted in the EU.

Permissible species

It is clear that the public is particularly concerned about the use of NHPs, cats and dogs, because of the additional suffering these species are liable to experience in the laboratory setting and (in the case of NHPs) before they get there.

Permissible purposes need to be heavily circumscribed so that public opinion is properly reflected.

Permissible suffering

The BUAV strongly believe that the notion of allowing suffering which is both severe and prolonged is obscene in a civilised society.

In Article 15(2) of its proposal, the Commission prohibited the infliction of severe suffering which is prolonged. This is the equivalent to the UK's "*severe pain or distress which cannot be alleviated*". The Parliament has passed two contradictory amendments. One, proposed by the BUAV, would prohibit severe suffering which was more than transient. The second, proposed by the Agriculture Committee, would allow suffering which was both severe and prolonged (subject to the weak safeguard of additional ethical scrutiny).

Re-use

Under Article 16 of the Commission's proposal, re-use would be limited to situations where both the first and subsequent procedures were of no more than "mild" severity ("double mild") (subject to the possibility of a derogation by the competent authority to allow "moderate/mild"). The Parliament (amendments 72–75) would allow repeated "moderate/moderate".

Ethical evaluation and retrospective assessment

It is obvious that proposals to experiment on animals should be subjected to close scientific scrutiny.Ethical evaluation involves weighing the anticipated harm to the animals against the anticipated benefit to humankind.

The BUAV believe that all projects involving animals should be assessed.

Transparency

Transparency is a key requirement for accountability, public debate and indeed good science (because it generates discussion). The Commission's proposals, as amended by the Parliament, are wholly inadequate. Transparency is important at a number of stages.

We fully accept that *genuinely* commercially sensitive information (information the disclosure of which would or might prejudice a patent application, for example) can be withheld as long as it retains its sensitivity.

Inspections

It is clear that member states should have comprehensive systems of inspection in place to make sure that experiments are being conducted only in accordance with authorisations and that suffering is kept to a minimum at all times.

Paragraphs 40 to 100

Care and Accommodation (Article 32)

Animals must be kept in conditions meeting the criteria set out in Article 32 of the Commission's proposal.

The overriding duty, here and in relation to experiments and the adverse effects they produce, must be to keep suffering to a minimum at all times and this must be spelt out clearly in the directive.

Paragraph 101

Alternative Methods

Responsibility with regard to alternative methods under the directive should rest with the Commission and other EU institutions, member states and researchers.

There must be a clear prohibition on the use of animals where there is an alternative which could in practice be used to generate the required information. Validity of the test method should be judged scientifically on a case by case basis, rather than whether the test has been through any one particular validation process (since this may have less to do with science than bureaucracy).

Paragraphs 102 to 106

Subsidiarity and Legal Base

It is appropriate to regulate at EU level in all of the proposed areas, or this would inevitably run counter to the harmonization objective and would lead to some member having lower standards than others.

There is nothing to prevent member states going further than the directive if they wish (under Article 95 of the EC Treaty and the Parliament's amendment 54).

Paragraph 107

21 May 2009

Main Submission by the BUAV

Introduction

(a) *Opening remarks*

1. The BUAV welcome this opportunity of contributing to the committee's inquiry. We will discuss both the European Commission's (the Commission) original proposal and the Parliament's amendments to it.

2. We have already expressed our concern about the composition of the committee. It appears to have very little expertise in the science of animal experiments—including non-animal alternatives and the capacity of animals to suffer in various ways—or in animal welfare ethics. These are massive lacunae. We attach our letter of 13 May to Lord Sewel as Annex 1.

3. The BUAV is generally regarded as the key organisation in Europe leading the debate against the use of animals in experiments. We lead an Europe-wide coalition of animal protection groups opposed to animal experiments (ECEAE). We are a member of the International Council on Animal Protection at OECD (ICAPO), which has observer status at the Organisation for Economic Co-operation and Development (OECD), which seeks to harmonise protocols for the testing of non-pharmaceutical chemicals. We are also an invited interested party at the European Medicines Agency and the European Chemicals Agency and participate in regular committee meetings at both. We are also a government-appointed member of DEFRA's Chemical Stakeholder Forum. We were members of expert working groups set up by the Commission which considered options for revision of EC Directive 86/609 (the animal experiments directive) and have participated in working groups looking at implementation of the animal test bans in the cosmetics directive. We have given evidence to European Committees, select committees and to the Royal Commission on Environmental Pollution. We have brought several legal challenges on the implementation of animal experimentation law, both here and in the EU and have an unrivalled reputation for conducting undercover investigations, usually the only way to get reliable information about the reality of animal experiments and the care of animals in laboratories.

(b) *The BUAV ethical approach*

4. The BUAV is opposed to all experiments on live animals. Our objections are principally ethical, although as we explain animal experiments are often scientifically very unreliable. We believe that it is wrong knowingly to cause suffering to sentient beings when it is not for their benefit and, self-evidently, they do not consent. The immorality is in direct proportion to the suffering caused—experiments causing a mild degree of suffering are mildly wrong; those causing severe suffering are very wrong indeed.

5. We strongly support, of course, the objectives of finding treatments for human illnesses and ensuring that products are safe. However, leaving aside the question whether animal experiments are scientifically the best way of achieving these objectives, a desirable end cannot of itself justify cruel means. If it could, we would experiment non-consensually on people, indisputably a far better model for human diseases and safety testing than non-human animals. Society rightly imposes a self-denying ordinance in this respect. If we are to be consistent in our ethics, the self-denial should be extended to sentient animals, who are just as capable of suffering as people and who have precisely the same interest in not being made to suffer when it is not for their benefit. Some people would extend the self-denial to research using human embryos, whatever the benefit such research could bring with debilitating human diseases.

6. Society develops ethical rules precisely because our behaviour may cause suffering to others. Suffering is inevitable with animal experiments, not just from the experiment itself but also from the inescapably confined and unnatural living conditions, and the capture, transportation and forced repeated breeding of some

animals. Why should it be any more acceptable, in ethical terms, to cause suffering to a species other than our own, for our benefit, than it is to cause suffering to members of a race, or a gender, or followers of a particular religion other than our own?

7. We appreciate that the question of prohibiting animal experiments altogether is not on the table in the current revision of EC Directive 86/609 (the animal experiments directive). However, ethics are nevertheless a key component of the debate (along with scientific efficacy). This is because ethical evaluation by member states of proposed projects involving the use of animals is a central feature of the European Commission's proposal (it has been watered down by amendments passed by the Parliament). The debate is all about where lines should be drawn—which species should be covered by the directive and which should receive particular protection, for which purposes should the use of animals be allowed, what level of suffering should be permitted, how is the trade-off to be made between limiting numbers of animals and limiting the suffering of those which are used, what level of compulsion should there be regarding alternatives to animal experiment, to what level of housing and care should animals in laboratories be entitled and so forth?

(c) *The BUAV scientific approach*

8. Statistics

According the latest statistics for the European Union for 2005 (released in 2007),[1] over 12 million animals are used in experiments that "may cause it pain, suffering, distress or lasting harm" . . . every year by the 25 member states. France, the UK and Germany are the largest users, using at least 2.3, 1.9 and 1.8 million animals respectively in those experiments captured by the statistics (the actual figures are considerably higher: see below).We estimate that at least 115 million animals are used worldwide[2] and the European Union would make up a large proportion of this. This is because animals that have been genetically modified, breed and killed for their tissues or as surplus to requirements are not yet counted in the EU. If they were, we estimate Europe's use would at least double to over 27 million. This is supported by the fact that the national statistics of each country are often much larger than those they submit to the EC, eg the UK claims to use over 3 million and Sweden over 7 million animals each year.

9. Types of animals

Although the majority of experiments are conducted on mice and rats (72%), researchers in the EU also use huge numbers of dogs (24,119), non-human primates (10,449), rabbits (321,681), guinea pigs (257,307), cats (3,898) and farm mammals (140,055), every year. Non-human primates are mostly used to test the safety of drugs and in invasive basic research related to the brain and behaviour. Contrary to popular belief only a tiny minority (13%) of primate use is testing the efficacy of new drugs. 73% of old world monkeys come from breeding centres outside the EU, usually Asia. Most are born in these centres from parents that were captured from the wild (known as F1 animals).

10. Uses of animals

Less than 50% of the animal experiments conducted in the EU (47%) constitutes research into human diseases, including relevant fundamental research in the areas of cardiovascular research, cancer and nervous and mental illness. 33% of animals (over 4 million) are used for fundamental research which is not conducted with the aim of directly benefiting human health and may not be directly related to human disease. Such research can nonetheless involve significant suffering as result of major surgery, electrocution and other psychological stressors. Research into the harmful effects of recreational drugs such as alcohol, tobacco, cocaine and heroin are just one of the more questionable use of animals in Europe. This research would fall under fundamental research because it is not about testing new treatments and is of limited use since the harmful effects of these drugs are already well known. 4% of all EU research is the toxicity testing of chemicals, used in food additives, agriculture, industry and consumer products. In 2005 this constituted over half a million animals and is set to rise with the advent of REACH, the new EU chemicals regulation which is likely in practice to involve a further 8–13 million animals[3] in chemicals safety testing over the next 10 years. A further unknown number of animals (in the UK a further 30%) are used to produce genetically modified animals who may well suffer significantly, partly as a result of the genetic modification and partly through living their lives in the laboratory environment.

[1] European Commission: *Fifth Report from the Commission to the Council and the European Parliament on the Statistics on the number of animals used for experimental and other scientific purposes in the member states of the European Union* COM/2007/675 final (2005)—http://ec.europa.eu/environment/chemicals/lab_animals/reports_en.htm

[2] Taylor *et al* 2008. Estimates of worldwide laboratory animal use in 2005. *Alternatives to Laboratory Animals 36, 327–342.*

[3] European Commission 2006. Briefing note on the number of animals expected to be used under REACH: summary of re-assessment performed by the JRC. *Joint Research Centre,* October 2006.

11. Efficacy of animal research

We believe that animal experiments are a poor way of testing if chemical or drugs are safe and/or effective. This is because animal experiments tell us about animals, not about people. The results of animal studies can never guarantee the safety or efficacy of human medicines or other products because of the fundamental biological differences between the species. It is not until a substance is tried in human clinical trials that we ever really know that it is safe for use. Surprisingly, the reliability and validity of animal experiments has not been properly assessed- they are only assumed to be effective through history of use.

12. However, where evaluative studies have been conducted, animal tests have been shown to be poorly predictive of human outcomes. For example, in one study 19 of 20 substances judged to be safe in humans caused cancer in rodents[4] and, in another, only 2 out of 6 drugs were the animal tests predictive of the human outcomes.[5] Indeed, an industry performed study found that rodents only predicted human toxicity 43% of the time.[6] It is not surprising therefore to learn that of those few drugs that successfully pass the animal studies, less than 90% actually make it to the pharmaceutical market, usually because they do not work in human trials.[7] As drugs become increasingly specialised, animal tests are going to become even less effective; a clear example of this is the trial of a monoclonal antibody (TGN1412) that nearly killed the six British volunteers testing it, even though it showed no effects in the 26 monkeys who were exposed to it at 500 times the dose.[8] In vitro tests conducted immediately after the event predicted the effects seen in the men.

13. The use of animals as "models" of human disease is a highly criticised practice since in most cases the animal has to be artificially induced with the disease. So, in addition to the obvious species differences, there are fundamental differences between the natural disease and the artificial one. This goes some way to explaining the monumental failure to develop effective and safe drugs and vaccines for important diseases such as HIV/AIDS, Alzheimer's, Parkinson's and stroke. Despite more than 85 different vaccines having been tested in around 200 clinical trials, protection and/or significant therapeutic effects have not been demonstrated by any vaccine to date in humans, despite decades of effort and extensive research funding.[9] At least 1,000 animal-tested neuroprotective stroke drug candidates have been tested in animals—with no success in humans.[10]

14. Use of alternatives

To determine if a chemical or drug is going to be safe, studies can be done using human cells or tissues in the test tube (in vitro studies); computer models can also be used to predict a chemical's activity based on its similarity to other chemicals (QSARS). Batteries of these tests can be employed to answer key questions such as whether the chemical is likely to be acutely toxic, irritant or cause damage to specific parts of the body such as damage to our genes that might lead to cancer. Some of these tests have been validated and shown to be as, if not more, effective than the animal studies they replace. For example, the Reconstituted Human Skin (RHE) Models are more predictive of skin irritation than the rabbit Draize test.[11] In vitro studies can also be employed to determine efficacy, for example, HIV and anti-cancer drugs are always tested using HIV or cancer cells in the test tube. Arguably, it would be better to test potential drugs first on human patients in "futility studies", once we know they are safe (using the techniques above), rather than wasting time developing animal models for which there is little evidence that they are effective.

15. It is fair to say that we do not have an "off the shelf" replacement for every single animal test. In many cases the researchers actually want to know what happens to the animal, we believe studies such as these should be challenged as they arguably add little to our key concern; human health. Another reason is that although alternatives exist, it takes many years and cooperation for industry and regulators to use them. The RHE skin models for example have been in development for over 20 years, and are still not yet accepted internationally, despite the fact that they are relatively simple models with reams of evidence in their support. It is vital that the revised Directive continues to mandate the use of alternatives that are scientifically sound. It is not acceptable that this "soundness" should be internationally agreed, because this has far less to do with scientific integrity than politics and bureaucracy. We should have enough faith in our European scientists to determine

[4] Ennever, F K *et al* 1987. The predictivity of animal bioassays and short-term genotoxicity tests for carcinogenicity and non-carcinogenicity to humans. *Mutagenesis.* 1987;2:73–78.
[5] Pound, P *et al* 2004. Where is the evidence that animal research benefits humans? *British Medical Journal* 328, 514–7.
[6] Olson, H *et al* 2000. Concordance of the toxicity of pharmaceuticals in humans and in animals. *Regulatory Toxicology and Pharmacology*; 32: 56–67.
[7] Mike Leavitt, Health and Human Services Secretary, Food and Drug Administration, 2006. *FDA Press Release* 12 Jan 2006.
[8] Department of Health, 2006. Expert Scientific group on phase one clinical trials: final report, *Crown copyright, 2006*.
[9] Bailey J 2008. An assessment of the role of chimpanzees in AIDS vaccine research. *Alternatives to Laboratory Animals* 2008; 36:381–428.
[10] O'Collins V E, Macleod M R, Donnan G A, Horky L L, van der Worp B H, Howells D W. 1,026 experimental treatments in acute stroke. *Annals of Neurology* 2006;59:467–477.
[11] Jirova, D, *et al* 2007. Comparison of human skin irritation and photo-irritation patch test data with cellular in vitro assays and animal in vivo data. *AATEX 14, special issue*, 359–365.

the validity of alternatives (indeed we are world leaders on this via the European Centre for the Validation of Alternative Methods) and should promote these as soon as they are shown to be scientifically valid, a concept that needs to be properly defined.

16. We also need more investment in alternative methods and greater support at the European level to make sure that promising techniques actually replace the animals they are designed to. As an example of how large the divide in spending between alternatives research and biomedical research is; the UK government via the Medical Research Council (MRC) and Biotechnology and Biological Sciences Research Council (BBSRC) provided the UK National Centre for the 3Rs (NC3Rs) with £2.6 million in 2007–08 for research into alternatives. In contrast, the BBSRC and MRC together funded research and training in science and biomedical research totalling £643 million in 2007–08.

(d) *The approach the revised Directive should take*

17. In the context of acute ethical controversy and dilemma, which inescapably accompany animal experiments, what should the overall legislative approach be? The answer must be that the legislation should reflect, as best it can, public opinion. It should not be a charter for the multibillion pound animal research and animal supply industries to carry on largely as they wish, away from the public gaze and applying only their ethical perspective or that of those they purport to represent. Moreover, the legislation must be sufficiently flexible to reflect public opinion as it evolves.

18. Divining public opinion is not easy. Opinion surveys need their health warnings (even though the European Union expressly relies on them when developing legislative policy [Eurobarometer surveys]). But nor can they be disregarded when they produce inconvenient results, and nor should legislators in this area adopt the paternalistic approach that they know what is best for people, despite what they may say. The BUAV, through the Europe-wide coalition it leads, recently commissioned an opinion survey from leading pollsters YouGov, in six representative EU countries—the UK, France, Germany, Italy, the Czech Republic and Sweden. The results, set out in Annex 2, are startling, and are remarkably consistent across the six countries. Very large majorities were opposed to any experiments on primates, cats and dogs causing pain or suffering (as all must inevitably do) and to experiments on any species causing severe suffering. A similarly large majority wants all information about animal experiments to be in the public domain, save that which is confidential or which would identify individuals.

19. Most telling of all, 79% of respondents will only tolerate animal experiments, if at all, where they are for life-threatening or serious human conditions. Included in the 79% are, of course, the very many who, as is apparent from a succession of other opinion polls, share the BUAV's view that animal experiments should not be permitted for any purpose. But, at the very least, the new directive, if it is to reflect rather than ride roughshod over public opinion, should limit animal experiments to those for important medical research or other overwhelming societal need.

20. The research industry always focuses on life-threatening and debilitating human illnesses in its public pronouncements and lobbying and seeks, disingenuously, to give the impression that all animal experiments are for this purpose. It creates a kind of Trojan horse by which animal experiments for all kinds of inessential purposes receive the PR shield of those conducted for important objectives. Regrettably, both the media and many politicians contribute to this deceit on the public by failing to investigate thoroughly or report in a balanced way. We attach as Annex 3 the recent statement by MEP Mojca Drcar Murko[12] when she took the extraordinary step of asking for her name to be removed as draftsperson of the Environment Committee opinion on the Commission's proposal. She complained about what can only be described as the emotional blackmail employed by industry:

> "This goes in particular for the following thesis [advanced by industry]: industry is trying hard to reduce, refine or replace animal experiments. No legislative incentives are therefore necessary. The consequence of this was the equation 'should you not allow that the experiments continue without (too much) interference from outside—people/children will be dying'. Conservative and some liberal members of the EP environment committee followed their line and accused me of being responsible for 'killing the research and therefore killing children . . .'."

21. It is worth stressing that nothing animal protection groups such as the BUAV are proposing would lead to the slightest risk of children dying.

22. As we shall explain, animal experiments take place, in their millions, for all sorts of purposes which have nothing to do with finding the cure to cancer, Alzheimer's and so forth. We concede, for these purposes, that basic research which has as its objective the making of a real contribution to finding the clue to serious human

[12] The full statement has not been published in the Report.

illnesses, and which has a realistic prospect of making that contribution, would fall within the category of important research. We would, however, exclude the development of "me-too"drugs where the primary motive (as with so much of vivisection) is commercial and the therapeutic benefit minor.

23. There is another important point about legislative approach. This is that every animal researcher says that he or she deeply regrets having to use animals and longs for the day when it is no longer "necessary". Some may view such a claim with skepticism, given the triviality of so many experiments, the callousness and sometimes outright cruelty which successive undercover investigations, here and throughout Europe and the wider world, have revealed and the fierce resistance which researchers show to meaningful transparency. But let us take the claim at face value. Professor Colin Blakemore, a passionate defender of vivisection, has described animal experiments as a "necessary evil". We dispute the "necessary" epithet. But it is obvious that society should do all in its power to eradicate an evil, particularly one on so massive a scale and causing such immense suffering. Legislation has a key role to play in the eradication of an evil. Restrictions, incentives (including funding for alternatives) and targets are needed to wean scientists—and regulators—off their traditional reliance on animals and encourage them into more modern, non-animal techniques, which often enjoy great (but sometimes largely untapped) potential. We attach as Annex 4 a paper about how targets would work which we gave to the Boyd Group, an organisation made up largely of animal researchers with some animal welfare representation, in 2005, and as Annex 5 the amendment we drafted to Article 53 of the Commission's proposal, about the need for periodic reviews and their objectives. The amendment was tabled at the European Parliament but not adopted.

Question 1: *Objectives of the Directive*

24. The existing rules on the protection of animals used in experiments and other scientific purposed were adopted in 1986. Despite the fast development of techniques of experimentation, the increased understanding of the capacity of animals to feel pain and the obvious need to take into account ethical concerns on the use of animals in laboratories, the existing rules have not been updated since their adoption.

Some Member States have taken the initiative to go further than the minimum standards laid down in the existing Directive, thereby creating huge differences in national legislation (regarding the requirements for authorisation and ethical evaluation, standards of housing and care, enforcement of the legislation, etc).

Inequalities linked to economic disparity, low standards of animal welfare, reflection of the public opinion in legislation justify the urgent need, in internal market terms, to harmonise the legislation on the protection of animals used in experiments in the EU.

25. In harmonisation terms, the draft Directive is a proportionate though not entirely satisfactory response to the different approaches which currently exist in the EU. The Commission has addressed a number of those issues (by extending the scope of the Directive, detailing the required authorisation and ethical process, introducing harmonised housing and care standards, data-sharing provisions, etc).[13] However some definitions, criteria and procedures need to be more detailed in order to be applied uniformly by Member States, and reduce existing disparities in the EU (for example, the assessment of suffering, application of the harm/benefit test, targets to reduce and replace animal experiments).

26. We believe it needs to be clearly stated at the outset of the revised Directive that it should reflect current evolving public opinion and that science should move away from its current unhealthy dependence on animals and to humane, often more reliable and often cheaper non-animal methods as soon as possible.

Question 2: *International Competition*

27. The revision of the current legislation on the protection of animals used in experiments is the best opportunity for the EU to take the lead and raise minimum standards for animal welfare much higher than at present.

28. There is no evidence—as opposed to claim and threat by the animal research industry—that strengthening the rules on the protection of animals used in experiments would result in displacing research in third countries. Decisions about where to conduct or source animal testing are influenced by numerous factors, such as fiscal policy, wage differentials, infrastructure and the availability of suitably qualified researchers.[14] Animal experiments in the UK are highly (though not always well) regulated and yet have one of the highest numbers of animal experiments in the world.

[13] For more details on the potential impact of the Commission's proposals for the revision of Directive 86/609/EEC, please refer to the Impact assessment based on an external study performed by Prognos AG: http://ec.europa.eu/environment/chemicals/lab_animals/pdf/ia_full.pdf

[14] Please refer to the European Commission Impact assessment: http://ec.europa.eu/environment/chemicals/lab_animals/pdf/ia_full.pdf

29. Raising animal welfare standards in the EU would encourage the European animal-testing industry, which claims to be deeply concerned about animal welfare, to maintain those high standards if it decides (for other reasons) to relocate in third countries or to only source research work outside the EU from companies operating those standards. In that way, standards will be raised to the EU level.

30. A number of third countries using animals in experiments have already in some aspects raised their standards of animal welfare or have already integrated processes of control of the use of animals.[15]

31. The BUAV has proposed that the directive should prohibit the import into the EU of monoclonal antibodies (MAbs) produced unnecessarily using the extremely painful mouse ascitic method and that Commission, in consultation with the European Parliament and stakeholders, should have the power to ban the import of other products developed by methods falling significantly short of those required by the directive. In this way, standards would have to be raised outside the EU if the countries concerned want to export to Europe and with it any incentive for EU companies to relocate or contract-out outside the EU.

32. There is also an ethical dimension to all this. No one would think of suggesting that fashion companies should be allowed to operate sweatshops in the EU, employing child labour, because otherwise companies will take their business to the developing world where sweatshops are endemic. Why, then, should animal welfare standards be depressed from what the public regards as acceptable in the face of a similar threat?

Question 3: *The proposed requirement to restrict research on non-human primates (Article 8)*

33. The BUAV is clear that non-human primates (NHPs) should not be used in experiments. They suffer hugely, not simply from the experiments themselves but also from the necessarily very confined and unnatural housing and, in many cases, capture and transport as well. The use of great apes is particularly objectionable and has been banned in the UK since 1995 (save in exceptional circumstances). We enclose a recent BUAV report on how we can replace the use of NHPs.[16] Furthermore, a recent YouGov poll[17] showed that 81% of people agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates. Recent BUAV investigations have shown the immense suffering involved in the primate trade.[18] A video summarising these investigations may be seen on the BUAV website.[19]

34. There is a very large and growing body of evidence that NHP experiments are not efficacious. For example, the drugs used in the Northwick Park monoclonal antibody clinical trial catastrophe had been tested on primates at 500 times the dose given to the volunteers and considered to be safe. Subsequent laboratory tests showed that the effects could have been predicted using *in vitro* methods.[20] Similarly, not one of the 85 or more candidate HIV/AIDS vaccines tested successfully on NHPs has worked in patients. And, over 1,000 potential neuroprotective stroke treatments have been tested in animal models (including primarily NHPs) but none of the 150 which have progressed to human trials has proved successful. We attach at Annex 6 the submission we made to the recent European Commission inquiry into the efficacy of NHP research and alternatives to it.[21] It is clear that, far from causing problems for important research, a ban would be scientifically beneficial, quite apart from the welfare issues, in encouraging medical research to modernize.

35. The Commission proposed (in Article 8) that NHPs should only be used where (*inter alia*) the research is "*undertaken with a view to the avoidance, prevention, diagnosis or treatment of life-threatening or debilitating clinical conditions in human beings*". The Parliament has removed this restriction, such that NHPs can now be used for just about any purpose. There has, once again, been disinformation propagated. The Parliament press office put out a statement on 5 May 2009[22] claiming that the restriction "*would hinder research into, among other diseases, some forms of cancer, multiple sclerosis and Alzheimer's disease*". Since these diseases would, self-evidently, come within the rubric "*life-threatening or debilitating clinical conditions in human beings*", this

[15] Please see note 2.

[16] The full "Ending Primates Experiments" BUAV report could be found online: http://www.buav.org/media/files/campaigns/primates-in-research/Ending_Primate_Experiments_2007.pdf

[17] Opinion survey commissioned by the European Coalition to End Animal Experiments (BUAV is the leading member), and carried out in six representative EU countries—the UK, France, Germany, Italy, the Czech Republic and Sweden.

[18] Please follow this link to look at the outcomes of the BUAV investigations: http://www.buav.org/investigations

[19] Please follow this link to access the video on the BUAV's investigations on the use of primates: http://www.buav.org/buavtv/thetimeisnow/thetimeisnowendingprimateresearchintheeu

[20] Duff, G W (2006) *Expert Group on Phase One Clinical Trials: Independent report to the Secretary of State for Health*. 7 December 2006. The Stationery Office; London UK.

[21] The report by the committee concerned, SCHER (Scientific Committee on Health and Environmental Risks), came down in favour of NHP research. The BUAV believes the report and the process which led to it is deeply flawed, partly because it assumed the efficacy of NHP research instead of critically appraising the evidence and omitted to refer to huge swathes of evidence showing that NHP research does not work and evidence setting out the efficacy or potential of alternatives. A complaint has been made to the European ombudsman and can be supplied if desired.

[22] Please follow this link to access the European Parliament press statement: http://www.europarl.europa.eu/news/expert/infopress_page/032-54955-124-05-19-904-20090504IPR54954-04-05-2009-2009-false/default_en.htm

is palpable nonsense. It is therefore our opinion that the commission's proposal should be reinstated and primate use limited to research related to life-threatening or debilitating primate diseases.

36. The Commission also proposed, in Article 10, that researchers be obliged to move away from using so-called F1 NHPs—where one or both parents was born in the wild—albeit under a far too leisurely timescale. The Parliament has replaced the obligation with a requirement for there to be a feasibility study, removing at a stroke any incentive for breeders and researchers to move towards using only F2+ (where both parents have been bred in captivity). It also elongated the timetables. We attach at Annex 7 a briefing dated February 2009 on the F1/F2 issue.

Question 4: *Extension of the scope of the Directive (Article 2)*

37. The existing Directive does not include the use of animals in harmful experiments when used for basic research (around of third of all use), education and training, breeding (including of genetically modified animals), and animals humanely killed for their tissues. The BUAV believes that all sentient animals housed and killed within laboratories should be covered by the revised Directive. This is on the basis that they are all liable to suffer in transport, housing, handling, marking, breeding and euthanasia. Any act carried out on an animal such as marking, toe clipping, ear or tail cutting, abortion or sterilisation, even if not as part of an experiment, should be included within the scope of the Directive and subject to authorisation by the member states and approval by a local Ethical Committee.

38. Currently, an "animal" covered by the scope of the Directive is considered to be a living non-human vertebrate, including free-living larval and/or reproducing larval forms. Therefore, invertebrates and fetuses for which there is evidence of sentiency, are not currently covered. A report by the Animal Health and Welfare Panel for the European Food Safety Authority (an EU agency) in 2005[23] concluded that cyclostomes (lampreys and hagfish), cephalopods (octopi, squid) and decapod crustaceans (lobsters, crabs) can feel pain, avoid noxious stimuli, learn, remember, behave as we would do if injured and even have emotions. In fetuses, there is evidence that they can respond to painful stimuli and even communicate with their mother (eg towards the end of gestation, chicks (ie birds) can communicate with their mother). Although there is evidence that they are not consciously aware (awake) when in the uterus, the delicate system that controls this can become unbalanced and it is possible that fetuses become aware periodically and if something happens to its mother. For this EFSA agreed that 50% gestation was a reasonable cut off time for protection, although sentience varies from species to species.

39. As a minimum we would support the inclusion of the above mentioned animals and fetuses and refer the committee to the EFSA report on this subject. We suggest that some degree of flexibility is included in the Directive at this point, so that as new scientific evidence comes to light about the degree of sentience of other animals, they can also be covered. It is important that where there is uncertainty over capacity to suffer, the animal is given the benefit of the doubt—the precautionary principle is well-established in EU law. In their initial impact (Prognos)[24] assessment, the Commission stated that the impact of including these invertebrates would be a small burden on researchers and Member States. "*The inclusion of selected invertebrates would lead to a better control of the use of these animals due to the application of already existing authorisation and ethical review criteria to a wider range of animals . . . The inclusion of selected invertebrates would lead to low additional administrative costs for most Member States. First analysis shows that about 1,000 experiments or scientific procedures with these species are carried out in the EU per year*".

Questions 5 and 6: *Authorisation of Persons, Requirements for Establishments, Inspections and Project Requirements (Articles 20–43)*

(a) Introduction

40. The Commission's proposals broadly mirror the requirements of ASPA (Animals (Scientific Procedures) Act 1986), under which persons, establishments (breeding, supply and research) and projects have to be authorised by the Home Secretary. A cost:benefit test must be applied for all projects, under section 5(4). This is in large part an ethical test, although the quality of the science is or should be a key element too. Ethical evaluation, first at the establishment and then by the competent authority, is required by the Commission proposal.

[23] EFSA 2005. Aspects of the biology and welfare of animals used for experimental and other scientific purposes EFSA Journal 292, 1–136.

[24] Results of the experts online questionnaire carried out by the European Commission in 2006, please see here, p 398 and p 411: http://ec.europa.eu/environment/chemicals/lab_animals/pdf/i_scope.pdf

41. We will focus on authorisation of projects, although we will touch on inspections. It is essential that individuals and establishments should be subject to rigorous authorisation and checking procedures and, in the case of individuals, training to ensure that they are both competent and empathic.

42. Everyone who supports animal experiments (other than research freedom militants) is agreed that there should be some restrictions on the use of animals in research. There are two ways in which restrictions can be imposed. First, by legislative measures and second by ethical evaluation, whether at establishment or member state level. An example of the first is the Commission proposal to prohibit the use of great apes, save in truly exceptional circumstances. The listing of permissible purposes in Article 5 necessarily means, too, that purposes falling outside the list are prohibited. Ethical evaluation necessarily contemplates that some use of animals will not be permitted—otherwise why have the evaluation?

43. We deal below with both types of restriction. We will first address the issue whether animal experiments should require prior authorisation by member states.

44. For whatever purposes animal experiments are allowed when the new directive comes into force, and on whatever species, it is essential that the Commission is given the duty to keep these matters under periodic review, so that the legislation can march in step with evolving public opinion and developing scientific consensus about the capacity of animals to suffer, in different ways and to particular degrees. The Commission should be required to consult stakeholders and the Parliament and bring forward proposals to amend the directive. We attach at Annex 5 an amendment we have drafted to reflect this. The amendment to Article 53 passed by the Parliament takes on board some of this.

(b) Authorization of projects by member states

45. The Commission is right to require authorisation for all projects based on an ethical evaluation by member states. This is the position in the UK. There is a great deal wrong with the way the Home Office operates the cost:benefit test in practice (in Annex 10 is an article about the BUAV's judicial review arising out of its undercover investigation of neuroscience research at Cambridge University) but the principle that animal experiments should only be permitted with governmental approval, and that this approval should only be given after rigorous scientific and ethical scrutiny, must be right.

46. It is important to remember that animal experiments would constitute an offence under the criminal law were an exception not made for them. In the UK, for example, section 58 of the Animal Welfare Act 2006 exempts animal experiments carried out under Home Office licence from the provisions of the Act. It is quite wrong that researchers should be able to grant their own exemption from the criminal law. Only with a system of governmental approval can there be accountability. The legislative deal should be: if you want to do something which would otherwise be a criminal offence, and about which the public is acutely concerned, you have to have governmental permission and be strictly monitored. Ethical evaluation by the establishment is no substitute because it carries no public accountability—the Commission's proposals and Parliament's amendments do not even require any transparency.

47. The Parliament has come up with a wholly unsatisfactory and unworkable compromise. Amendment 167 stipulates that only projects classified as "moderate" or "severe" (or those involving NHPs need authorisation. All other projects need only be *notified* to the competent authority following local ethical review.

48. This would exclude millions of animal experiments from authorisation. It is therefore wrong in principle. It is also unworkable. Under Article 15(1) of the Commission proposal, it is for *member states* to ensure that procedures are classified as "mild", "moderate", "severe" or "non-recovery" in accordance with Annex VIIa (proposed by the Parliament). That is clearly intended to be part of the authorisation process, because member states cannot fulfill this duty unless they have *detailed* information about what is proposed. Annex VIIa is itself very detailed. Member states' duty under Article 15(1) is, of course, to ensure that projects are *properly* classified.

49. It is not possible to have a system which is part regulated and part self-regulated, particularly given the graduated nature of severity. Researchers would have an obvious interest in claiming that their projects involve no more than "mild" suffering because they would thereby avoid the need for authorisation. The proper classification of suffering should be for member states to decide objectively on the evidence. This matters because effective ethical evaluation cannot take place without a true appreciation of the suffering involved, as well as an objective assessment of the science and potential societal benefits.

50. There might be an implied power entitling competent authorities to check whether a classification in a particular case is realistic (although there is no sanction for a researcher getting it wrong). However, this provides no comfort. Spot-checks will not address the fact that projects which are not checked—in practice, the vast majority—may include many which have wrongly escaped governmental scrutiny.

51. There can only be two options—all animal experiments should require authorisation or none should. The latter is clearly unacceptable. The Commission's proposal should be adopted.

52. Even with NHPs, the animal research industry is desperate for as much self-regulation as it can muster. Under Article 8(1)(b) of the Commission's proposal, there has to be a scientific justification that the purpose of the procedure cannot be achieved by the use of species other than NHPs. The Parliament's amendment 58—promoted by industry—replaces this with a requirement that "the applicant provides a scientific and ethical justification" (emphasis added) that other species would not suffice. A researcher's inevitably self-interested opinion that there is justification may be very different from objective analysis.

53. Article 54 of the Commission proposal requires member states to designate one or more competent authorities responsible for implementation of the directive and says that a body other than a public authority may be designated. This would apply not only to authorisations of projects but throughout the directive. The thinking behind this proposal is not known. It is wholly unacceptable. Only regulation by a public authority can achieve accountability (not least to member states' parliaments) and enjoy public confidence. Under the proposal, a member state could, in principle, designate a body representing animal researchers. This shows the absurdity of the proposal.

(c) Permissible purposes: general

54. Article 5 of the Commission proposal sets out the purposes for which animal experiments can take place. It is a very widely-drawn list, far wider than public opinion would tolerate. Permissible purposes need to be heavily circumscribed so that public opinion is properly reflected.

55. Experiments for household products, alcohol and tobacco products, weapons, psychology testing, food additives, shellfish safety (which involves very painful tests), plants, education and training (where there are ample alternatives), research aimed at the preservation of a species and forensic inquires are particular examples of types of animal experiments which should not, on any footing, be allowed. There are plenty of others. We are happy to develop this further with the committee.

(d) Permissible purposes: imports

56. We believe that the revised directive should give the Commission, in consultation with stakeholders and the Parliament, the power to prohibit the import into the EU of particular products which have been developed under standards significantly below those mandated for the EU under the revised directive, or in circumstances which would not be permitted in the EU.

57. An example of the former is where unacceptable suffering is caused by an experiment or the husbandry is inadequate.

58. An example of the latter is where there are alternatives methods which could have been used. We believe that the directive should on its face prohibit the import into the EU monoclonal antibodies (MAbs) produced using the mouse ascites method (save where, exceptionally, there is scientific need to use animals). Non-animal alternatives, validated by ECVAM, have been available for over 10 years but there is nothing to prevent EU companies from importing MAbs produced with the ascites method and many do.

59. Apart from the huge welfare implications—the ascites method is universally regarded as causing a great deal of suffering—this puts EU companies at a competitive disadvantage. We explained above that there is little evidence that higher welfare standards in the EU cause EU companies to move their animal testing work elsewhere. The power we are suggesting would underline that point—clearly, there would be no point outsourcing animal testing to countries with lower standards if the resultant products could not be imported into the EU. The power would also help raise animal welfare standards. We are advised that exercise of the power it would be WTO-compliant because it would reflect the moral views in the EU which led to the revised directive.

60. With the exception of MAbs, this would be a power to prohibit rather than a duty. In exercising its discretion, the Commission would no doubt take into account the societal utility of a product—there would be no question of important medicines being banned.

(e) Permissible species

61. Similarly, it is clear that the public is particularly concerned about the use of NHPs, cats and dogs, because of the additional suffering these species are liable to experience in the laboratory setting and (in the case of NHPs) before they get there. Some female dogs and cats are forced to breed repeatedly, with obvious welfare detriment, as demonstrated by the BUAV's undercover investigation at Harlan-Hillcrest, a multinational laboratory animal supply company.[25]

(f) Permissible suffering: severe suffering

62. Animal suffering lies at the heart of the public's concern about vivisection. The concern is almost certainly in direct proportion to the level of suffering.

63. A key question is whether there is a level of suffering which should not be allowed, irrespective of hoped-for benefit. At present, the UK does have such a level. It does not permit "*severe pain or distress which cannot be alleviated*".[26] This is based on the Government's interpretation of Article 8 of the existing directive.

64. In Article 15(2) of its proposal, the Commission prohibited the infliction of severe suffering which is prolonged. This is the equivalent to the UK's "*severe pain or distress which cannot be alleviated*". The Parliament has passed two contradictory amendments. One, drafted by the BUAV, would prohibit severe suffering which was more than transient. The second, proposed by the Agriculture Committee, would allow suffering which was both severe and prolonged (subject to the weak safeguard of additional ethical scrutiny). The Parliament's officials have purported to resolve the contradiction by coming up with their own wording, but one which in fact favours the principle behind the Agriculture Committee's wording. The Parliament also passed an amendment (an amalgamation of amendments 71 and 185) stipulating that the criteria which the Commission is to develop for severity classification "*shall include an upper limit of severity beyond which procedures on animals will be prohibited*". This is unsatisfactorily vague—the position needs to be clear on the face of the directive—but it does at least acknowledge the principle that there is a point beyond which suffering should not be tolerated, irrespective of hoped-for benefit.

65. The notion of allowing suffering which is both severe and prolonged is obscene in a civilised society. This would in principle allow severe suffering indefinitely. The YouGov poll shows that European citizens are firmly opposed to the infliction of *any* duration of severe suffering.

66. Important medical research involving animals for chronic illnesses such as cancer, arthritis and multiple sclerosis takes place in the UK without their being any suggestion that the bar on particular levels of suffering acts as a restriction. Nor need it elsewhere in Europe, with proper use of pain-relieving methods and monitoring.

67. It is important to understand that, in the UK, which has similar classification labels as is proposed for the EU, so-called "moderate" suffering can involve a very high degree of suffering. At Cambridge University (the subject of the BUAV undercover investigation), for example, individual marmosets received multiple surgical procedures including painful craniotomies followed by the inducing of strokes or Parkinsonian symptoms (as a result of which some were unable to self-care), sometimes with multiple seizures, and were then forced to undergo a stressful series of tests over a period of months whilst on a severe water restriction regime—the Home Office categorised these experiments as "moderate".[27] There is every reason to fear that the UK approach would be replicated elsewhere.

68. As a flavour of what a "severe" (or "substantial" under the Home Office nomenclature) experiment looks like, here is the description given by the chief inspector to the High Court in the BUAV judicial review of a licensed experiment:

> "The systemic administration of the neurotoxin MPTP to non-human primates produces the full-blown clinical condition as seen in human clinical practice [Parkinson's disease] although, contrary to the human experience, the clinical signs may improve rather than worsen with time. This model produces, even with treatment, persistent, severely disabling and distressing clinical signs (with rigidity, tremor, and paucity of spontaneous movements being the main hallmarks of the condition) requiring a prolonged

[25] Please see the outcomes of this investigation here: http://www.buav.org/investigations/makingakiling
[26] See the final subparagraph of paragraph 5.42 of the Home Office's *Guidance on the Operation of the Animals (Scientific Procedures) Act 1986*.
[27] Please see the outcomes of the BUAV investigation in Cambridge here: http://www.buav.org/investigations/cuttingedge

> period of intensive care and leaving residual neurological damage requiring high-dependence special-care thereafter. Although not generally believed to be a painful condition in the animal models (it is essentially painless in man) it is considered to cause distress in the affected animals … producing devastating welfare costs".

Does a civilised society really wish to tolerate this level of suffering to animals, let alone on a prolonged basis?

(g) Permissible suffering: re-use

69. The re-use of animals clearly has huge implications for suffering. It is important to understand what is meant by re-use. The Parliament has voted this definition (amendment 43):

> "the use of an animal already used in a procedure, when a different animal on which no procedure has previously been carried out could also be used".

70. Where the same animal has to be used in other procedures for the benefit of the overall experiment, this is termed "continued" or "single" use. A single use can involve a number of invasive procedures. This is an example of a "single" use at Cambridge:

> 20 marmosets were trained on various discrimination tasks while confined in a container. All 20 then underwent their first operation. Anaesthetised and in a stereotaxic frame, they received a total of 18 injections to nine different locations on each side of the brain. Cognitive testing started after two weeks. Five to 11 months after the first operation, the marmosets were again anaesthetised and a dialysis probe inserted into the brain to find out whether the damaged brain cells had recovered in any way. This operation lasted 8.5 hours and the marmosets were allowed 7–10 days' recovery before testing recommenced. They were all eventually killed but only after 18–24 months.

71. Under Article 16 of the Commission's proposal, re-use would be limited to situations where both the first and subsequent procedures were of no more than "mild" severity ("double mild") (subject to the possibility of derogation by the competent authority to allow "moderate/mild"). The Parliament (amendments 72–75) would allow repeated "moderate/moderate". Under the Cambridge example, a marmoset subjected to numerous, invasive procedures could be used in another experiment involving numerous, invasive procedures, indeed repeatedly so.

72. We recognise there is a tension, in animal welfare terms, between wishing to keep the numbers of animals down, on the one hand, and minimising suffering, on the other. However, that tension should not be resolved in a way that allows an unacceptable level of suffering for an individual animal. That is why we support the Commission's "double-mild" approach. We strongly suspect that it is cost rather than concern about welfare which is driving the industry's push for "moderate/moderate".

(h) Ethical evaluation: scientific benefit

73. It is obvious that proposals to experiment on animals should be subjected to close scientific scrutiny, and that this can only be done objectively and with accountability at governmental level. It is not enough for researchers to claim that their research is important and of good quality—this has to be rigorously tested.

74. This is particularly important with basic or fundamental research. We totally reject the argument advanced by many animal researchers that they should be allowed to do any basic research involving animals they wish, just in case some piece of knowledge is generated which might in time contribute to treatment for some illness. The mere generation of new knowledge—inevitable from any experimental process—should not be considered a qualifying benefit for the purpose of the legislation. We appreciate that basic research is part of the discovery process. However, if it is to be allowed, for the time being, on animals, it must (i) have as its objective the making of an important contribution to the understanding of a serious human condition; and (ii) have a realistic prospect of making that contribution.

75. The cost:benefit note produced by the former chief inspector[28] accepts that a causative link needs to be made between basic research and actual benefit. Rather in contradiction, the Home Office's statistics show that hundreds of thousands of experiments are allowed each year when there is no direct benefit in view other than the generation of knowledge. In Annex 8 we give examples of trivial basic research which has taken place in the UK and elsewhere in Europe.

[28] *Guidance on the operation of the Animals (Scientific Procedures) Act 1986* (Home Office 2000), Annex I: Cost: benefit assessment, http://www.archive.official-documents.co.uk/document/hoc/321/321-xi.htm More detailed guidance is found in Home Office (1998). Cost/benefit assessment. A note by the Chief Inspector. Chapter 2, pp 50–59, in: *Report of the Animal Procedures Committee for 1997*. TSO: London. www.apc.gov.uk/reference/ar97.pdf

(i) Ethical evaluation: harm to animals

76. Ethical evaluation involves weighing the anticipated harm to the animals against the anticipated benefit to humankind. (It is sometimes argued that animals also benefit from animal experiments. In the majority of cases, however, animal experiments conducted into animal diseases are for the farming, pet food and racehorse industries—ie where human economic gain is the predominant motivating factor. And, in ethical terms, it is no more justifiable to experiment on, say, a dog, for the benefit of other dogs than it is to experiment non-consensually on a person for the benefit of other people).

77. As far as the harm or cost side of the equation is concerned, it is obvious that a realistic view should be taken of all the detriment which an animal may suffer as a result of being made to be involved in the vivisection process, from cradle to grave. At Annex 9 is an amendment we have proposed which reflects this [Article 15(1)].

78. Given that animals cannot articulate their experience, and the damage caused if an assessment underestimates the detriment, it is essential that a precautionary approach should be taken to suffering. The precautionary principle is, of course, well-established in environmental law and has some application in animal welfare law too. It should be enshrined in the directive. The precautionary principle is particularly important with genetically-modified animals, where the harm may not become apparent for a generation or two. (The BUAV is particularly opposed to the genetic modification of animals because of the potential for great suffering).

79. Similarly, the presumption should, as the former chief inspector has acknowledged, be that animals suffer in situations where humans would. That may be displaced by clear scientific evidence—and in some cases an animal may suffer to a greater extent than a human would.[29]

(j) Retrospective reviews

80. The Commission proposed (Article 38) that ethical evaluation should determine whether projects classified as "moderate" or "severe" severity should be retrospectively assessed at its conclusion, to consider whether the objectives were achieved, the harm caused to the animals and "elements that may contribute to the further implementation of the requirement of replacement, reduction and refinement". Projects involving NHPs would always have to be retrospectively assessed; projects of "mild" severity involving other species would never have to be.

81. The Parliament, astonishingly, has amended Article 38 so that only "severe" projects and those involving NHPs would need to be retrospectively assessed. This is wholly unacceptable. All projects involving animals should be so assessed, to make the judgements specified by the Commission. This is no bureaucratic burden because researchers will, surely, assess projects when they are completed anyway. Funders will certainly require this. But quite apart from this, where researchers have been allowed to do things to animals which would normally constitute a criminal offence, society as a whole has a stake in ensuring that that the decision was a reasonable one, so that lessons can be learnt for the future.

(k) Transparency

(i) *Introduction*

82. Transparency is a key requirement for accountability, public debate and indeed good science (because it generates discussion). The Commission's proposals, as amended by the Parliament, are wholly inadequate. Transparency is important at a number of stages.

83. In all that follows, we fully accept—and will not repeat each time—that genuinely commercially sensitive information (information the disclosure of which would or might prejudice a patent application, for example) can be withheld as long as it retains its sensitivity.

84. We also fully acknowledge that information which could lead to the identity of individuals or establishments should be withheld, because of any risk to personal safety in a particular case (albeit that the risk in general terms is very small, largely historical and often hugely exaggerated). This would not encompass,

[29] For example, researchers wanted to see if NHPs had a preference for looking at the left or right side when looking at a picture of a human face. For this, three NHPs had metal coils inserted into their eyes and were restrained by their heads into chairs and forced to watch computer images. They found that, like humans, monkeys also looked for longer at the left hand side of the face. *Left gaze bias in humans, rhesus monkeys and domestic dogs. Animal Cognition 2008 Oct 17.*
To conduct this study in humans, either with external eye coils in contact lenses or using infra red eye tracking devices, completely voluntarily and without restraint, causes much less suffering to the human than the monkey, especially when one factord in the deleterious effects of housing and transport on the NHPs.

however, information which could identify individuals where it is already in the public domain that the individuals concerned are involved with particular animal research. Researchers often voluntarily publish articles about their animal research and it follows that, to the extent that there is any risk to their safety, it is one they have voluntarily assumed (which almost certainly means that they do not, in fact, think there is a risk). The Information Commissioner understood the point in a recent series of successful complaints made by the BUAV following the refusal by a number of universities to disclose very basic information about their NHP research under the Freedom of Information Act 2000[30] (FOIA). Researchers attached to the universities had published extensively about their NHP work.

85. In addition to publication, animal researchers are encouraged by pro-vivisection pressure groups to talk about their work. We welcome this. But those same researchers cannot then hide behind the cloak of secrecy when asked for further information about their animal research.

(ii) *Comment period*

86. Competent authorities should publish proposals to carry out animal experiments to enable interested parties to comment, about the quality of the science, the availability of alternatives and the ethical evaluation more generally. In this way there can be proper accountability for regulatory decisions and public confidence will be increased.

87. There are precedents—for example, the evaluation stage under REACH has a compulsory comment period of 45 days for proposals to test chemicals on animals, and there is a similar comment period under the High-Production Volume Program in the US. The comment period need only be short.

(iii) *Detailed information about proposals*

88. Linked to this, full information about proposed or actual animal experiments (subject to the two exceptions discussed above) should be made available on request. The Commission proposes only that "non-technical summaries" should be provided. The UK experience has shown that this does not work. Under the UK system, licence applicants are encouraged—they are not obliged—to include a short "abstract" with their application for a project license. The Home Office then publishes the abstracts under its publication scheme under section 19 FOIA. This is what the Information Tribunal said about the five abstracts representing the project licenses for which the BUAV sought disclosure under the FOIA:[31]

> ". . . the abstracts appear generally to adopt a style and tone intended to persuade the reader as to the value of the proposed experiments. This is in contrast to the style of the license applications, which are more neutral in tone. This perception of a positive spin having been applied to the published information was increased by the absence from the abstracts of the detail about the experiments themselves . . .".

This is a damning statement by a judicial body and confirmed the BUAV's perception that abstracts are used by animal researchers as PR tools. Only full information will satisfy the public. It is patronising to suggest, as some have, that the public and in particular stakeholders such as the BUAV are unable to understand or deal responsibly with complicated scientific information.

(iv) *Ethical evaluation*

89. Details of the ethical evaluation, at both local and national level, should be made public so that the public can see the process of reasoning.

(v) *Duplication of experiments*

90. By "duplication" we mean animal experiments which are repeated either because a researcher does not know that they have taken place or he cannot access the results. This is distinct from the situation where an experiment is repeated for scientific reasons. Duplication should be prohibited because it serves no scientific purpose and therefore leads to unnecessary animal suffering. REACH has strong anti-duplication provisions, as does other EU legislation such as the pesticides directive, so there are precedents.

[30] See http://www.ico.gov.uk/upload/documents/decisionnotices/2009/fs_50160902.pdf (University of Oxford) and related cases against the Universities of Cambridge and Manchester, King's College London and University College London.

[31] http://www.informationtribunal.gov.uk/Documents/decisions/buavdecisionwebsite1.pdf The decision was overruled on a different point by the High Court.

91. Robert McCracken QC, when he was a member of the Animals Procedures Committee (the statutory advisory body), said this in his memorandum to the House of Lords select committee:[32]

> "3. Unnecessary harm to animals is built in to the system as the absence of any requirement to publicise results leads to duplication. Pharmaceutical companies have a "strong commercial interest" in not publishing blind alley research results [according to a Glaxo Wellcome company representative who expressly agreed that her views could be made public].
>
> 4. Medical progress may be hindered and the cost of drugs increased because of secrecy and the unnecessary duplication of research".

92. We are pleased that the Parliament has passed amendments, based on a draft propose by the BUAV, to tackle the problem of duplication. However, amendments 135 and 136 only bite if authorisation is needed, underlining why this is essential for all projects. We are concerned that the introductory phrase "Subject to the safeguarding of confidential information" in amendment 134 should not be interpreted in a way which emasculates the provision. By definition, the data which member states have to ensure is shared between researchers is likely to be prima facie confidential. The amendment must be intended to refer to other types of confidential information, but this needs to be made clear.

(vi) *Retrospective reviews*

93. The reviews must not only take place, they must be published so that the public can see what has happened. Lessons are more likely to be learnt if there is public scrutiny and duplication is less likely to take place.

(vii) *Infringement reports*

94. It is essential, for reasons of public accountability, that reports of infringements should be made public. Neither the Commission's proposals nor the Parliament's amendments contain this requirement.

95. In 2007, in a case brought under the FOIA by the BUAV,[33] the Information Commission ordered the Home Office to disclose documents about particular infringements. The Commission decided that, although particular exemptions prima facie applied, the public interest required disclosure. This was particularly so in light of the very light sanctions the Home Office normally imposes for infringements.

(viii) *Statistics*

96. Statistics are an important source of public information about animal experiments. Under ASPA the Home Office has to publish annual statistics. They are reasonably comprehensive but the House of Lords select committee on animal procedures (2002) was critical of them and recommended changes. An obvious criticism is that an animal is only counted for the year when its involvement in an experiment begins, so the fact that it is used during a subsequent year is hidden from public view. Similarly, the statistics give the false impression that the vast majority of animals are only subjected to a single procedure whereas many are subjected to several (see the definition of "re-use" above).

97. The Commission proposed (Article 49) the publication by member states of annual statistics but said little about what they should contain. We have proposed the following amendment:

> "The Commission shall in accordance with the regulatory procedure referred to in Article 51(2) by [within six months from the entry into force of this Directive] and after consulting the Parliament and stakeholders set out in detail the type of statistical information which is required. In doing so it shall be guided by the principle that the primary purposes of the statistics should be (a) to inform, to the maximum extent possible achievable by statistics, the public about the use made of animals for procedures in Member States, the purposes for which they are used, the development and use of non-animal alternatives and the level of suffering animals experience, and (b) to enable the public to assess whether appropriate ethical evaluations and regulatory decisions are being made".

98. Not only animals actually used in experiments but also breeding animals and those deemed unsuitable or surplus to requirements should be recorded, so that a proper picture of the extent of live animal involvement in science is given. There is evidence that animals falling into these categories exceed those which are used.

[32] Please follow this link: http://www.publications.parliament.uk/pa/ld200102/ldselect/ldanimal/999/1121102.htm
[33] See http://www.ico.gov.uk/upload/documents/decisionnotices/2007/fs_50108125.pdf

(l) Inspection

99. It is clear that member states should have comprehensive systems of inspection in place to make sure that experiments are being conducted only in accordance with authorisations and that suffering is kept to a minimum at all times. Authorisations should if necessary be varied or revoked in light of experience (for example, because the suffering is greater than had been anticipated or the benefits are not being realised). As many inspections as possible should be unannounced.

100. Article 33(2) of the Commission's proposal requires national inspections to be carried out by the competent authority at least twice a year (although Article 33(3), correctly, puts the level of frequency at that which is needed to ensure compliance with the directive). The Parliament has amended this to an average of one a year (subject to a risk analysis). That could mean, of course, that some establishments are not inspected at all during one or more years. That is clearly not satisfactory.

Question 7: *Care and accommodation (Article 32)*

101. We will not comment in detail in this submission about the standards set out in Annex IV to the Commission's proposals. We will confine ourselves to the key principles:

(a) Animals must be kept in conditions meeting the criteria set out in Article 32 of the Commission's proposal.

(b) As scientific knowledge about animals' needs develops, higher standards should be applied without the need to amend Annex IV (which would inevitably take considerable time).

(c) The overriding duty, here and in relation to experiments and the adverse effects they produce, must be to keep suffering to a minimum at all times and this must be spelt out clearly in the directive.

(d) There must be sufficient staff on site at all times to ensure that this duty is in practice being met. There must be adequate 24 hour cover.

(e) Similarly, an appropriately experienced veterinary surgeon should be on call at all times.

Question 8: *Alternative methods*

102. Responsibility with regard to alternative methods under the directive should rest with the Commission and other EU institutions, member states and researchers. There is an ethical imperative that alternatives are developed as quickly as possible, for animal welfare reasons but also because they are often more reliable (and cheaper).

103. It is wrong to think of alternatives simply as direct substitutes for animal methods. What matters is that they generate the required information. Similarly, it is a mistake to think solely in terms of scientific techniques. Governmental policy also has a part to play. For example, a policy of presumed consent for organ donation, as some member states have, could solve the organ shortage and thereby remove the incentive for xenotransplantation research (which causes immense suffering to animals).

104. The Commission should co-ordinate, share information and keep a database of alternatives. We welcome the extension of ECVAM's remit proposed by the Parliament (amendment 139).

105. The directive should make it clear that member states have a responsibility to help in the development of alternative methods, particularly replacements, with adequate funding, training and a suite of pro-active policies. The Commission's proposal, as amended by the Parliament, goes some of the way along this path.

106. We believe that these are the principles which should govern alternative methods as far as researchers are concerned:

(a) There must be a clear prohibition on the use of animals where there is an alternative which could in practice be used to generate the required information. Validity of the test method should be judged scientifically on a case by case basis, rather than whether the test has been through any one particular validation process (since this may have less to do with science than bureaucracy).

(b) In particular, there should be no suggestion—as some have made—that an alternative is only available if it is "internationally accepted" (whatever that means). That would inevitably reduce the pace of development of alternatives to that of the slowest country and remove any incentive to develop them.

(c) It should be made clear that additional cost is not relevant, save where the cost would be significant.

(d) Researchers should have a duty proactively to search for and devise alternative strategies and explain how they have done so, and not simply to apply one if it is readily available.

Question 9: *Subsidiarity and Legal Base*

107. It is appropriate to regulate at EU level in all of the proposed areas. It would be artificial to hive off some areas to member states. This would inevitably run counter to the harmonisation objective and would lead to some member states having lower standards. There is nothing to prevent member states going further than the directive if they wish (under Article 95 of the EC Treaty and the Parliament's amendment 54).

Annex 1

BUAV letter to Lord Sewel

Call for Evidence by the Environment and Agriculture Subcommittee
Inquiry into the Revision of the Directive on the Protection of Animals used for Scientific Purposes (the animal experiments directive)

I am writing to express our concern about the composition of the subcommittee. It appears to us to be ill-suited to the task of considering the European Commission's proposal to revise the animal experiments directive.

As you will appreciate, as well as being hugely controversial animal experiments cover a wide range of highly complicated scientific disciplines (including animal welfare science and non-animal alternatives). A range of different ethical and therefore legislative approaches is possible.

As far as we can tell, none of the sub-committee members has any background in animal welfare or animal ethics, and very little parliamentary or extra-parliamentary involvement in these issues. Similarly, there appears to be very little scientific expertise on the committee. Expertise in all these areas is we believe essential.

It may be that this particular subcommittee has been chosen because the lead committee at the European Parliament is the Agriculture Committee. In fact, it was illogical for that committee to be given the dossier, given that there is little overlap between agriculture and animal experiments. There are, we would have thought, more appropriate subcommittees.

The overriding imperative, however, is to ensure that there is a fair representation of interests and expertise on the subcommittee which holds the inquiry. I do not know whether members with the appropriate interest and experience can be co-opted?

Annex 2

Public opinion poll results on the revision of Directive 86/609/EEC

The ECEAE commissioned leading polling company YouGov to carry out a poll in February and March 2009 in the UK, France, Germany, Italy, Sweden and the Czech Republic on the revision of Directive 86/609/EEC.[34] The results show that public opinion is strongly at odds with proposals currently on the table.

Results from the opinion poll

- 81% of people surveyed agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates.
- 79% of people agree or strongly agree the new law should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions.
- 84% of people surveyed agree or strongly agree the new law should prohibit all experiments causing severe pain or suffering to any animal.
- 80% of people agree or strongly agree all information about animal experiments should be publicly available, except information which is confidential and information which would identify researchers or where they work.

[34] All figures, unless otherwise stated, are from YouGov Plc. Total sample size was 7,139 adults. Fieldwork was undertaken between 24 February and 4 March 2009. The survey was carried out online. The figures have been weighted and are representative of the population sizes of the countries surveyed.

— 73% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to cats.

— 77% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to dogs.

Individual Country Analysis

Czech Republic

— 73% of people surveyed agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates.

— 70% of people agree or strongly agree the new law should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions.

— 80% of people surveyed agree or strongly agree the new law should prohibit all experiments causing severe pain or suffering to any animal.

— 74% of people agree or strongly agree all information about animal experiments should be publicly available, except information which is confidential and information which would identify researchers or where they work.

— 71% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to cats.

— 76% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to dogs.

France

— 86% of people surveyed agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates.

— 81% of people agree or strongly agree the new law should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions.

— 85% of people surveyed agree or strongly agree the new law should prohibit all experiments causing severe pain or suffering to any animal.

— 79% of people agree or strongly agree all information about animal experiments should be publicly available, except information which is confidential and information which would identify researchers or where they work.

— 72% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to cats.

— 77% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to dogs.

Germany

— 85% of people surveyed agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates.

— 82% of people agree or strongly agree the new law should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions.

— 89% of people surveyed agree or strongly agree the new law should prohibit all experiments causing severe pain or suffering to any animal.

— 84% of people agree or strongly agree all information about animal experiments should be publicly available, except information which is confidential and information which would identify researchers or where they work.

— 75% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to cats.

— 79% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to dogs.

Italy

— 82% of people surveyed agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates.

— 79% of people agree or strongly agree the new law should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions.

— 86% of people surveyed agree or strongly agree the new law should prohibit all experiments causing severe pain or suffering to any animal.

— 83% of people agree or strongly agree all information about animal experiments should be publicly available, except information which is confidential and information which would identify researchers or where they work.

— 76% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to cats.

— 82% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to dogs.

Sweden

— 75% of people surveyed agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates.

— 76% of people agree or strongly agree the new law should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions.

— 84% of people surveyed agree or strongly agree the new law should prohibit all experiments causing severe pain or suffering to any animal.

— 81% of people agree or strongly agree all information about animal experiments should be publicly available, except information which is confidential and information which would identify researchers or where they work.

— 78% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to cats.

— 83% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to dogs.

UK

— 71% of people surveyed agree or strongly agree the new law should prohibit all experiments causing pain or suffering to primates.

— 72% of people agree or strongly agree the new law should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions.

— 78% of people surveyed agree or strongly agree the new law should prohibit all experiments causing severe pain or suffering to any animal.

— 74% of people agree or strongly agree all information about animal experiments should be publicly available, except information which is confidential and information which would identify researchers or where they work.

— 66% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to cats.

— 67% of people disagree or strongly disagree that the new law should permit experiments causing pain or suffering to dogs.

Annex 5

BUAV amendment to Article 53 of the European Commission draft Directive

Amendment

Proposal for a directive
Article 53

Text proposed by the Commission	*Amendment*
The Commission shall review this Directive by [10 years after the date of entry into force] taking into account advancement in development of alternative methods not entailing the use of animals, and in particular of non-human primates, and propose any amendments, where appropriate.	The Commission shall review this Directive ***within 3 years after the date of entry into force and every three years thereafter, in consultation with stakeholders,*** and propose any amendments, ***including in relation to which species may be used in procedures and which types of project may be authorised. In doing so, it should be guided by the following principles:*** ***(a) The Directive should reflect (i) evolving public opinion about when the use of animals in procedures is justified and the care to which they are entitled; and (ii) scientific developments*** ***(b) The priority is the reduction and elimination of procedures causing the greatest permissible pain, suffering, distress or lasting harm and those which are not designed to alleviate life-threatening or debilitating clinical conditions in human beings*** ***(c) The eventual goal, accepted by all stakeholders, is the elimination of procedures on live animals***

Justification

The revision process of the Directive should be flexible enough to take into account future changes in public concern, the understanding of the ability of particular species to suffer and the state of development of alternative methods and science more generally. A review of all essential elements of the Directive on a regular basis is essential to ensure that the legislation in the EU reflects the current minimum animal welfare standard, evolving scientific knowledge and public opinion, and best practices.

Annex 9

BUAV amendment to Article 15 of the European Commission draft Directive

Amendment

Proposal for a directive
Article 15—paragraph 1

Text proposed by the Commission	*Amendment*
1. Member States shall ensure that all procedures are classified as "up to mild", "moderate", "severe" or "non-recovery" on the basis of the duration and intensity of potential pain, suffering, distress and lasting harm, the frequency of intervention, the	1. Member States shall ensure that all procedures ***and projects*** are classified as "up to mild", "moderate", "severe" or "non-recovery" on the basis of: ***(i)*** the ***nature,*** duration and intensity of potential pain, suffering, distress and lasting harm, ***(ii)*** the

deprivation of ethological needs and the use of anaesthesia or analgesia or both.

use of anaesthesia or analgesia or both, ***(iii)*** the frequency of intervention ***for a particular animal, (iv) methods of restraint used, (v) any deprivation of physiological needs (such as food or water) (vi) method of capture (where relevant), (vii) transportation (where relevant), (viii) breeding, (ix) housing and (x)*** the deprivation of ethological needs. ***In this Article, the criteria listed in paragraphs (vi) to (x) are referred to collectively as an animal's "whole life experience"***

Justification

The level of suffering needs to be clearly defined as the harm/benefit test required needs to be rigorous and realistic.
It is also logical that the entire lifetime experience of the animal be included in the assessment of harm. The additional parameters allow for a more complete assessment of the harms inflected on the animal. There is a wealth of scientific information that shows that such parameters also contribute to "pain, suffering and distress" and can impact on scientific outcomes.

Examination of Witnesses

Witnesses: **Dr Katy Taylor,** Scientific Co-ordinator, **Mr David Thomas,** Legal Adviser, and **Ms Samira Gazzane,** European Policy Officer, examined.

Q337 ***Chairman:*** Thank you very much for coming to see us. It is very good of you to help us with our inquiry. Although I hope it will be quite relaxed it is a formal session of evidence. A recording will be taken and you will see a transcript within a day or two so that if you feel any errors have crept in, either in the interpretation of what you said or even if what you said was not quite what you meant, which happens to all of us, please let us know. We are being webcast, although we are not very certain whether anyone at all is listening out there. I know you have a note of the areas of questioning we want to go into. Do you want to make any preliminary statements?
Mr Thomas: Yes. May I first of all thank you, my Lord Chairman, for inviting us this morning. I will make the introductions and then, yes, we would like to have the opportunity of making a brief statement. My name is David Thomas. I am Legal Consultant to the BUAV. The reason I am here this morning is that Michelle Thew, the Chief Executive, is on maternity leave at the moment.
Dr Taylor: I am Dr Katy Taylor. I am the Scientific Co-ordinator at the BUAV. I represent the BUAV in its expert status at Defra, at the European Chemicals Agency in relation to chemicals testing, and at the European Medicines Agency. The BUAV is also part of a much larger international co-operation called the International Council on Animal Protection and we have expert status at the OECD which is the international body for chemicals guidelines.
Ms Gazzane: My name is Samira Gazzane. I am European Policy Officer for the BUAV. I also work closely with the European Coalition to End Animal Experiments. The BUAV holds the secretariat of this organisation which is composed of 17 members of animal protection organisations across Europe.

Q338 ***Chairman:*** Thank you very much. I should have said at the beginning apologies from our Chairman, Lord Sewell, who is away on NATO business at the moment, so I am standing in.
Mr Thomas: I will make a few brief comments if I may, my Lord Chairman, about what the BUAV thinks should guide the revision of the directive. The BUAV is strongly pro-science provided that the research methods are humane and reliable. Its position of principle, as we have explained in the written evidence, is that knowingly causing suffering to innocent animals when it is not for their benefit is ethically wrong and the wrongness is in direct proportion to the degree of suffering caused. Although a complete ban is not on the table, ethics nevertheless play a crucial part in the debate because ultimately it is about where lines should be drawn: for which purposes should the use of animals be allowed, what level of suffering should be permitted, which species should receive particular protection, to what standard of housing and care should animals in laboratories be entitled, what priorities should be given to developing alternatives and so forth. As your Lordships know, animal experiments are deeply controversial and, as with all controversial issues, legislation dealing with them should aim to reflect public ethical opinion as best that can be determined. A recent YouGov survey across six representative European Union states showed consistently very strong majorities against causing any suffering to primates, dogs and cats, and against the causing of

severe suffering to any species and for maximum transparency with only confidential information and information which could identify individuals and labs withheld. Most significantly, a resounding 79% of people thought that the new directive should prohibit all animal experiments which do not relate to serious or life-threatening human conditions, and, of course, very many people share the BUAV's view that even those experiments should be banned on ethical and scientific grounds. In all its public statements and lobbying industry focuses exclusively on such experiments, no doubt for its own tactical reasons, but the reality is very different. To experiment on an animal would in any other context constitute a criminal offence under general animal protection laws. That is what takes animal experiments out of the private realm and into the public. In this context, in order to reflect public opinion and achieve some measure of public confidence, the legislation must, we think, first, require decisions to be made by Member States and thereby achieve democratic accountability, not leave it partly to self-regulation. Second, it must insist on maximum transparency. Third, it must ensure that animal experiments, where they are permitted, are truly a last resort with duplication and inadequate habit-based, tick-box science rooted out and with rigorous, prospective, ongoing and retrospective review of the alleged scientific benefits from particular animal use. Fourth, the directive must ensure that animal suffering is cut to the absolute minimum at all times, which certainly does not happen at present. Fifth, it must ensure that maximum use of alternatives is made, again, contrary to what happens at present. Finally, the directive must be frequently reviewed so that it reflects evolving public opinion and scientific developments with a targeted approach to ending animal experiments at the earliest possible time as the overriding objective. Judged by those criteria, the current directive is a miserable failure. The Commission's proposal makes important strides but still falls far short, and some of the Parliament's key amendments take us back into the dark ages. No doubt we will explore some of these issues. The BUAV is looking to Member States, aided by inquiries such as your Lordships', to get the exercise back on track.

Q339 ***Chairman:*** Thank you very much. That is very clear. In the written evidence that you submitted to us you indicate that there are big differences that have developed across the EU in regard to authorisation, care and enforcement, and I was just wondering whether you could explain in more detail in that context the need for the proposed legislation. I think you have already explained what would happen if the legislation did not come into force.

Mr Thomas: My Lord Chairman, I think everybody is agreed, looking at your previous sessions, that there is a crying need to update this directive. Aside from internal market and harmonisation issues, which, if you like, are the technical peg on which the directive revision has been hung, the BUAV sees the existing directive as woefully deficient in a number of respects. Fundamental research and education and training are outside its scope; there is no authorisation at Member State level, no requirement of ethical evaluation, very little control over which experiments can be conducted or which species are used, no requirement for transparency, which is a key area. The BUAV and many others want to see maximum transparency at all stages, subject in each case to genuinely confidential information and personal information being withheld. There is no prohibition in the current directive against duplication or measures to address it. Some species for which there is strong evidence of sentience are excluded and the provisions dealing with alternatives are inadequate, so, aside from technical harmonisation reasons, the BUAV believes that the new directive should address these and other deficiencies.

Q340 ***Lord Brooke of Alverthorpe:*** You referred to the 1986 directive as a miserable failure. Would you say that applied equally to the UK?
Mr Thomas: I think the BUAV would talk in terms of relative failure. The UK has gone further than the minimum standards which the directive requires. For example, it requires authorisation at Member State level which we think is very important. It has a cost/benefit test, which again is very important if you accept the premise that animal experiments are going to happen. There are numerous areas, however, where the BUAV thinks that the UK legislation (a) does not go far enough and (b) in its implementation there are considerable deficiencies, and, either today or in a subsequent paper, we can deal with some of those if that would assist.

Q341 ***Lord Brooke of Alverthorpe:*** It may not be an easy task but on a scale of one to ten where would you put the UK in terms of its application of the 1986 directive?
Mr Thomas: In terms of transposition, what it has to do?

Q342 ***Lord Brooke of Alverthorpe:*** What it did with the 1986 directive.
Mr Thomas: In terms of its technical duty to transpose, the UK does pretty well, and in relative terms is better than a lot of other Member States, much better than some Member States, but in a sense the BUAV would say that is not the criterion. You

should not be measuring against the worst; you should be measuring against what is achievable.

Q343 ***Lord Brooke of Alverthorpe:*** Which is why I am asking if it is possible to see what you would have thought on a scale of one to ten. I am trying to get in my head is it five or is it seven or is it three?
Mr Thomas: In terms of comparison with what it should be?

Q344 ***Lord Brooke of Alverthorpe:*** In terms of application in the sense of what would be acceptable to you so that it would not be described as a miserable failure or woefully deficient.
Mr Thomas: It is a difficult question for the BUAV to answer because clearly the BUAV is against animal experiments causing pain and suffering and therefore it is working within something that should not be there. I am not sure I can say much more than that.
Lord Brooke of Alverthorpe: That is fine. It is not an easy one.

Q345 ***Baroness Sharp of Guildford:*** Moving on from, so to speak, the UK's relative position you reject in paragraph 28 of the evidence that you gave us the concern of the industry that the directive as drafted is likely to displace research out of the EU and you note that investment decisions are likely to take account of a range of factors. Amongst those factors, do you think the speed of securing authorisation for a project is one of them? Secondly, it has been suggested that the impact of the directive might be to "leak" poor animal welfare standards from the EU to third countries. What is your view on that issue, and perhaps I could add how far do you feel that there is likely to be leakage from the UK—and you were indicating earlier that you felt that the UK standards were relatively better than in other EU countries—to other EU countries which might be less efficient in monitoring what goes on?
Mr Thomas: I will ask Katy to start off.
Dr Taylor: If I can answer the first part of your question, in relation to the time it takes to grant licences in the UK it is important to note that the Home Office Inspectorate report for 2007 stated that 85% of new projects were granted within 35 days and the average is 18 days[1], so we cannot understand why amendments to licences would take longer than this. The point is that in the UK, which some people would argue has the most bureaucratic and the highest standard amongst Europe, it is only taking 18 days to grant a licence. Secondly, I think we need to view that in the context of concerns about speed and the development in particular of new drugs, and so that 18 days needs to be seen in the context of how long it takes to develop a drug and bring it to market, which on average is 10-14 years. If it is about a month to accept a project licence against 10-14 years then let us see it in that context. Thirdly, a really important point to make is that the UK is the largest animal user in Europe and has been for some time. It uses three million animals every single year and the numbers have been increasing. Since this Government came to power it has increased by over 20%, so that is in the last 12 years. If the alleged burdens of the revised directive were likely to have an effect would we not have already seen this in the UK if we were arguably already coping with these increased bureaucratic burdens?
Mr Thomas: On the more general point, the first point to make is that Europe must do what is right, what its citizens want to see. No-one suggest that we should allow child labour here because otherwise fashion companies would continue to outsource their work to sweatshops in the developing world. The second point is that the Commission has looked at this very carefully and has concluded that there is little or no evidence to suggest that the research will migrate if animal protection improves in the EU. Decisions about where to locate or conduct research are governed by a huge array of factors, of which differential labour costs and skills availability are by far the most important. As Katy has said, the UK, and Switzerland too, have relatively higher standards and yet they have relatively high use. There is no linkage of the sort suggested. Looking at your previous sessions, two really crucial points emerge from the evidence given by the animal researchers. The first is that the academic witnesses made it very clear that high animal welfare standards equate to better science and there is indeed lots of evidence to support that, so why would anyone countenance dropping those animal welfare standards if that leads to worse science? The second point is that all your research witnesses have made it clear that their companies insist on European animal welfare standards when setting up facilities or contracting outside the EU, and therefore again it is clear from that that high animal welfare standards in the EU cannot be the driver.

Q346 ***Chairman:*** Do you support that view? Would it worry you, bearing in mind your concerns, if leakage did happen? If the standards are the same around the world in the research organisations would you be concerned?
Mr Thomas: If the standards were indeed lower? We do not accept the premise but if standards were lower and therefore there was more animal suffering, of course, that would be a concern.

Q347 ***Chairman:*** But you have no evidence to indicate that they are lower, or do you? That is not really my question. Do you endorse the statement that the standards are now the same throughout the

[1] 18 days from submission to decision

world and therefore leakage is not necessarily relevant to your agenda?
Mr Thomas: No. I think it is fair to say that there is a disparity in standards but not universally. Some of the evidence you were given indicated that China has now some very good facilities, for example. There is disparity within Europe too but I think the key point here is that there is no evidence of European-linked standards, if and when research takes place outside Europe, being any lower. There is one final point which I would like to make, and this is a point which is often missed, which is that the European Union as a member of the World Trade Organisation can prohibit the import of products which have been developed in a way which offends the moral susceptibilities of its citizens under Article XX (a) of GATT. Indeed, the EU have done that with cosmetics tested on animals outside the EU. Such cosmetics are now prohibited from being imported into the EU. It has also done it very recently with banning the import of seal products because of the perceived cruelty of seal hunting. In the present context therefore the directive should, as I said in opening, if it is doing its job, reflect the ethical consensus, the ethical settlement if you like, and animal research elsewhere which fails to meet directive standards by definition offends the moral sensibilities of EU citizens if the resulting products are then imported into the EU. The EU could, and BUAV would encourage it to, signal that it will invoke this WTO power which then immediately takes away any incentive there might otherwise be to chase the lower standards. I am conscious of time but I can give quite a pertinent example of this if it would help the Committee.

Q348 ***Chairman:*** Very quickly.
Mr Thomas: Monoclonal antibodies in the vast majority of cases can now be produced without using animals. The animal method is extremely cruel. What happens is that the animal method is banned essentially in Europe, but they are still produced outside Europe and imported into Europe. We would like to see the directive, using this as an example, prohibit that importation on the basis that it is against the moral view of EU citizens and therefore one could use the GATT XX(a) exception because it is cruel and because the cruelty is completely unnecessary because you can do it another way.

Q349 ***Chairman:*** Thank you very much. You did not quite answer Baroness Sharp's question about leakage from Britain to the continent.
Mr Thomas: I am sorry, my Lord Chairman. I thought Katy did.
Dr Taylor: I personally do not think there is any danger of that because the UK, you can argue, has got one of the highest standards already and has had for 20 years, and, yes, it is the largest user in Europe, so bringing everybody else up to that level is not going to lead to leakage throughout Europe. If anything, it might increase the UK capacity because we are already doing it, we have already got the facilities in place and all that.

Q350 ***Chairman:*** We are going to Brussels next week to talk to various Member State representatives. Are there any particular representatives you feel we ought to question with more perspicacity than others?
Ms Gazzane: In terms of transparency, we have seen some disparity between Member States. The Swedish and Danish systems, for example, are much more transparent than the UK system in terms of publishing more information such as project authorisation. This is another example of countries doing better than the UK.

Q351 ***Chairman:*** My question was more about countries doing a lot worse.
Mr Thomas: It is fair to say that normally the UK is relatively better but the BUAV would say not good enough by a long way.

Q352 ***Lord Livsey of Talgarth:*** You argue that research using non-human primates should be ended and that there is sufficient evidence to suggest that this would be scientifically beneficial. I would like you to explain why you think that. Some of our witnesses have acknowledged that research on non-human primates is not 100% secure in all cases but that in many instances it is nevertheless the best option for testing and remains, at least for the moment, necessary. How do you respond to that?
Dr Taylor: Before I discuss the scientific merits of primate research I do think it is important to reiterate the strong ethical objections to their use, and in our recent YouGov poll across six Member States 81% of people thought the new law should prohibit all experiments causing pain or suffering to primates, so let us not forget the very strong ethical argument.

Q353 ***Lord Livsey of Talgarth:*** Can I just stop you there? How many people were surveyed?
Dr Taylor: I thought you might ask that.
Ms Gazzane: We have provided you with the results of the YouGov opinion poll.

Q354 ***Lord Livsey of Talgarth:*** Can I ask you if you would give us that information in writing?
Dr Taylor: It is probably 1,000 in each Member State.

Q355 ***Chairman:*** Perhaps you could let us have a note on that. That is the best answer. We are a bit pushed for time this morning.
Dr Taylor: In terms of the scientific objection to the use of primates, just because primates are used does not mean that they have to be used or that they

should be used. I think we need to separate out the concept of usage from the concept of utility. This point has been supported by the NC3Rs whom you saw last week, who have noted that there has yet to be a comprehensive scientific review of the rationale for primate toxicity testing. Primates are used mainly to test for toxicity in pharmaceuticals. There is very little scientifically gathered evidence supporting the use of primates in safety studies, and in fact there is growing evidence that they are poor predictors of the human response. What we need to remember, and we made this point to the recent European Commission's Scientific Committee on Health and Scientific Risks (SCHER) report on the use of primates, is that we are not trying to replace a model that works; in fact, we believe that there is plenty of evidence to suggest that the model should be scrapped regardless of the presence or absence of alternatives. If I could give you some figures, the FDA acknowledged that the success rate of a new drug through clinical studies (once it has successfully passed pre-clinical studies which are animal tests including primate tests) is in fact less than one in ten, so if primates were really predictive of what happened in humans you would not have a drop-out rate of 92%. We have trialled over 85 HIV vaccines on people and none of them has worked even though they have all been shown to be effective in monkeys. We have tested over 1,000 neuroprotective stroke treatments on animals and yet so far there is still no effective drug for treatment on humans. Similar stories exist about Alzheimer's and Parkinson's and Hepatitis C, which are the main uses of primates. At what point do we need to stop and look at the efficacy of the primate model? One success in a mountain of failures does not a valid or an efficient model make. We believe a ban would be therefore beneficial because it would force the industry to change their approach to testing, reduce wastage, because this industry is extremely wasteful of animals and also money, and it would maximise the use of alternatives which can be cheaper, faster, and more predictive. This kind of radical sea-change approach has already been suggested by the US National Academy of Sciences which has foreseen a future where we do not use animals to test the safety of chemicals, so we would like to see a similar sea-change in approach to the testing and safety of pharmaceuticals. Perhaps I can finally make the point that we need greater investment in alternatives, that is definitely the case. I will just make the point about how vast the disparity[2] is at the moment. The UK Government, via the MRC and the BBSRC, provided the NC3Rs, which is our kind of alternatives body, with £2.6 million last year in funding, but by contrast the MRC and the BBSRC together funded research totalling £643 million for medical research. That is a funding alternative to the tune of less than 1%, I think it was 0.4%, so we need much bigger investment in alternatives. Your witnesses made a really good point last week when they said it was unrealistic to assume that science cannot do better.

[2] Between the funding specifically for the development of alternatives and funding of general medical research

Q356 ***Lord Livsey of Talgarth:*** You have stated your position very clearly there so we will study it. Turning to a totally different aspect, you agree with the Commission that any non-human primate research should be restricted to second generation primates. Could you express your main concerns regarding the use of F1 primates? Do you agree with the time limits proposed by the Commission for the restriction to come into force, ie, 18 months for marmosets, seven years for macaques and 10 years for other species? Could you explain your position on that, please?
Dr Taylor: By definition the F1 situation depends extremely heavily on the wild-caught trade, so any wild-caught ban is limited if you allow the use of F1s, which are monkeys that are born in captivity from wild caught parents, so our concerns about the use of F1s arise from the massive welfare and conservation consequences of the use of wild-caught primates. This is well known and has also been recently documented in various investigations that we have done into breeding centres in Cambodia, Malaysia and Vietnam, some of which export to Europe. I would just like to make the point that this is not just our opinion about the use of F1s. The European Commission's Scientific Committee on Animal Health and Welfare in 2002 said that for as long as the use of primates in research is necessary only purpose-bred animals should be used, so that is F2s. Most recently the SCHER said that the use of wild-caught non-human primates for experiments should be discouraged for both scientific and animal welfare reasons. I think it is fair to say there is quite a large consensus now, not just among the animal protection community but also the Commission and their scientific committees who are extremely independent, that we should move to F2s. In terms of a timeline, our main concern is the timelines for macaques. Macaques are used very heavily in testing pharmaceutical safety, more than marmosets. The Commission deadlines of seven years from transposition would effectively mean, at the rate we are going with this directive, that that would be a ban in 2020. That is a very long time, we feel. If we limit primate use to research on serious and debilitating human conditions and we increase our investment in alternative methods this might help reduce our dependence on them, but at the moment the use of 10,000 monkeys a year in Europe is unsustainable. Researchers have been trapping and importing monkeys since the 1950s and they have known about the conservation impacts since the 1970s and those

figures have come from the European Commission's Scientific Committee on Animal Health and Welfare, so they have had since the 1970s to develop breeding centres and move to an F2 situation. Our argument is that we need legislation to help push this through, and that position is agreed by the Commission in their statement to yourselves. They have also said that we need something to morally enforce this change in the status quo. It is not going to happen voluntarily because it is cheaper to trap wild monkeys and they do not breed very well in captivity.

Q357 ***Earl of Caithness:*** Given what you said in reply to Lord Livsey's first question, and given the fact that scientists want positive results and that people spending money on research do not want to waste money, why are people still using these animals and why is it increasing?
Mr Thomas: Is that in relation to primates or more generally?

Q358 ***Earl of Caithness:*** To non-human primates. Dr Taylor was mentioning that the numbers had gone up.
Dr Taylor: They continue to use primates because they are expected to show primate studies when they want to market pharmaceutical drugs, so there is a regulatory barrier for them there. Even though they themselves may not feel that the primates are particularly useful, the regulators are very slow to change their regulations, so there is not a driver to encourage industry to change the way they do things. I find it quite hard to believe but it is true that there has not been a scientific evaluation of the productivity of primate research, and again there is no driver to incentivise people to do that, so at the end of the day it comes down not to science but emotion. They feel better knowing it has been through a primate, basically, but there is not an awful lot of scientific evidence to suggest that that is the best thing to do.
Chairman: Thank you very much. Can we move on to severity classifications?

Q359 ***Lord Palmer:*** We have asked all our witnesses very much the same question. As things stand at the moment the proposal contains a system of "severity classifications", of which I am sure you are aware ("up to mild"; "moderate"; "severe"; or "non-recovery"), which will determine important aspects of the application of the directive. However, the criteria for these classifications are only to be finalised after the adoption of the directive, which I think seems totally illogical. (a) Would you like to see these agreed within the text, as proposed by the European Parliament, and (b) what is your view of the definitions proposed by the European Parliament under amendment 161? Some of our witnesses thought there ought to be more classifications within this band. What are your thoughts?
Mr Thomas: I can answer (a) quickly, my Lord—yes. I will ask Katy to deal with (b).
Dr Taylor: We broadly welcome the annex where the classification system is placed. However, we do have a number of concerns. First, there should be an upper limit on the amount of suffering imposed on an animal and the Commission, in their original Article 15(2), say that Member States should ensure procedures classified as severe are not performed if the pain or suffering is likely to be prolonged. However, if you look at the annex and you look at the "severe" category under this new annex, it would allow "prolonged suffering" or "severe injury", which we believe is unacceptable. If we have to have a "substantial" or "severe" category, we would prefer it to be more like the wording of the UK, which is "a major departure from the animal's usual state of health or wellbeing". "Severe" and "prolonged suffering", we believe, as do the public, based on our YouGov opinion polls, and the Commission believe, should not ethically ever be allowed. Secondly, generally speaking, we think the approach to assessing animal severity should be an individual-centred approach. We need to look at the animal's whole life experience and not just focus on procedures and not just have an over-emphasis on pain. We need to take into account capture, breeding, transport, handling, husbandry procedures including marking, procedural-related practices such as food or water restriction, training for procedures, restraint, which is particularly relevant when we are talking about restraining non-human primates in primate chairs for procedures, and also housing. In relation to recent primate neuroscience experiments at Cambridge University, which were subject to judicial review, Professor David Morton, who is an animal welfare expert, considered that the marmosets in question would have suffered moderately even before they had started their surgical procedures. Finally, in terms of the broadness of the severity system, yes, we would like to have seen a broader system, so maybe a four-point system rather than the three-point system that has been proposed. They are proposing "mild", "moderate" and "severe".

Q360 ***Lord Palmer:*** What would you add in?
Dr Taylor: We would like to see whatever is covered under the "moderate" category split because in the UK 59% of procedures fall under "moderate", so that is a massive catchment for a lot of procedures, some of which can be really quite severe. We do not really mind how it is worded, but we would like to see "moderate" split. So, for example the system is graded; one, two, three, four. That was the opinion of the Animal Procedures Committee in 2003, and the House of Lords in 2002 said that there should be a

more transparent scoring system as well, so this is not new. With the revision of the Directive we have got an opportunity to revisit the way we look at severity classification. It would have been nice to go to a four-point system but it looks like this is not on the cards. I am going to the discussions in Brussels tomorrow about this. They are being strict about this; they want the three-point system.

Q361 ***Lord Palmer:*** Is there a case to split "moderate" into three rather than two?
Dr Taylor: I think it is a trade-off between that and making it as simple and easy as possible for researchers. I think maybe to split it into three would be too difficult and then you raise the risk that it is down to the individual researcher and their opinion and where they put it in the category reducing the objectivity of the system. Four I think is a good compromise. Three is too broad, but maybe a five or six system would be too unwieldy.

Q362 ***Earl of Dundee:*** In terms of animal welfare, you note a tension between keeping the numbers of animals down on the one hand and minimising suffering on the other. In what circumstances do you consider that the re-use of an animal should be permitted?
Mr Thomas: It is a difficult and uncomfortable issue. The BUAV's fundamental position, of course, is that animals should not be used at all, let alone re-used. The next point to understand is that even a single use or a continued use, as the Home Office calls it, can involve multiple operations and other procedures on a single animal where the same animal has to be used for scientific reasons, and we give a graphic example of this at Cambridge University in paragraph 70 of our written evidence. So, we are talking about potentially allowing repeated multiple use in invasive experiments which the BUAV clearly thinks is unacceptable. We think the correct approach, given that some animal experiments will continue for the foreseeable future, is to focus on the overall suffering of individual animals rather than engage in a crude numbers game or allow principle to be overridden by considerations of cost, which, I have to say, is what we suspect is really at the heart of this. The BUAV would limit re-use to what we call the double mild situation, a mild first procedure, a mild repeated procedure. What is particularly important is that the repeat procedure is genuinely mild only, taking into account, of course, the cumulative effect of the fact that the animal has already had one procedure. We would also put a strict limit on the time animals can be used in this way because of the distress which they would experience simply from being kept in unnatural confined conditions and their memory from previous use, quite apart from the repeat procedure itself. These principles, we believe, need to be built into the directive and then rigorously enforced by competent authorities on an individual case-by-case basis, which is indeed what the Home Office does in this country.

Q363 ***Earl of Dundee:*** Would you like to tell us a bit more of how you would specifically build it into the directive? We learned that Article 16(2) would prevent the re-use of dogs fitted with telemetry devices in drug metabolism studies. Which further restrictions on re-use might you wish to see also imposed?
Mr Thomas: I think we can deal with this at the principle level, which is what I have tried to do. It is difficult to be overly prescriptive apart from that about particular situations, which is why we say that on this occasion, and the BUAV does not always agree with the Home Office, the specific approval for a re-use, looking at what the animal has already experienced and ensuring that any further suffering really is genuinely mild, is the way to deal with this.

Q364 ***Lord Brooke of Alverthorpe:*** If I may turn to the authorisation process, you were very unhappy with amendment 167 of the European Parliament. Could you explain to us what you believe would be the most appropriate definitions in these areas as opposed to what has now been produced as a compromise?
Mr Thomas: We are unhappy because, as a matter of principle, accountability at Member State level, as I explained in opening, is key. Only requiring authorisation for some procedures is also unworkable. We think that to have a part regulated and part self-regulated system, particularly one which is graduated depending on severity, means there is an obvious incentive, without casting any aspersions, on researchers to downplay suffering so that they can call it mild and therefore avoid official scrutiny and bureaucracy. Article 15 of the Commission proposal puts an obligation on Member States to determine severity but, of course, they cannot do that unless they have full information about what is proposed. In addition the severity classification is only part of the ethical evaluation. Member States should also be taking into account societal benefits, the quality of the science, issues like duplication, and that really can only be done at Member State level, so we do feel very strongly that the Commission has got this right and it has to be authorisation across the board. How would we like to see authorisation work? It is a big topic but I can perhaps just list the main elements that we would like to see with maximum transparency at each and every stage. First of all we would like to see a local ethical review with independent animal welfare and

alternatives expertise; secondly, a short public comment period as with REACH, the chemicals legislation; thirdly, rigorous authorisation by Member States looking at the science, animal suffering, societal benefit, alternatives, et cetera; and, fourthly authorisations drawn tightly to enable proper ethical evaluation to be made. There should be no question of automatic authorisation, as the Commission is suggesting, for required-by-law projects or multiple authorisations because that disables you from looking at the societal benefit from testing a particular substance. There should be a duty on applicants and Member States to take reasonable steps to avoid duplication, and we can expand on that if you would like us to. There should be ongoing review and adjustments made, if necessarily, including revocation of licences, and amendments too need to be at Member State level because amendments can have as much impact on animal welfare, and indeed the quality of the science, as the original proposal, and finally we think that there should be a retrospective review in each case.

Q365 ***Lord Brooke of Alverthorpe:*** You were critical earlier of the UK by comparison with, for example, with what is happening in Scandinavia. Do you think you could drop us a note afterwards on what you believe is deficient in current arrangements in the UK and what will continue to be deficient?
Mr Thomas: Yes, with pleasure.

Q366 ***Earl of Arran:*** Turning to permissible purposes, you are well aware of your own arguments in paragraph 54 that animal experiments are too widely drawn. How would you like to see this worded in the directive? What are your views on this, in a perfect world?
Ms Gazzane: Obviously, the primary position of the BUAV is that we should not experiment on animals but in the context of the revision of this directive we believe that the purposes of procedures should be restricted to those acceptable by the public, meaning the procedures to develop treatments for serious illnesses. Public support for animal experiments is solely dependent on their perceived direct benefit to human health and our opinion poll, carried out by YouGov in six countries, has shown that 79% of people agree or strongly agree that the revised legislation should prohibit all experiments on animals which do not relate to serious or life-threatening human conditions. 33% of animals are used for fundamental research which is not conducted with the aim of directly benefiting human health, so we would restrict those purposes to those acceptable to the public. We do not believe that other purposes are justified, such as animal testing for tobacco products, alcohol, food additives and household products. We have seen in Germany, for example, that the law prohibits animal testing for detergents, so why not expand this to other countries in Europe? Even for basic research we do not think it is unrealistic to ask researchers to require that the knowledge gained from the experiments has a realistic prospect of benefiting human health.

Q367 ***Earl of Arran:*** You have very strong hopes and aspirations. What chance do you think you have of getting the directive additionally worded to your effect? Have you had any influence so far, do you think?
Mr Thomas: There has certainly been a degree of influence, not specifically on that issue but, as Samira has said and as I said in opening, the key thing is to match the directive to public opinion as closely as one can do that. There is no evidence at all that a big chunk of the public accept anything other than animal research into life-threatening and serious diseases.

Q368 ***Chairman:*** Is there any evidence that either the Commission or the Parliament are listening to public opinion?
Mr Thomas: I have to say, the Parliament, no, very largely. The parliamentary stage in the process has been very disappointing. I think the Commission have to some extent but, of course, we are only some way through the process. One final point is that it is not just that section of public opinion that accepts animal experiments at all that says it has to be only for those limited purposes. That is also all the public messages and, as far as we can tell, all the lobbying messages which are given by the industry. No-one ever talks about household products or the whole range of other experiments that Samira has talked about. There is a kind of disingenuity to the whole debate and we would very much like to see honesty in the debate and the focus being on what industry is talking about and what the public will at most accept.

Q369 ***Chairman:*** In your evidence to the Boyd Group you mentioned the question of targets in relation to alternative methods. I just wonder whether you could expand a bit on what you mean by setting targets in this respect.
Mr Thomas: In relation to alternatives in particular?

Q370 ***Chairman:*** Yes, specifically in relation to setting alternatives.
Mr Thomas: The full investment in, and the full exploitation of the potential of alternatives is a tool which is relevant to the stringency of targets and the achievement of targets to end animal research more generally.

Q371 ***Chairman:*** And who should be setting the targets and monitoring them? It is the system I am looking for.
Mr Thomas: With a directive that would be at Commission level. Obviously, there would be a lot of discussion with stakeholders, including Member States, but we would see alternatives as in the broad sense. As Katy mentioned earlier, it is not only a technique-on-technique kind of comparison, but also alternatives has a real policy element to it. To give one example, if one had, and I can never remember which it is, an opt-in or an opt-out system in relation to organ donation, a presumed consent, then you immediately produce a lot more organs and therefore you take away the incentive to research using animals. It is called xenotransplantation research. That is just one example of where you have to look at alternatives in a very broad policy sense rather than in a simple scientific technique-upon-scientific-technique sense. If you would like, my Lord Chairman, we can expand on the whole targets thing in relation to alternatives or more generally separately because it is a big issue.

Q372 ***Chairman:*** OK, that would be very helpful; thank you very much. Are there any other points you feel you want to make?
Mr Thomas: I am conscious that we are already eating into the next session, so we will leave it at that.
Chairman: Thank you, all three of you, very much.

WEDNESDAY 8 JULY 2009

Present	Brooke of Alverthorpe, L	Dundee, E
	Caithness, E	Livsey of Talgarth, L
	Cameron of Dillington, L (Chairman)	Palmer, L
		Sharp of Guildford, B

Memorandum by Animal Defenders International, National Anti-Vivisection Society and Lord Dowding Fund for Humane Research

OBJECTIVES OF THE DIRECTIVE

1. *What degree of harmonisation of rules governing the protection of animals in research is required to avoid distortions of the Single Market? To what extent are such distortions causing problems at present, and is the draft Directive a proportionate response to those problems?*

1. There are huge differences in laboratory animal welfare standards amongst EU and EEA countries. It affects the EU scientific community as whole by increasing the risk of variable research results due to inconsistent scrutiny of experimental design; this multiplies the risk of duplication of procedures. It affects the free movement of researchers due to the difference of requirements in education and training, which is an obstacle to cross-border scientific projects in the EU. Low EU standards also discourage innovation in alternatives to animal testing. These problems contribute to the fragmentation of European research and negatively affect its competitiveness in the world.

2. Animal Defenders International (ADI) and the National Anti-Vivisection Society (NAVS) believes that the appropriate response to this problem is to harmonise to a high level, so that European scientists can better compare their experimental results, increase their cross-border cooperation, which will boost the EU's scientific dynamism and competitiveness as whole. Harmonisation must be achieved to the highest animal welfare standards, because low standards—such as the "old" Directive 86/609/EEC—will allow wide variations in the Common market. The EU legislation must also achieve high animal welfare standards to respect the EC Treaty's Protocol on Animal Welfare and public opinion.

3. As a whole we believe that the draft directive is a proportionate response to this problem. It is a significant step forward from Directive 86/609/EEC. It includes an authorisation process for all animal experiments; the 3Rs as a cornerstone of the legislation; ethical reviews; a licensing system for suppliers, establishments and individuals using animals; an upper limit of pain; uniform implementation of Council of Europe standards of housing; the extension of the scope of the Directive to some invertebrate species, and so forth. It also limits the use of primates to studies into life-threatening and debilitating diseases, includes a phase-out on the use of all wild-caught primates in testing and breeding, and the creation of national reference laboratories (NRLs) dedicated to alternatives methods.

4. However, the proposal also has some shortcomings, and could be improved. Bans on the use of great apes and endangered species contain unacceptable loopholes and exemptions. ECVAM (European Centre for the Validation of Alternatives Methods), an institution key to the dissemination of alternatives in Europe, is not mentioned.

INTERNATIONAL COMPETITION

2. *How might high(er) animal welfare standards in the EU impact upon the international competitiveness of the EU's private and public sector research base, and that of commercial establishments carrying out routine testing?*
Is there a risk of displacing research using animals to third countries and, if so, what would be the consequences of such a trend?

5. There is no evidence that high animal welfare standards are detrimental to the competitiveness of the pharmaceutical industry and scientific research. Claims made by some sectors of the industry are unfounded. It is argued by some that a new Directive will drive research out of the EU to China and other countries. However, ADI/NAVS have been unable to find any evidence—neither anecdotal, nor statistical—to support this claim. There are already vast discrepancies amongst EU countries, and yet British animal research has not gone to France, for example, where regulation is weak.

6. If high animal welfare standards were driving research abroad, the effect would be most obvious in countries which already operate strict regulatory controls over the use of laboratory animals, such as the UK and Switzerland. In fact, in 2007, the pharmaceutical industry became the most competitive industry in the UK, as it ranked number 1 in trade surplus, beating all other British industry sectors. Statistics of the Association of the British Pharmaceutical Industry (ABPI): http://www.abpi.org.uk/statistics/section.asp?sect=2. As in the UK, the Swiss pharmaceutical industry operates under tight laboratory animal welfare regulations. Globally, Switzerland leads the world in terms of trade in pharmaceuticals with £10.8 billion (€11.46 billion) in trade surplus, beating the UK (£4.2 billion), Germany (£5.5 billion) and the USA (minus £18.3 billion) ABPI statistics: http://www.abpi.org.uk/statistics/section.asp?sect=1.

7. Increased animal welfare standards and a governing framework for scientific research have a beneficial impact on the appeal of conducting research in a specific country. The introduction in 1986 of the UK Animals (Scientific Procedures) Act, which went much further than the 1986 European Directive in its controls, licensing and codes of practice, has not affected the growth and effectiveness of the British pharmaceutical industry. By comparison, the USA is a long way behind. It has the largest trade deficit in pharmaceuticals in the world, poor standards of animal protection and welfare, with poor controls over standards of science and animal use. Clearly, lax regulation and poor controls have not helped the USA to perform better in this sector.

8. The UK will be at a particular advantage if stricter regulation of science and protection of animal welfare is introduced in the EU, since many of the measures in the Commission's proposals are already in place in the UK. That means that UK standards will be exported to the rest of the EU, which could give British researchers a competitive advantage in Europe.

The Proposed Requirement to Restrict Research on Non-human Primates (Article 8)

3. *Are the proposed restrictions proportionate, and what might be their impact?*

9. The Commission's proposal limits the use of non-human primates to experiments "*undertaken with a view to the avoidance, prevention, diagnosis or treatment of life-threatening and debilitating clinical conditions in human beings*", or aimed at the conservation of the species (Article 8, paragraph 1, point a). Swiss case-law already provides for similar restrictions. There is broad consensus that the high cognitive development of these wild animals calls for, at least, strict regulation. One of the aims of Directive 86/609 was to reduce the use of primates in experiments, but instead their use has steadily risen. According to the latest EU Statistical report on animals testing, the use of New World monkeys has jumped 31% from the previous report, to the detriment of wild populations and innovation in advanced techniques.

10. For that reason, ADI/NAVS believes that their use should be phased out and the Commission's restrictions are a first step. This would be an appropriate response to public opinion: in a European Commission survey, 80% of the public felt that the use of primates was "*not acceptable*". In 2007, The European Parliament adopted a Written Declaration which sought to "*establish a timetable for replacing the use of all primates in scientific experiments with alternatives*".

11. Furthermore Report A5-0387/2002 adopted by the European Parliament on 13 November 2002 states that "*the need for the continued use of non-human primates in research and testing should be critically evaluated in the light of scientific knowledge, with the intention of reducing and eventually ending their use*." http://ec.europa.eu/environment/chemicals/lab_animals/pdf/evans_report.pdf The case for ending their use is indeed supported by a growing number of scientists who use alternatives to primates in the field of neuroscience.

12. ADI therefore proposes that the use of primates in research should be subject to periodic scientific and ethical review, including opportunities for replacement. Such reviews must be Commission-led and involve all stakeholders; reviews would be permitted to set timetables or targets for specific areas of primate use, as appropriate. Amendment 59 by MEPs Brian Simpson and Lily Jacobs was adopted in the Plenary session of the European Parliament and adds a new paragraph 2a to Article 8:

> *"Every two years, and for the first time two years after the entry into force of this Directive, the Commission shall, in consultation with Member States, conduct a review of the use of non-human primates in procedures and publish the results thereof. The review shall examine the impact of developments in technological, scientific and animal-welfare knowledge, and set targets for the implementation of validated replacement methods."*

We strongly support this amendment, however we regret that the European Parliament has also deleted the restrictions to primate use in Article 8, paragraph 1, point a.

13. Reviewing, limiting and replacing the use of non-human primates will have a *very positive impact on*:

- *Conservation and welfare*: the use of primates in Europe is only possible with the catching of monkeys from the wild in their home range states. At a time when governments in primate range states are desperately working to discourage trade in wild-caught animals, the European research trade forms part of the problem. It is known that taking monkeys from the wild causes damage to wild populations (sudden losses of either females, or random catching of groups), to their environment; separation from family groups. Capture and transport over long distances causes great suffering.
- *Science and research*: reviews will stimulate the dissemination of existing advanced alternatives—more reliable than animal models—and the innovation into new alternatives relevant to human diseases. It will allow stakeholders to critically assess the results obtained from primate experiments. This will boost the competitiveness of European research.
- *Public opinion*: It will send a clear signal that governments are listening to the concerns of EU citizens by establishing a clear and reasonable policy framework to address the issue of the replacement of primates in testing. Such a framework is currently non-existent.

Important Remarks on the Use of Wild-caught Primates (Article 10)

14. Article 10 and Annex III of the Commission proposal provides for a seven-year phase-out on the use of wild-caught primates in experiments and in breeding. ADI/NAVS feel that these articles deserve special comments, due to the vast campaign of disinformation launched in the European Parliament by the pharmaceutical industry on this issue.

15. Approximately 7,000 macaque monkeys (cynomolgus and rhesus) enter Europe each year, for research. Some wild-caught primates continue to be used, which in itself can lead to compromised scientific outcomes. Significantly, some breeding establishments still take animals from the wild to supplement their breeding stock (those that are supplying F1 animals are of course, taking from the wild). However as yet, there is no real incentive to make the change to advanced scientific replacements within a reasonable timeframe. Such a change is essential in order to end unnecessary suffering and preserve the world's primate populations. We therefore welcome and support Article 10 and Annex III of the new directive, as drafted by the Commission.

16. The Commission's Impact Assessment (IA) concluded that a seven-year phase-out was feasible. This is based on the reproductive cycles of various species, and knowledge of existing production levels. Most macaque monkeys (mainly cynomolgus, with smaller number of rhesus) used in European laboratories are believed to be F1 animals (born in captivity from wild-caught animals). Europe is self-sustaining in F2 marmosets (second generation born in captivity) so no transitional period is needed. The seven-year phase-out was deemed "reasonable" for macaques. The Commission estimates that to satisfy current European laboratory demand for macaques with F2 rather than F1 animals will require an increase of 10,000 animals to the current breeding populations. We support these conclusions, and our reasoning is summarised below.

17. It is estimated that this would leave 800 surplus males, because a larger number of females are used for intensive breeding strategies. Some industry representatives have claimed that they are concerned that these surplus male monkeys will be humanely killed on the farms. On the other hand, they appear comfortable with ongoing wild capture, with the attendant suffering, deaths, damage to wild populations and environmental destruction it causes. They also appear content with the animals being sold for research and testing. The reality is that these surplus males are more likely to be sold for research or to others in the industry.

18. Macaques have an average life span of 25 years, reaching sexual maturity aged three to five years. Macaque gestation is about 164 days, and females have a minimum 15 year reproduction period. *Therefore if we assume that a breeding farm would replace females as they become less productive, it is possible that over a period of seven years as many as 50% of a breeding population would be replaced anyway, the same period as the Commission's proposed phase-out*. The question is, whether the replacement animals will be snatched from the wild, or captive-bred.

19. This means that over five years the estimated 800 surplus males would be made up of 160 males per year, spread across the whole industry. Some would argue that being humanely killed is preferable to life on a breeding farm or death in European laboratory. However, it is unlikely that there would be no customers for these animals. If females are wild caught, there is the potential for the social balance of wild populations to be disastrously disrupted, and alternatively, if trappers take both sexes it is possible that the males are killed once they have been sexed, anyway.

20. The Commission's proposals on primates (Article 8, Article 10 and Annex III) are reasonable and should receive the full support of the British Government.

Extension of the Scope of the Directive (Article 2)

4. *Are the proposed extensions to the scope of the Directive justified, and what might be their impact?*

21. The Commission's proposal to include foetal forms in their last third of gestation is justified, but does not go as far as the UK's legislation, where mammals, birds and reptiles are protected from half way through gestation. Since animals become sentient at different stages of gestation depending on their species, there needs to be a more flexible approach.

22. We suggest the final third of gestation as the minimum protection, but with provision for a species-by-species table to allow for sentience at different points, eg once a specific area of the brain has developed and is functioning. This should be established by the Commission through consultation. ADI/NAVS suggests a precautionary approach similar to the one of New Zealand's 'Good Practice Guide for the Use of Animals in Research, Testing and Teaching: "*Unless there is specific evidence to the contrary, investigators must assume foetuses have the same requirements for anaesthesia and analgesia as adult animals of the species*". http://www.biosecurity.govt.nz/files/regs/animal-welfare/pubs/naeac/guide-for-animals-use.pdf

23. The Commission's proposals on the inclusion of some invertebrates are justified, considering recent scientific findings regarding pain in decapod crustaceans Barr, S, *et al* (2007) Nociception or pain in a decapod crustacean? Animal Behaviour doi:10.1016/j.behav.2007.07.004. Additionally, the Biosciences Federation, has issued an opinion that "*squids and cuttlefish have similar nervous system and complex behavioural abilities to those found in octopods, and are at least as complex as those found in fish*". They concluded that all cephalopods should be included in the scope of the EU legislation http://www.bsf.ac.uk/responses/eu_directive.htm. Cyclostomes have also been recognised to possess a similar pain system and brains to some other fish http://www.efsa.europa.eu/cs/BlobServer/Scientific_Opinion/ahaw_op_292_labanimalwelfare_summary_en1,0.pdf?ssbinary=true making their protection justified. If the directive is to remain restricted to the species described, it is essential that provision is made for regular thematic review of the species within the scope, in order to keep pace with advances in scientific knowledge, animal welfare, alternatives to animal use and evolving public opinion. It is essential to regulate the use of all species within the scope, but it is not always necessary to include everything in the statistics—see below.

24. The proposed extension of the scope keeps pace with current scientific knowledge of capacity for suffering in the species listed. It provides protection for those animals not currently covered in the legislation of certain Member States. It would benefit harmonisation. Furthermore, we urge that the level of protection for foetal forms should, at least, be expanded to match that of the UK standard. In the UK, details of procedures are collected, but these animals are not included in the statistics, thus reducing the perceived "bureaucratic burden" on industry. http://www.homeoffice.gov.uk/rds/pdfs08/spanimals07appc.pdf.

Authorisation of Persons, Requirements for Establishments, Inspections and Project Requirements (Articles 20–43)

5. *Are the administrative demands that the draft Directive would impose overall proportionate to its objectives?*

25. The objectives of the directive are to harmonise the use of animals across Member States. The Commission proposal provides for a basic level of authorisation, as well as provisions for education and training, reporting, reviews etc. Many Member States (including the UK) already have well developed regulatory systems in place including for example, an authorisation process for all experiments. This is good laboratory practice, and in our view the Commission is not making exorbitant administrative demands. It is logical to bring those countries with poorer animal welfare standards, up to the level of Member States which have gone beyond the requirements of Directive 86/609. This will then ensure harmonisation and a "level playing field" for the internal market.

26. If the new directive were to require less of the Member States than that which is currently in place in the more advanced nations such as the UK, the aims of harmonisation and implementation of high levels of protection of animals used in the EU will not be achieved.

6. *Do any of the provisions relating to the authorisation of persons, the requirements for establishments, the inspection regime, or project requirements require further consideration and/or amendment and, if so, why?*

27. Authorisation of persons (Article 20 and Annex VI) in the new directive should include requirements for obtaining, maintaining and demonstrating competence and lifelong learning. All Member States have set a legal minimum requirement for the competence of personnel performing experiments with animals, but only

35% of Member States require that this competence is demonstrated/maintained. The outline given at Annex VI would be improved with the addition of a Commission-led initiative on Europe-wide training programmes. Compulsory education and training should be required regardless of previous experience, and should be considered to be an ongoing process. The Commission should, at Annex VI, suggest penalties for non-compliance, as a harmonisation measure.

28. The registration and licensing of establishments (from Article 21 to Article 32) is a step forward. However, ADI/NAVS would suggest the setting up of a Commission-led Europe-wide co-ordinating inspectorate with expertise in the 3Rs to provide advice, guidance and training. Noting the limitations of any system of inspection, this would aim to compare and report upon compliance to the directive by Member States and ensure that uniform standards are applied throughout the EU, again to improve harmonisation. It would ensure best practice everywhere in the EU, would ease cross-border science projects and facilitate scientists' mobility in Europe.

29. National inspection (Article 33) bodies are essential and should be required to produce an annual report, as in the UK. This would include all their activities, including breaches of the regulations, referral of issues of public concern to the national ethical and scientific review body and any issues highlighted by inspections. The inspection reports should be made available to the public.

30. The Commission's proposals to authorise individual projects (from Article 35 to Article 43 and Annex VII) with compliance checks will improve the welfare of those 750,000 animals used in the four Member States which do not, as yet, have a system for project authorisation. All projects should be subject to an independent ethical, scientific and replacement evaluation, before authorisation is given. Within this framework, ADI/NAVS would prefer to see point 2 of Annex VII more clearly defined to require applicants to list the alternative methods that have been considered and why they have been rejected. The Annex should also require the application to contain the recommendation of independent local ethical and scientific review committees. We believe that independent ethical and scientific review bodies should include experts in the field (not connected to the laboratory), experts in ethics, welfare and replacements and more than one lay person. The Article should state that applications are open to wider scientific and public scrutiny. We suggest that the independent scientific, ethical and replacement review process, which should feed advice into the competent national authority, be adapted from the Human Research Ethics committee model, in the UK.

Care and Accommodation (Article 32)

7. *Are the care and accommodation standards set out in Annex IV to the Directive appropriate, and will they produce an adequate level of harmonisation across the EU?*

31. Article 32 and Annex IV are essential in terms of harmonisation, good laboratory practice and animal protection and welfare. We have some reservations about Para 1(b) of Article 32, which could be interpreted to cover the restriction of animals during procedures—eg when held in metabolism cages. It would seriously compromise welfare if it were determined that this would be the standard of general day-to-day care, rather than part of a procedure.

32. Animal establishments should provide standards of accommodation, environmental enrichment and care which allow all species to freely express their natural behaviours and to enjoy freedom of movement. Annex IV incorporates elements of the European Convention for the Protection of Vertebrate Animals (ETS No. 123). The implementation of this Council of Europe Convention is not compulsory in Europe, although the UK largely follows these guidelines. Annex IV will make these accommodation standards compulsory for all EU countries: this harmonisation is welcome.

33. However, we believe that this is should be an ongoing process and that the Commission should regularly consult further following the entry into force of the new Directive. These guidelines should be improved and updated in the future to take into account the development of knowledge of the physical and psychological needs of animals. In particular, Annex IV contains very little about enrichment.

Alternative Methods

8. *How satisfactory are the provisions on alternatives to animal testing and National Reference Laboratories (Article 46)?*

34. *Article 45* provides for a general obligation for Member States and the Commission to "contribute to the development and validation of alternative approaches". We welcome this article, but support Amendment 138 voted by the European Parliament, which specify that this support should be financial, and not only symbolic.

35. It is disappointing that the Commission's proposal does not mention ECVAM. This innovative body has played a key role in the implementation of the EU ban on cosmetic testing and has been emulated by Japan and the USA. We therefore strongly support Amendment 139 voted by the European Parliament creating a new Article 45a. This new article firmly anchors ECVAM to the Directive and establishes it as the coordinating body for the National Reference Laboratories (NRL).

36. We welcome the Commission's proposed NRLs for the validation of alternative methods (Article 46). Disappointingly, the Impact Assessment presents a tiny budget for the NRLs, indicating that the Commission has a very different vision for this than one might interpret from the Articles of the revised Directive.

37. In general, more emphasis is needed on development of replacement methods. Advanced scientific replacement methods are at the leading edge of scientific and technological development and as such, would keep Europe at the forefront of science. The citizens of Europe want replacements; most people think of an alternative to animal use as a replacement; therefore replacement should be higher up the agenda within the Directive.

Subsidiarity and Legal Base

9. *Is it appropriate to regulate at the EU level—as opposed to lower tiers of government—in all of the proposed areas? Is the legal base for the proposal adequate in light of the content of the Directive?*

38. The new Directive has the same legal basis as Directive 86/609 on animal experiments. Article 95 of the Treaty establishing the European Community allows the Commission to propose harmonisation when divergences in the legislation of Member States are detrimental to the functioning of the Single Market. We have explained in our answer to Question 1 why we believe that vast variations in animal welfare standards amongst EU countries are indeed a problem for the Single Market.

20 May 2009

Examination of Witnesses

Witnesses: **Ms Jan Creamer,** Chief Executive, **Mr Tim Phillips,** Campaigns Director and **Mr Helder Constantino,** Head of Parliamentary Affairs, National Anti-Vivisection Society and Animal Defenders International, examined.

Q373 ***Chairman:*** Welcome. Thank you very much for coming. You have heard my introductory remarks before, but, just to repeat them, there will be a transcript taken, you can amend it as and when you get it in a few days, and we are being webcast. If you would like to introduce yourselves or make any opening statements that would be very helpful to us. *Ms Creamer:* Certainly. First of all, our grateful thanks, my Lord Chairman, for inviting us to give evidence today. My name is Jan Creamer. I am Chief Executive of the National Anti-Vivisection Society and Animal Defenders International. I have been Chief Executive for the past 23 years, after having joined the NAVS in 1976, so I have some experience of campaigning under both the 1876 Act and the 1986 Act. This is a rare privilege and we are very pleased to be here. I am joined by my colleagues today. Tim Phillips is our Campaigns Director and has similar experience to myself of the legislation. Helder Constantino is our Head of Parliamentary Affairs and he has extensive experience in the European Union. We represent three NGOs today. The first is the National Anti-Vivisection Society, which was founded in 1875. We are opposed to all animal experiments but we have a long tradition of campaigning for laboratory animal protection, and we take a step-by-step approach. That possibly leads us into the reason for having our non-animal research wing, which is the Air Chief Marshall the Lord Dowding Fund for Humane Research. This was founded in 1974 and we award grants to scientists who are conducting non-animal scientific and medical research. I suppose two of our key achievements have been a new British standard test for the testing of dental filling materials and currently we are funding the full cost of the FMRI unit at Aston University. Thirdly, we have Animal Defenders International, which we founded in 1990. This advances the group's objectives on the international stage but also allows us to campaign on wider issues, such as environmental issues, conservation and other animal welfare issues. We have offices in London, San Francisco and Bogotá, and we have a network of representatives throughout Europe. These are the people who are presenting evidence to you today and, as I say, we are very pleased to be here and are very much looking forward to answering your questions.

Q374 ***Chairman:*** Thank you very much, that is very helpful. In your written evidence to us you suggest that there are wide-ranging differences across Europe at present, which obviously is encouraging for the purpose of a new directive. You say that this increases the possibility of duplication but also produces

inconsistent results, which cannot be very helpful to those carrying out the experiments, and also produces less innovation, more fragmentation and reduced international competitiveness. I am just wondering whether you can expand a bit on that and say why there is a need for the proposed legislation and what the impact would be if the legislation were not revised.

Ms Creamer: First, on the variation in legislation, I think that is inevitable over such a long period of time. It is 23-year old legislation, we have new members of the European Union, and so we have a variation in structures, in administration. There are certain key countries, such as the UK, that have quite sophisticated systems of regulation and control, and other countries which are way behind, so, certainly in terms of harmonisation, there is a need for new legislation. The other key reason to modernise the 1986 directive is that the legislation we have now is not structured in a way that helps it to keep pace with developments in modern science and technology and that is what we need in this kind of legislation. We need to have it structured so that we can have regular reviews of specific uses of animals and the advancement of alternatives, which is why we have put forward the suggestion of the thematic regular reviews so that particular uses of animals in particular experiments can be focused upon. Secondly, with the introduction of alternatives you need to look at individual issues and individual cases. I suppose one of the greatest weaknesses we would see of the legislation in the UK and in Europe is that public transparency and accountability have been extremely poor and in the new legislation we need to see a much more open structure. We need to see true public accountability, public involvement, transparency. One of the key issues which I know you will want to talk about in detail is the authorisation and ethical review process, and we would very much like to see that open to public involvement in a way similar to the structure of the human research ethics committees that we have here in the UK where you have members of the public as lay people involved and also other scientists. Beyond the ethical review process being open to public accountability, I would say there should be public involvement in the authorisation process over the internet. One of the problems with the debates we often have about the use of animals in research is that we are debating the issue after the experiment has taken place. We frequently investigate the uses of animals in specific industries and we suggest that non-animal alternatives could have been used instead and we find out that the researchers did not know that they existed or did not look, so even with the 1986 Act in the UK, where there is a requirement to look at the alternatives, we frequently find that does not happen. Public access to anonymised authorisation applications would assist with that over the internet where we could have some input into the decision-making process before the licence is granted, and we could then call in our non-animal research scientists to advise on what alternatives might be available.

Mr Phillips: I have one very short point to add. I think this is also an opportunity, and it enhances the need for this review, for the gulf between animal welfare as perceived within the laboratory and what the public perceive as good animal welfare to be bridged, at least to a degree. For example, at one of the recent hearings the representative from Huntingdon Life Sciences spoke of very large primate cages with verandas for the primates. I think in most people's minds they would envisage something like London Zoo. We investigated that facility last year and we measured the cages and so forth. They are not the worst primate cages I have seen, so by industry standards you might be able to make that claim, but we are talking about less than a metre square per animal in what are pretty much metal boxes with a handful of perches and certainly no view of the outside world. We do need to bridge this gap when the public are told that the UK has very high standards. What does that mean? I think the opportunity to push those standards up further should be seized. Also, on the replacement issue, the key deciding factor on the use of animal replacements, where there are replacements, is nearly always availability, and I think Europe-wide we need to address that. Are the facilities there to do the experiments in another way and what incentives should there be to get the experiments from A to B and to do them elsewhere where an animal might not be used?

Q375 ***Chairman:*** Earlier on you mentioned that some countries are way behind the UK, to use your words. Do you want to give us some examples of EU countries that might be way behind?

Mr Constantino: I believe the new incoming countries are quite far behind but we have to take into account that their research industries are much weaker. The main users of animals are France, Germany and the UK. With regard to these three countries, it is clear that France is behind Germany and the UK. For instance, there is not even an authorisation process in France for animal testing. There is one for individuals in establishments but not for the project itself, so I think France is a country which is really behind the others.

Q376 ***Baroness Sharp of Guildford:*** I think you heard the discussion that we had earlier about the international competition and you too, as do the BUAV, reject the concern of industry that the directive as drafted is likely to displace research out of the EU. How do you respond to the argument that

the burdensome authorisation procedures might particularly threaten international competitiveness in terms of the length of time that it takes, particularly in this country, to get an authorisation?

Ms Creamer: Before I ask Helder to take that question, as he has done quite a lot of research on the economics of the international competitiveness issue, I would like to point out that we do have a concern about the evidence given by Dr Brooker of Huntingdon Life Sciences, where he said that the European Union can take six months to get a project licence. In fact, the European Commission have said that it is usually 70-100 days and exceptionally it might be 200 days, and in the UK the Home Office has said that 85% of their project licence applications are dealt with in 35 days and their average is 18 days, so I do think that claim of six months should be revisited. Certainly, we have not seen any evidence of any disadvantage to European science and pharmaceutical industries by having more sophisticated, stronger regulation of the science industry and of the pharmaceutical industry, and in fact the research that Helder has completed for us indicates the opposite.

Mr Constantino: I do not think there is any leakage of poor standards out of Europe. I think it is quite the contrary, that Europe is taking the lead when it comes to alternatives and standards and the rest of the world is following. For instance, we have taken the lead for chemical testing when it comes to REACH, and now the US has published a very ambitious strategy to also phase out the use of animals in chemicals. Dr Brooker from HLS mentioned last week that more and more of his clients, whether it is in China or in the US, are asking for European-style standards, so that clearly means that the European standards are better as they provide for better science and so they are more competitive. As far as the big picture is concerned, it is clear that the UK pharmaceutical industry is very competitive; it is the most competitive industry in the UK. The trade surplus of this industry was £4.2 billion in 2007, which is an increase of 361% from 1985 when it was only £1.1 billion, and the sector has also become much more research-and development-intensive between 1995 and 2003. It is not only that it is exporting more; it is also investing more in research. This is reflected, unfortunately, in the figures on animal testing which have risen in the UK from 2.6 million in 1997 to 3.2 million in 2007. Similar figures were given to you earlier. One of the things we have to keep in mind when it comes to competition is how we want to enter into this competitive industry. I would like to talk a little bit about the competitiveness of alternatives. The critical difference between animal testing and alternatives is that any country can do animal testing. China can do it, any developing country can start building breeding centres and making their own testing facilities. However, when a company or a laboratory invents a new alternative the alternative becomes the property of the company, so it can become a commercial market. I would like to give two examples. Commissioner Günter Verheugen, who is also the Vice President of the Commission, said in a speech a couple of years ago that alternative methods, developed to replace the rabbit pyrogen test for bacterial impurities in drugs, had proved a major success and had a worldwide market volume of €200 million, so that is a key example where companies and business can benefit from making alternatives. Another example, which is perhaps a little bit more ironic, is in terms of cosmetic testing. When the cosmetic testing ban came into force, of course, the major industries were against it, but now L'Oréal, which is a world leader in cosmetics, has bought a company, Episkin, which is now commercialising an *in vitro* test on skin culture. They were against the phasing out of animal testing but now they say they have made some profit from selling alternative *in vitro* methods. That is why I think we have to keep in mind that for the benefit of the EU and the UK we should really concentrate on competing on alternatives rather than trying to lower the cost of animal testing.

Mr Phillips: If I could make a very broad point on the bureaucracy of the authorisation process, we believe that it is not bureaucratic, as you might perhaps predict, but that it is basic good practice, good planning and record-keeping. Something else where there has been in a sense slight misinformation amongst lobbyists in the European Parliament is the way regulatory tests are authorised. Currently in the UK these are given thematic authorisations. There is not an application process for most of the research done at the contract research organisations and most of the regulatory tests for the pharmaceutical companies. They simply follow a course and sporadically the Home Office will check that, so they are not delayed in any way whatsoever. The directive proposal already has provision in Article 4 for a group authorisation process which we assume would address those issues of regulatory requirements, "These tests must be done, it must proceed", as it were. We do believe that the current UK system is too lax. An example we had last year was rodent experiments on the same product proceeding at exactly the same time as primate experiments, so when there were severe adverse effects in the rodent experiments they started to happen simultaneously in the primates experiments. Clearly, one set of experiments should have logically informed the others, whichever way round it was, rather than just get them done as quickly as possible. So, whilst we are opposed to group licensing, there is likely to be something like that which is going to limit very dramatically the authorisation process for commercial companies.

Q377 ***Baroness Sharp of Guildford:*** Can I pick you up on this group licensing issue? My understanding had been that on the whole it was in the academic research community where a new piece of research was being undertaken that involved animals where it was necessary to get specific authorisation through the Home Office.
Mr Phillips: That is correct. I am talking about commercial and regulatory testing, which is about 45% of research in the UK.

Q378 ***Baroness Sharp of Guildford:*** Pharmaceutical companies that contract out?
Mr Phillips: That type of research. For the type of work that you are talking about, the authorisation process, yes, that kind of academic research would need to be authorised. However, having viewed several applications for licences, including ones which have been passed in very rapid time, they often group together a quite complex series of experiments on different species with different aspects covering, as you probably know, up to five years. In a way there is a very large amount of streamlining already going on in that process which is perhaps not being indicated.

Q379 ***Baroness Sharp of Guildford:*** Can I take you on to the question of leakage? I take it from what you have been saying that, just as you are doubtful about the degree of displacement that might take place from the EU, you do not accept the notion that the Directive might leak poor animal standards from the EU to third countries.
Ms Creamer: No. The reason the pharmaceutical industry and the science base here is so strong is because the skills are here. We think the investment has been traditionally in the places where the people can be found to do the work. In a previous House of Lords inquiry on animal experiments, many people from the industry were interviewed and not one could cite an example of people or work going abroad because of strict regulation in the UK. There simply does not seem to be evidence of a case for this. When companies are talking about their reasons for moving abroad to the countries in Asia and the emerging markets, their reasons are mostly economic. In those companies are saying on the one hand that they would not reduce their standards and they export their standards abroad, therefore their animal welfare standards are just as great, when you analyse their arguments, the real reason is that those are emerging markets.

Q380 ***Baroness Sharp of Guildford:*** This is as true of the contracted-out research. Given that a lot of the animal experimentation is contracted out to places like Huntingdon Life Sciences and so forth, there is not a tendency to put these out for example to eastern Europe?
Mr Phillips: In the case of Huntingdon Life Sciences, one might argue that this facility was tested to the full in that it had a national exposé on it, it lost a lot of clients because of that exposé and the way the data was being handled, the British Government threatened it with losing its licence so it had the full weight of the bureaucratic burden and then it had a series of protests some of which, most would agree, were extremely unpleasant. But here it still is using more animals than ever, expanding its primate use in the UK and making more money than ever. If any industry was likely to move, it would have been the contract research organisations and there has not been any indication of that happening.
Mr Constantino: What is going to happen is that the EU will export its legislation, a bit like the great ape ban. It started with the UK experiments and then the EU followed and in the US they stopped breeding great apes for testing. It seems to start from the UK; then it goes to Europe and it extends all over the world.

Q381 ***Earl of Caithness:*** Do you think that research on NHPs will ever be phased out and, if so, over what timescale?
Ms Creamer: Timescales are always difficult but we are confident that the use of non-human primates can be phased out because fundamentally on the scientific level there are genetic, cellular and biological differences between ourselves and other primates. It is important to see that there is already a drive and a new impetus to finding better ways of conducting medical research and that is where the advanced techniques and technologies come in. We are looking for something better than the rather crude animal experiments. Primates are not only different from us, but the stress that is caused to those animals by their presence in the laboratory causes variation in experimental results, even in the best facilities. Studies have looked at the same species and sub-species of animals and the same experiments in different laboratories and pound variation in results. It just seems to be that they can be affected by so many factors. There is that driver to look for better methods of research. In terms of how we would break this down and address it, the majority of primates in the EU are used for product testing, principally pharmaceutical, so this could be addressed first. There are already sophisticated replacement techniques for drug testing such as micro-dosing and accelerator mass spectrometry, AMS. This is where human volunteers are given tiny, tiny doses of product, too small to cause any damage, and this is analysed for the effect. The EU has conducted a study of micro-dosing and AMS and found that it was 80% predictive of what might happen in a human being. It is a very good, new system. To give you an example of what this means and how it would work, you may

recall the incident at Northwick Park Hospital a few years ago when human volunteers suffered extreme and life threatening side effects from an experimental drug, TGN 1412. That drug had been given to laboratory primates in doses 500 times that given to the human volunteers and there had been no side effects. We do need to look at scientifically better methods. Another use of primates that could be looked at for replacement would be brain research, neuro-imaging for example for Alzheimer's, Parkinson's and similar diseases. The functional imaging techniques, the FMRI that we are sponsoring at Aston, have advanced significantly over the last few years and they now are at a level of quality and sensitivity that makes them a viable alternative. The advantage this has is that, if you are non-invasively recording the brain activity in a human being, they can tell you how they feel. They can tell you what they are experiencing, so this is superior to using animals because you are understanding what is happening in a human being. This is one of the reasons we have suggested these thematic reviews. We do not think this is a case where you can say at X date we will end all primate experiments in one go. It needs to be looked at on a case-by-case basis and you need to look at the science, the effects on the animals, the public opinion, what alternatives are available. At thematic review is where you could set your deadlines and timetables for alternatives to be introduced.

Mr Phillips: One of the big issues on setting timetables and so forth is the availability issue. We can cite clear examples where an alternative method is superior to an animal one. One of the most common conversations I have with my head in my hands with our research grant holders is, "Why are not other people doing it? They are not wilfully cruel so why do they not do this instead of the animal research?" They do what is easily available. It is nearly always the case that, if you do animal research, you tend to keep doing that. If you do non-animal research, you tend to keep doing that. One of the key challenges for this Directive is to marry those two things. If you look for example at the study which Jan mentioned, the Europe wide study of using micro-dosing and AMS to examine absorption, distribution, metabolism and excretion of drugs, which is a classic experiment done on primates as a second species, that was 80% predictive of the human results. The primate experiments are about 60% predictive. It is clearly superior on any graph. The issue then is how can we create the availability to get the research currently in primate laboratories to the limited AMS facilities that there are and to provide an incentive for there to be greater investment in having an expensive AMS machine. That is what will affect the timetable. We need to do that on a case by case basis. The other examples that Jan mentioned, the FMRI/MEG combinations in neuroscience, are doing examinations of people which 20 years ago would have been considered incredibly invasive because micro-electrodes would have been used. The animal research community said, "Ah, but you cannot get the level of detail that you can get from the micro-electrodes." You can now. Our team at Aston University compared research data from primate experiments on vision and their own human subject experiments on vision. If the baseline of validation is whether you can get the same information from the non-animal model, then clearly you can. That might be a fairly limited use. At the moment, there is no mechanism to look at 100 primates used across Europe and how we can stop that.

Q382 ***Lord Brooke of Alverthorpe:*** The previous witnesses said that no matter how you try to reduce the numbers, maybe by using alternatives, there still may be a problem with regulatory demands which require that before products are marketed they have to be tested on animals. What is your comment on that and, if there is validity in that, how do you set about trying to change it?

Ms Creamer: Regulatory demands are a problem. This is the place where we hope to change that. It is something that has grown up historically. If you look back over the last 30 or 50 years of the use of animals in research, in terms of safety testing and regulatory requirements, we have rather bumbled along. When someone has come up with a test using animals for something, it has been applied to safety testing. A couple of the older tests remind me of this where people were looking at specific lines of research and it has been found that those were useful for safety testing and they have just been adopted by regulators. There has not been much critical assessment of whether these tests are the best tests. Unfortunately, once an animal test is incorporated into the regulations and it sinks into the minds of the regulators and the government administrators, it is very hard to make that change. The change has to be political and it has to be at this level that change is made. What we are asking for in this Directive is that there is an opportunity for making change. When I first started campaigning on this issue we had an Act of Parliament that had been in place for over 100 years. Then we made a certain step forward. It was quite minimal but we made very positive steps forward in the UK and still here we are, 23 years later, where we have not been able to put replacements for the use of animals at the heart and centre of the legislation. Only the legislators can do that. Only the people making the political decisions can do that. This new Directive and the new legislation in the UK needs to be structured so that there can be regular

reviews of specific uses of animals and specific experiments. The legislation can be adapted to developments in scientific knowledge.

Mr Phillips: The key is that the regulators have to be involved in this. In areas of fundamental research you might argue that the universities will gradually come to it themselves—although that is not occuring. With these tests which are locked into regulations and law, somehow the regulators have to be involved. We saw that with cosmetics testing. It would not have happened but for that timetable. The timetable was ultimately successful. I will not go into it except for this detail: that was a fairly complex, start-to-finish testing process that people were attempting to replace. People thought it was OK to set a timetable on this because ultimately we do not really need cosmetics. We can make do with what we have. In research terms, you were talking about products which were applied to the mouth, the eyes, worn for decade after decade, entire lifetimes, so the toxicity issues and all of those things were complicated to resolve if you were going to hit the timetable. If we look at the primate issue for example and how we can phase out primate experiments, these are nearly all used as a second species in animal testing, as are dogs at the moment. It seems to us logical to start attacking that back end of the animal testing process to say, "Can we start finishing this animal testing earlier? Can we draw that line back and back until ultimately we do not do experiments on animals?" There are researchers who agree that, because animal models are an approximation that you are attempting to extrapolate to humans, there is only so much information you can get. Adding species upon species to that is of very limited value. We think a logical approach is to have these mechanisms by which you can start saying, "Could we get that into a human model earlier? Could we move from the rodent tests into AMS when it comes to the absorption trials?" and so forth. We believe that is possible and at least people should be examining how we could go about that.

Q383 ***Earl of Caithness:*** You agree with the Commission that any research on NHPs should be second generation. What do you think of the Commission's timescale for that?

Mr Phillips: We think this is a very, very important issue. It is one of the few areas where it addresses head-on a serious animal welfare issue. There is great suffering to these animals that are taken from the wild. They are often then put into appalling conditions. To move on from the welfare, environmental impacts of this onto the issues of the seven year phase-out, we would like to see it done as soon as possible. We believe that the seven year phase-out is a more than realistic timetable for this. The problem area is the macaque species, which tend to come in from imports. If I deal with marmosets which can have multiple offspring bred in captivity, generally the import data for Europe supports the Commission position that they are self-sustaining. 18 months to implement that seems no problem. About 7,000 macaques come into Europe every year. The global export output of China, Vietnam, Mauritius, the Philippines, Indonesia and Cambodia alone, the big suppliers for Europe, is 78,000 macaque monkeys, so we are looking at attempting to influence 8% of their export production. The protestations that this will turn primate production on its head are a nonsense in terms of scale. In fact, global output is probably twice that because the US produces a huge number of primates. China and other countries are producing them for domestic use. We are possibly attempting in seven years to influence about 4% of global output. The Commission have said that this would need about 10,000 primates added to the breeding stock over the seven years. Those are 10,000 which, if they do not implement this process, will almost certainly be replaced with animals from the wild anyhow. The absolute breeding period for a macaque female is 25 years and that is if you breed from her until the day she dies. Realistically, the peak breeding period for a macaque monkey is about 15 years, which is what we believe they are currently using. Roughly half of all these breeding monkeys are going to be replaced in the next seven years. They are either going to take them from the wild or they are going to be under pressure to breed animals and replace them internally. There are good, scientific arguments for why an animal with a known genetic background, a known disease history, a clear age, known parentage should be a better research tool. There are all the animal welfare arguments and so forth. There is also the impact. If you keep taking these females, you are talking about depleting huge numbers of females rather than males from the wild. There have never been any studies of what impacts that has, apart from the fact that we can be sure that they severely disrupt the right balance in wild populations. We also think there is a very high likelihood from what we have seen that males are caught anyway and just killed because the dealers do not want them. We think this is a measure that can be met and we believe it is a very, very important one.

Q384 ***Earl of Caithness:*** What about the 10 years for the other species?

Mr Phillips: If cynomolgus and rhesus macaque breeding can be dealt with in seven years, which we believe it can, it is probably reasonable to expect it can be done with other primate species. However, I think the question should be addressed: why are there these disparate, little experiments on a handful of

lemurs here, a handful of prosimions here, the odd baboon over there and so on, when the argument from the animal researchers is that you want to gather baseline data on a single species to attempt to iron out the species differences? We think all of these models are flawed but it seems to hugely add to the problem if you are not focusing on a single species. We think there is a strong scientific case for putting in straight away that those other disparate primate species which are almost used *ad hoc* be phased out altogether.

Q385 ***Lord Palmer:*** You probably heard the answer we had from our previous witnesses who were remarkably brief in their answers. As we all know the severity classifications for procedures, up to mild, moderate, severe or non-recovery, will determine important aspects of the application of the Directive. However—and I do not find this at all logical—the criteria for these classifications are only to be finalised after the adoption of the Directive. Would you like to see these agreed within the text as proposed by the European Parliament and what is your view of the definitions proposed by the European Parliament under amendment 161?
Ms Creamer: Firstly, we would certainly like to see the severity classification system agreed before the Directive is finalised. We did oppose the definitions in amendment 161. We felt they needed more work. We would not like to be in a position where definitions and a system is rushed through just to get it into the legislation and then there may be no opportunity to review it later. We have produced a briefing on severity classifications which we can send to you as a supplementary memorandum, and also on primates. We have suggested that we think there need to be possibly six classifications. They would be mild pain, moderate/low, moderate/high, severe pain, severe and prolonged pain and non-recovery. The reason we have added the split on severe pain is, as you were discussing earlier, that the description in the European Commission's proposal does include an element of prolonged pain. Later on there is a discussion of how much is prolonged and how long that should go on. The UK Home Office has contended that they have concerns about the use of primates in Parkinson's research who clearly, when they are suffering the effects of the condition that has been inflicted on them, are suffering severe and prolonged pain. The reason we have suggested another category is that we would prefer to have the definitions more finely tuned so that we know what is going on, rather than having perhaps a blunter system which would mean that something which is severe and prolonged just gets classified as severe or, even worse, something that is severe gets reclassified as moderate.

Q386 ***Lord Livsey of Talgarth:*** The evidence that we had from the multinational companies said that they preferred amendment 161 to what was contained in the Directive. Why do you think that is?
Ms Creamer: Amendment 161 makes things easier for them. Throughout this lobbying effort over the last couple of years, one of the key things that we achieved in the European Parliament was Written Declaration 40. Yet our sense from the multinational companies was that they wanted to minimise regulation as much as possible, minimise the bureaucracy and regulation.

Q387 ***Earl of Dundee:*** You approve of the authorisation process subject to an ethical review. Indeed today I think you have emphasised the desirability of transparency and of public involvement. Would you just like to say a bit more about how you see the authorisation process and ethical review working?
Ms Creamer: Yes, certainly. We can provide a supplementary memorandum on this as well. We believe the important elements of authorisation are that it must be administered by a government or public authority, not by private bodies, as has been suggested in some quarters. It needs to be transparent and accountable to the public. It should report annually to Parliament and the public. It should be comprehensive. It should cover all animal experiments. We do not believe in derogation of the authorisation process for certain types of experiments. This would cause confusion and debate over what should be authorised and what should be notified. We also think that derogating authorisation defeats the objectives at the heart of the Directive to consider alternatives. If there is no authorisation and ethical review, you cannot consider the alternatives. It needs to include a severity banding system and a retrospective review element. Our thoughts on retrospective review are that, when you are at the end of your project, you review what you have done. You think about what has gone wrong, what has gone right, what you could have improved, where you should go in the future. Retrospective review would be part of the work that you are doing anyway. It is not an additional burden because, if you are conducting your science properly, you are doing that review yourself. Obviously it should include exploration of replacement methods, including when someone applies for a licence. They should be able to demonstrate that they have explored replacement methods and provide scientific references. The independence of the ethical review body is probably one of the most important things because in the UK there is no access to what ethical review bodies do and they are dominated by the colleagues of the researcher making the application. This is entirely unacceptable. We would see it much more like the

human research ethics committees, where they are completely independent of the establishment and of the person making the application. Currently, 21 Member States covering nearly 90% of animal use require some form of authorisation. A comprehensive system is already in place in 78% of the Member States. We think it is very important that those with the more sophisticated regulations, such as the UK, are not required to make a step backwards. The level playing field should mean that other countries rise to the authorisation here. That is not to say we are entirely happy with everything in the UK, especially the limitations on transparency and accountability. Having spent a lifetime negotiating with government departments, I can assure you they still find it very difficult to talk to the public and NGOs. Other governments in other countries have made that step on freedom of information and involvement of the public in the governing process. Very briefly, that is the outline of our authorisation system. The ethical review body should include at least one member from an animal welfare background, one alternatives expert or a relevant consultant, one external expert in the relevant field, three lay members, and should be able to consult scientists and experts in alternatives or a relevant field, importantly, independent from the laboratory and reporting to the competent national authority, not to the establishment.

Q388 ***Earl of Dundee:*** We learn of the European Parliament's recommendation that mild projects should only be notified to the competent authority following ethical review at the institutional level. What do you think about that?
Ms Creamer: I think it would be a disaster. It will cause confusion. There will not be an opportunity for implementation of the three Rs. There will not be wider scientific scrutiny of proposals to use animals. For the researchers themselves, they will be confused about what should be notified and what should be authorised.
Mr Phillips: That is the key. If the authorisation process is there to ensure that there is no duplication and that the information is not available from another source, that this is absolutely necessary and that there is not a replacement available to do this experiment, that affects experiments whether they are mild, moderate or severe. In fact, in rodent research there is a case that people are likely to be more cavalier in going into those experiments than they would be with more expensive species like a dog or a primate. We think prior authorisation has to be across the board. It may be possible to replace with thorough scrutiny millions of mild experiments rather than perhaps hundreds on this or that species in the severe category. There needs to be an acceptance that this has to be an effective authorisation process. It does have to test the research and so forth. If it is going to be meaningful and the public are not being misled when they are told, "We only allow animal experiments when they are absolutely necessary", there needs to be a reasonable time to do it. Obviously that cuts both ways. We believe that 60 days would be a good minimum for assessing project applications. We do not think it is burdensome in terms of the way research operates. We are involved in research in terms of grant applications. In terms of planning, especially when animals are involved, where you are looking well ahead to get the animals bred and online, at the right age and so forth. We do not think this application process is burdensome in the way it is portrayed. There needs to be access to input into it, to challenge it and to start looking to seriously replace animal experiments.

Q389 ***Earl of Arran:*** I know you are pretty scathing about the draft Directive, about the lack of promotion of alternatives particularly. How constructively would you like to see this amended?
Mr Constantino: That is a very good question. We strongly support ECVAM. It was created on the basis of a Commission's communication in 1991. That is the only legal basis it has. However, it has a very important role in validating alternatives and it has shown that it was efficient for the cosmetics ban. It is making some progress on toxicity. A similar institution has been created in the US, Canada and Japan because it is an excellent system to develop the use of alternatives. Despite a weak budget and a weak legal basis, it counts as a world leader in the validation of alternatives. That is why we really would like ECVAM to be firmly on course in an Article in the Directive. The Commission's proposal does not include that. However, amendment 139 adopted by the European Parliament is adding a new Article 45(a) which talks about ECVAM, and we support this.

Q390 ***Earl of Arran:*** The researchers who carry out the experiments on animals must be distressed and find them abhorrent at times. Are they indoctrinated when they first start doing this that really animals are the only way to do this? Are they encouraged to think laterally about alternatives?
Mr Constantino: It is an interesting question about scientific culture in general. It is clear when students arrive at the university and they start testing on animals they might lose sight of the fact that animals can suffer. I think it is the same in all areas of cruelty against animals. Yes, you could say there was a kind of indoctrination.
Mr Phillips: In any industry there is a tendency to lock into the way that you are trained and have operated. Reform of industry is traditionally hard.

There was not a surge from the car industry to move to lead free petrol. Particularly in animal research, where you grow up extrapolating data from a different species, it heavily locks people into that methodology. I also think that there is a physical lock in to it. I was once speaking to a researcher on funding fertility research in Birmingham and they were doing this excellent work. They were using human cells and developing new models and they were racing ahead with it. "Why is there so much mouse research going on? More and more than ever." He said, "They do not have this. They are not attached to a hospital. They have a room full of rodents instead." Again, that is where the regulators need to get involved. They need to create an incentive to move from having rooms full of rodents, breeding and breeding, to having rooms full of different equipment and possibly a new range of graduates coming in. If I could just add one other point on the F1 primates, it is inevitable that those monkeys are going to be more expensive. If you get your monkeys free from the wild aged five years and you put them straight into a breeding programme, you have just saved five years of rearing costs. There is clearly an immediate disincentive to change unless there is some reason to go to F2, such as a legislative requirement.
Ms Creamer: There is also a problem with the status of the alternative methods of research because of the tradition that there has been built up over the years of using animals. As I am sure you can find out from organisations such as NC3R, there has been a difficulty over the years with the status of researchers using alternative methods and with a focus on alternative methods. The attitude in the science community has been, "I just want to do this research in the way that I have always done it" without looking at the other ways of doing the research. Training, education, improving the status of non-animal researchers all needs to be part of the mix in this new Directive. The suggestion we have made for the European Centre for the development of alternative methods and for training and centres of excellence and certainly the national reference laboratories that have been suggested would help to raise the status of the advanced technologies which at the moment are running alongside the use of animals. Getting the advanced techniques at the heart and centre of the Directive is one of the key solutions to making progress.

Q391 ***Chairman:*** I have found this a very good evidence session. Are there any more points?
Ms Creamer: I would like to summarise one point on the primates and the reason that we have given that so much emphasis. As I mentioned, we instigated the Written Declaration 40 in the European Parliament which gained 55% of the votes. Something to consider on the use of primates is that in the 1986 Directive there was an undertaking to treat primates as a special case and to look at how the use of primates can be reduced. The International Union for the Conservation of Nature has announced that 48% of primate species are now either endangered or critically endangered. One of the drivers for removing primates from the wild is the laboratory primate industry, as you have heard. They want to be able to take animals from the wild for breeding stocks and sometimes for research itself. If this Committee could take anything on board in terms of the use of primates, it would be how long do we think we can carry on taking these animals from the wild without wiping some species off the face of the earth. 23 years later, we are still taking animals from the wild. In terms of what these creatures are, they are intelligent, emotional beings. They communicate. They use tools. These animals can anticipate what is going to happen to them. We conducted an investigation of Huntingdon Life Sciences just last year and one of the points that our investigator made was that on the killing days, all the monkeys fell silent. They knew what was happening to their cage mates. They suffered prolapses and self-mutilated. Some bit through fingers, all because they could anticipate what was going to happen to them.
Chairman: Thank you very much for all your evidence.

TUESDAY 14 JULY 2009

Present	Arran, E	Cameron of Dillington, L
	Brooke of Alverthorpe, L	Sewel, L (Chairman)
	Caithness, E	Ullswater, V

Memorandum by the European Federation of Pharmaceutical Industries and Associations (EFPIA)

Introductory Remarks

— EFPIA is the voice of the pharmaceutical industry in Europe. Via its direct membership of 32 national associations and 43 leading manufacturers, it represents 2,200 R&D based biopharmaceutical companies.

— The industry acknowledges and supports the need for the review of Directive 86/609 to reflect technological and scientific progress. The industry constructively contributed to all expert and public consultations in the preparation of the review, and is keen to continue this collaboration.

— Europe has the highest animal welfare standards in the world today, with all aspects already highly regulated and controlled. Animal studies are fundamental for the biopharmaceutical industry's ability to conduct R&D in Europe. This is in turn critical to the industry's future contributions to innovation in healthcare and to Europe's economic wellbeing.

— While reduction and refinement measures bring short-term tangible welfare benefits, the entire replacement of animals in medical experiments remains a long-term objective; however scientifically this is not yet feasible. Therefore such research remains a key component of the study of diseases, their mechanisms and of maximising patient safety. Thus any new legislation must have a clear objective of improving animal welfare without unnecessarily hindering research.

— This review is the opportunity to strike an appropriate balance between animal protection, research reality and patients' needs. EFPIA calls for a honest and open debate, and stresses these aspects as vital to fundamental and applied biomedical research projects in Europe.

Animal Welfare and Good Science Go Hand in Hand

— EFPIA welcomes the explicit reference to the 3Rs principles (reduction, refinement and replacement of animals in experiments). These principles are already embedded in our research.

— A formal ethical review prior to any animal experimentation work is a positive step. This will instil confidence that animal studies are only used when other methods are not available. Ethical review bodies are already widespread within the EU and delivering clear benefits.

— Improved standards for animal housing and care have been developed by the Council of Europe over recent years and are now included in the Directive. EFPIA welcomes this; good animal care is entirely consistent with collection of good quality data. Proper implementation will require appropriate supportive investment, particularly in academia.

— The revision of the Directive means developing training and assessment for individuals who conduct work in animals. The industry welcomes this focus upon skills development, and is eager to explore training opportunities to sustain delivery of leading-edge technical capabilities in the EU.

— EFPIA applauds addressing unnecessary duplication of animal experiments, and will work constructively with all stakeholders to identify and eliminate those rare areas where this may occur in pharmaceutical and vaccines research and development.

The Proposed Text Suggests some Measures that would Reduce Levels of Animal Welfare

— Extensive restrictions on the re-use of animals may actually diminish overall animal welfare and could result in an increase in the total number of animals used. Certain long-living species undergo special training to make experiments less stressful for them. This is only practicable if the individual animals can be part of several studies in their lifetime, with full recovery after each trial. Preventing appropriately controlled re-use responds neither to research objectives nor animal protection.

— The requirement to use only 2nd and subsequent generations of monkeys (F2) born in captivity would be detrimental. Any benefits of a short or medium term ban on the capture of animals from the wild for breeding purposes would be outweighed by the consequences of demanding F2 use only. Primates live in harems, with one male to approximately eight to 10 females. Thus many 1st generation males would need to be culled, and numbers kept in captivity to sustain supplies would increase dramatically. The feasibility of this should be established before it is included in any unilateral legislation, including an assessment of any potential shortage of F2 animals during the transition periods and the potential to establish self-sustaining breeding colonies in the longer term.

— The prescriptive detailed list of euthanasia methods provided in the proposal will reduce the scope for application of improved methods and is therefore counter to good animal welfare. Appropriate scientific guidance, which can quickly adapt to technological developments and reference to good veterinary practice for detail should be preferred. This should be controlled through ethical review.

Limiting Possibility to Study Monkeys Contradicts Calls for More Research in Certain Fields

— The industry accepts that research in non-human primates (NHP) is a sensitive topic. However, it remains crucial in many important biomedical research projects to generate new therapies and biotech-derived medicines to treat, for example, cancers and neurodegenerative diseases. NHPs are also essential to the development of vaccines vital to prevent some pandemics. Restrictions, banning or phasing out their use in the absence of valid alternative models as suggested in some debates would not remove the need, it would drive it out of Europe and away from its scrutiny.

— Proposals to limit NHP use to debilitating and life-threatening diseases could restrict research not linked directly to a specific disease at the outset, such as improving understanding of biological processes. In addition, it could also restrict research into treatments for chronic conditions where no satisfactory treatment is available. Europe is a world leader in a number of areas of major fundamental research; including somewhere an understanding of underlying biology is vital. The EU should work to maintain this scientific leadership.

Red Tape without Tangible Welfare Benefit should be Avoided

— The proposals should reflect the EU's Better Regulation and Simplification agenda, which is aimed at reducing administrative and bureaucratic burdens, whilst not compromising animal protection.

— Any new provisions should avoid duplicating administrative processes between authorisation and ethical review. For example, studies that are demanded by law and where the requirements for them (scientific justification and ethical review) have already been established.

— The pharmaceutical industry is built upon protecting intellectual property. Therefore, although EFPIA fully recognises the value of better understanding of animal research, this should not mean divulging confidential information on research projects or personnel.

— The scope of the Directive includes certain life forms, such as many invertebrates, where the scientific evidence of sentience is poor. Furthermore, including embryonic and foetal forms could lead to a substantial increase in the administrative burden with no benefit. For example, including eggs used in vaccine production will mean millions of reported procedures with no benefit at all.

EFPIA hopes that the co-decision process will offer an opportunity for a factual debate on the best options for the protection of laboratory animals and sustain the EU's place as a location for high-quality empirical research.

11 December 2008

Examination of Witnesses

Witnesses: **Dr Gabriele Kuesters,** Sanofi Aventis—Chair of the EFPIA Group on Research and Animal Welfare, **Mr Steven Spanhaak,** Johnson & Johnson—Chair of the EFPIA Group on Safety, **Dr Karin Blumer,** Novartis on behalf of the EFPIA Research Directors' Group and **Ms Magda Chlebus,** EFPIA, Director, Animal Welfare, examined.

Q392 ***Chairman:*** Thank you very much for coming in such formidable force to help us with our inquiry. I have to go through a little bit of formality, just to say that this is an evidence session of a House of Lords Sub-Committee and a note will be taken of the meeting. Pretty shortly you will get a transcript of what has been said and you can then correct any errors that may have crept in. You will have a chance

to look at it. It would be enormously helpful if you could just identify yourselves and perhaps introduce yourselves to begin with.

Ms Chlebus: My name is Magda Chlebus. I work for the European Federation of Pharmaceutical Industries and Associations in two different roles: as Director Animal Welfare, and Central Europe. I deal with all issues relating to the revision of Directive 86/609 and other issues related to animal research.

Dr Kuesters: My name is Dr Gabriele Kuesters. I am a veterinarian and have worked with Sanofi Aventis in Germany and its predecessor companies for 25 years. I work in a department called LASW, Laboratory Animal Science and Welfare, which is a globally organised department. At the same time, I am Chair of EFPIA's Research and Animal Welfare Group which is a multidisciplinary group dealing with all issues around animals, animal research and animal welfare which might have an impact on our industry.

Dr Blumer: Good morning. My name is Dr Dr Karin Blumer and I am a trained veterinarian and philosopher. I worked on the ethics of animal experimentation in academia prior to joining Novartis where I now work in the Global Public Affairs team responsible for research and development policy issues. I am here to deputise for Professor Paul Herrling from Novartis who is a member of the Research Director Group of EFPIA.

Mr Spanhaak: Good morning. My name is Steven Spanhaak. I work for Johnson & Johnson here in Belgium. I am a toxicologist and senior scientific adviser to the Toxicology Department. Furthermore, I am Chair of the EFPIA Safety Group, which deals with regulatory requirements regarding pre-clinical safety testing.

Q393 ***Chairman:*** Thank you very much. As I said, a formidable array! Would you like to start by making any opening statement and then go on to the questions that we have indicated? It would be helpful if you could make an opening statement on your general position if you wish to do so.

Ms Chlebus: Thank you very much. First, thank you for giving us an opportunity to give you some information today and for the questions that we received in advance. I would like to make one brief statement consisting of two parts: one, about EFPIA and the importance of the pharmaceutical industry in Europe that might set the scene for some other questions, and then our global position about the revision of Directive 86/609 and the key drivers that should be taken into account when revising this piece of legislation. I will pass you a booklet, which is *The Pharmaceutical Industry in Figures*, which shows you some of the key figures about our sector across Europe, EU27 and beyond. First of all, EFPIA, which is the European Federation of Pharmaceutical Industries and Associations, represents the pharmaceutical industry which operates in Europe. We do not represent European companies, but we represent companies that place their investment and research work in Europe. I think it is important to make that point. In our membership we have both corporate companies, about 40 of them, and about 35 national associations. Altogether, we represent about 2,000 companies, all of them doing research and development of new medicines, vaccines and treatments. We have two specialised groups and I would like to highlight one of those, which is the European Vaccine Manufacturers. The reason why I highlight that is because 80% of all vaccine research, development and manufacturing for the worldwide market is done in Europe. That brings a new perspective to some of the issues, like the use of non-human primates, et cetera.

Q394 ***Lord Cameron of Dillington:*** Sorry, what percentage?

Ms Chlebus: 80% of all worldwide production, be it flu or childhood diseases. That is quite an important point. The other specialised group which also brings a new perspective to some of these issues is the European Biopharmaceutical Enterprises, which is composed of big biotech companies but also biotech start-ups, very small and medium-sized companies as well, which might be affected by some of the provisions especially from the procedural point of view. The main objective of EFPIA is to create a positive legislative environment which will attract investment in Europe and help us continue to flourish and invest here in Europe—not elsewhere, in Europe—and also help strengthen the science base to develop the European research area. One example is a project called the Innovative Medicines Initiative which is a huge public-private partnership which will address both vaccine and medicine development. This is between EFPIA and its members and the European Commission. These are our objectives. I would also like to draw your attention to a few figures that are important from the research and development point of view. The first is the figure of 19%. The pharmaceutical investment in R&D constitutes 19% of all private research and development investment in Europe, and that is probably a higher percentage than any other industrial sector here in Europe. The second is that we provide for highly qualified jobs. The pharmaceutical industry across Europe employs 635,000 people. It can be considered that one direct job could create three to four indirect jobs as well, and in a time such as the current economic crisis I think that is quite important. I would like to highlight the fact that 117,000 of those jobs are directly employed in R&D. Finally, our sector has one of the highest contributions among high-tech sectors to Europe's trade balance. We have a very important trade surplus of €52 billion. The value of the sector for Europe and, therefore, the importance of maintaining pharmaceutical research and investment

in Europe are highlighted by some of these figures. I now turn to the revision of Directive 86/609 and I would make only a few comments because the rest is addressed in the questions that we will discuss later. First of all, the pharmaceutical industry supports the need for the revision of 86/609. This Directive is 20 years old and needs to be adapted to technological and scientific progress. EFPIA has contributed to that process since 2002, so it is a very old story. This revision now gives the opportunity to strike a balance between animal welfare and research and patient needs. In our case this is all about maintaining biomedical research in Europe, so it is quite an important piece of legislation. A way of achieving that balance could be done through three main principles. The first one is that the Directive should focus on objectives and outcomes and not necessarily on the processes. For us, a level playing-field does not mean identical playing-fields. If we harmonise the outputs, the objectives, the processes could be different because they are embedded in different countries, in different administrative systems, but what is important is that the output from any process is the same harmonised across Europe. The second is that the provisions of the Directive should reflect a real policy driver, a real objective. Today we are not 100% sure that there is always a clear policy objective behind every provision of the Directive, again clear objectives rather than what is perceived to be public pressure or public opinion. The third is that the administrative burden should not be disproportionate to the potential animal welfare impacts. We will come back to this proportionality element later. For us, good welfare means good science and good science should drive good policy. Therefore, as an industry, we would support very strongly some elements which are already in the Directive today as written by the Commission and which contribute directly and in a tangible way to improving or harmonising animal welfare: explicit reference to the replacement, reduction and refinement principle; formal mandatory ethical review, which will now be the centre-piece of this legislation; improved standards for housing and care; training and assessment of individuals. These are important issues that have been rightly captured by the Commission in the text. However, there are some areas of concern. If we consider ethical review is the central piece of the legislation, we are surprised by the lack of trust that the Commission text places in that ethical review because there are a number of conflicting additional limitations, or barriers, which are redundant. If we consider all existing safeguards provided by ethical review, scientific justification, harm benefit assessment, retrospective reviews, all these layers of controls make any additional blanket limitations, like the ones on non-human primates, completely redundant. I would like to stress the need to regulate outputs and not the processes. As I said, the processes can diverge across Europe, and we will come back to that in one of the questions. Finally, I would also like to highlight the fact that the European Parliament has addressed many of the shortfalls of the European Commission text and placed the ethical review as the centre-piece of the legislation and at the centre of decision-making about doing animal research. This is reflected in some of the provisions proposed by the Parliament on access to and use of primates, severity classification and the re-use of animals, and proportionality of administrative burden to the security and complexity of research. To conclude: these three issues—proportionality, clear policy objectives and focus on the outputs rather than processes—should be the elements that contribute at the end of the day to striking this balance between animal protection, research and patient needs.

Q395 ***Chairman:*** Thank you very much. I think we will explore the whole business on outputs rather than processes as we go through the questions. The Commission's argument, or justification, is the one that you have given us, that the need for the Directive is that there has been a lack of consistency in the way the 1986 Directive has been applied and the requirement to establish a level playing-field can only be achieved through a new Directive. That is your position as well, is it not?

Dr Blumer: It is definitely our position that a level playing-field adds an element of certainty in terms of investment, that if you invest in one part of the Community you want to make sure there is a consistency throughout the European Union. This is why EFPIA as an organisation is fully supportive of creating a more level playing-field. However, as my colleague has already mentioned, this does not necessarily mean that this harmonisation can or should occur via harmonisation of the processes.

Q396 ***Chairman:*** That is what I do not understand.

Dr Blumer: This is where we are fully with the Commission, that animals being used for experiments in the UK should not be treated substantially differently from animals used for experiments in other parts of the Community. There seems to be the perception, and I cannot state whether this is fully supported by evidence, that animals in the UK are treated differently from animals in other parts of the Union and a novel piece of European legislation could help to eliminate these different areas. As Ms Chlebus has already mentioned, we do see that there are some discrepancies in implementation throughout the different Member States. For example, not all

Member States have a mandatory ethical review, which is a core element we would like to support. If this is the case, then it makes sense not to regulate the processes but the fundamental outcome-based elements of animal welfare legislation throughout the Community. These are the areas where a new law would benefit.

Q397 ***Chairman:*** Obviously you are talking in conceptual terms here, the difference between process and outcome. Can you give us some idea of what it means on the ground?
Ms Chlebus: I can give one example on the authorisation part because I think this is the most obvious. If we look at the Commission's Impact Assessment Report it states that certain countries do not approve projects, and they mention Sweden amongst those. Our question is: does that really impact on animal welfare? Sweden is approving studies but through a different process, not at the level of approving the project but of reviewing the procedures through a regional ethical committee and the authorisation comes with the positive outcome of that approval. Here we have an example of a very well-functioning administrative system, but if you wanted to adjust to what is in the European Commission text you would have to add another layer of authorisation which would be authorising the project per se. Would that necessarily add to animal welfare and help to better implement the 3Rs? We are not convinced that this is the case. What we want to try to get out of the process is a sound scientific justification, a sound ethical review and to make sure that the 3Rs—reduction, replacement and refinement—have been applied, that we have done the harm benefit assessment. This can be done by a variety of bodies or systems, but we want to make sure that this will be done prior to the start of the study. That is really what matters. When we say, "harmonise the outputs and not the processes", that does not necessarily mean implement the same administrative system across Europe. That would not work anyway because there are too many different administrative systems across Europe and it would create a lot of bureaucracy if we wanted to do so.

Q398 ***Lord Cameron of Dillington:*** How do you police your system?
Ms Chlebus: Through national inspections. Establishments are being inspected. There is no carte blanche for doing anything you want. The systems could be at regional level, establishment level or national level, it depends on the country. There are a lot of different systems that exist. At the level of the establishments you would have an inspection level. By the way, the Commission has included a new element in the revision of Directive 86/609, which is inspecting the national inspection systems to make sure they work properly and according to the same standards. This is one of the ways of policing the system consistently across Europe.
Dr Blumer: I have served on two ethical review bodies, one in Germany and one in Switzerland. A sound and strong ethical review that also has a part in policing is probably the most pragmatic and deliverable system to ensure animal welfare. There seems to be a misconception on the part of the Commission of what an ethical review body does. It is not just a committee including ethicists. There is an ethicist, but that is not the key part. The key part of such a body is diverse expertise from the different scientific angles. I am sure my colleagues will support me that very often the most critical person in such an ethical review body is the statistician who helps you to fine-tune your studies, so you use as few animals as possible and as many as required to come to sound results. Such a review body does policing in a way that it reviews the protocols, helps to fine-tune the protocols, to determine any misconduct in the protocols, for example if there is an anaesthesia that is not appropriate to the species, and it may also have a part in auditing the facilities. If you have behavioural scientists on an auditing body, they may do the policing part and help the authorities which do not necessarily have the scientific and technical skills to ensure that animal welfare is taken into account in the most appropriate way. From our perspective—and this is an area where harmonisation may be required—a sound, strong, empowered ethical review is the most important element in improving animal welfare.

Q399 ***Chairman:*** I think we are on common ground on the importance of ethical review, I do not think there is any difference between us there. Could I go on a little? The Commission's point is that there is a lack of consistency. When we had Professor Hammond giving evidence in June he said "there has been a big difference in implementation across Europe" of the 1986 Directive. The question then is does the fact that there has been this lack of consistency and difference in implementation mean that some Member States are going to be in quite a difficult position to implement the new one because it is going to be far away from where they are now? Is that fair?
Dr Blumer: It is difficult to make a prediction from the knowledge we have today, because much of this definitely depends on the final version of the text. If the text is a simple text, more like umbrella legislation that gives specific objectives to be achieved while not going into too much detail, implementation may not be overly difficult because national animal welfare legislations can be adapted to include the additional elements being asked for by Europe. However, if it is

a highly detail-orientated text with a lot of mandatory annexes that go into areas such as the provisions for euthanasia, which euthanasia methods would be allowed, then implementation will certainly be more of a challenge. It is difficult to be specific on the question for which countries it might become a challenge. Recently I attended a government workshop in Germany, an expert workshop on transgenic animals where, amongst other things, it was being discussed whether a new law would be required. At the moment the German law that regulates this area is the Animal Welfare Act; if the new legislation becomes very, very specific on the use of animals in scientific studies, it would mean eventually we would need a new law and, aside from the Animal Welfare Protection Act, there would have to be an act on the use of animals in experiments and this is more of a legislative process. It is very difficult today to say what will be the final European legislation and from then on who will have difficulties.

Ms Chlebus: Maybe if I could answer that one point. It is where the differences lie in the implementation. The differences stem from the differences in administrative systems: sometimes you have formal authorisation, sometimes not; sometimes you have a formal ethical review, sometimes not. The second is that certain provisions are mandatory or guidance. As an example, housing and care provisions would be considered mandatory in some countries and not in others, but that does not mean that establishments will not strive to achieve the implementation and application of these standards. There is also different statistical reporting, you count animals differently, either prospectively or retrospectively, and this varies hugely across the European Union. There are different severity classifications. These are the differences, but at the same time when we look at the outputs from the different national systems, if the policy objective is to make sure that you have good welfare of laboratory animals these systems do not seem to have any impact on the final objective, which is the welfare of animals. Yes, there are some huge differences but one should question whether they are differences in standards or just in simple administrative procedures that might be justified.

Q400 ***Chairman:*** This inevitably raises questions about implementation and monitoring implementation. I suppose we start off by asking how do you monitor implementation and is there a role for the Commission?

Ms Chlebus: There is definitely a role for the Commission. The Treaties provide for a variety of tools to police implementation of legislation. First of all, Member States implement the legislation and have an obligation to report back to the Commission on how they have done so. Then, based on a third party complaint, or the Commission itself on its own initiative, the Commission can launch an infringement procedure against a country that fails to properly implement the legislation. This is to translate the European text into national legislation. Similarly, on the practice, if there is a very systematic breach of the provision of legislation that is brought to the attention of the Commission, the Commission has tools through infringement procedures. The Commission would be in a better position to address this through the variety of tools they have. There is one additional point which I mentioned earlier on which the Commission has embedded in the new Directive, and this is inspecting the inspections, making sure there are adequate inspection standards and provisions in every country.

Q401 ***Chairman:*** You see that as a critical role of the Commission, to inspect the inspectors?

Ms Chlebus: This might be one of the important points of enforcement because this has not been checked until now. I am not sure whether this is really critical but it would certainly help to have common inspection standards and that would also contribute to the level playing-field from that point of view.

Chairman: Thank you. Let us go on to the next topic, which is international competition.

Q402 ***Lord Brooke of Alverthorpe:*** Good morning. I am probably staying on the same subject for a little while longer. We heard some very forceful evidence from the UK ABPI's representatives about their concern that the proposal might diminish the bioscience sector's international competitiveness. They focused their concern on the risk of unnecessary bureaucracy that would, for example, slow down the process for authorising animal procedures. They said that in their opinion authorisation processes in the UK could be slower than in other Member States, and also much slower than in other parts of the world too. Do you agree that there are differences between the Member States in the authorisation process in the time taken, which they very strongly claimed there was?

Dr Kuesters: Yes. We can only agree that there are indeed differences between the Member States on the speed of the authorisation process. This has been shown in a Commission survey and our own experience confirms this. Harmonising timelines to speed up the approval processes would indeed contribute to a level playing-field, which is something the Commission clearly has in mind. However, if you look at the current drafts from the Commission and also the EP amendments then it is not clear if the authorisation timelines include the time for delivering an ethical review. Should this not be the

case then we would have a reasonable time for a compliance check, which means the authorisation, that is 30 days, but no timelines at all for the ethical review process. This is a shortfall in both proposals so far and should be included in the final legislation. In Germany that is already the case. In Germany we have a deadline included in the national legislation within which the authorisation has to be granted or rejected and, because the ethical review body is reporting to the authorisation authority, it is very clear that the time needed for the ethical review is included in this timeline. If I may give another example leading to differences in the speed of the authorisation processes, and this is an example from Germany again. In Germany they apply notifications for regulatory testing simply because these tests are obligatory by law and that has the effect that the ethical review is done by the lawmaker and an additional ethical review and authorisation is not needed, it is deemed redundant. As is the case in Germany, the responsible authority receives detailed information on the planned experiment, which is called notification, and then they have an opposition deadline of two weeks and only if you do not receive any comment then you can start with the work.

Q403 ***Lord Brooke of Alverthorpe:*** Would you see the German system being faster than the one operating in the UK?
Ms Chlebus: For regulatory testing, probably yes.
Dr Kuesters: For sure. Two weeks is quite quick to be able to start.

Q404 ***Lord Brooke of Alverthorpe:*** So the arguments advanced to us were correct, there is quite a difference between two or three of the major producers in the UK, let alone between the Eastern European countries?
Dr Kuesters: And we do not have any complaints about bad animal welfare or that things should be changed, so the system works well and is accepted.

Q405 ***Lord Brooke of Alverthorpe:*** So we have some very active welfare animal campaigners in the UK then, you think?
Ms Chlebus: Yes.
Dr Kuesters: You have.

Q406 ***Lord Brooke of Alverthorpe:*** This brings us back to an issue that you raised earlier about the difference between science and public opinion and the extent to which that may be the science but one cannot disregard public opinion and the movement of public opinion too.
Dr Blumer: Would you allow me to briefly comment here?

Q407 ***Lord Brooke of Alverthorpe:*** Certainly. This is not in the questions; this is a supplementary.
Dr Blumer: This is a key point. Coming professionally from a country where perceived public opinion is checked on a regular level by public referenda. The perception of public opinion is not necessarily what real public opinion is, because you may have highly vocal groups who can display an argument in a very popular manner but who are not necessarily supported by the majority of the public as a whole. We have seen this in Switzerland where we have had three public referenda on the use of animals in experiments.
Ms Chlebus: The European Parliament is another example of the voice of the European public. This is what the European Parliament is. The opinion adopted by the European Parliament seems to completely contradict some of the perceived public opinions before us. Yes, you are right, both have to be taken into account.

Q408 ***Lord Brooke of Alverthorpe:*** Do you mean the amendments?
Ms Chlebus: Many of the amendments contradict completely what was perceived to be public opinion.

Q409 ***Lord Brooke of Alverthorpe:*** Yes. The allegation has been made to us that the European Parliament has been nobbled by the industry!
Ms Chlebus: I will not comment on that.

Q410 ***Lord Brooke of Alverthorpe:*** This is again an argument that was put to us by the UK industry. Do you agree there is a real risk that adoption of the new Directive might mean that research is lost from the EU? To what extent is such research already being diverted to other parts of the world? How far can any such diversion be attributed to differences in the regulatory control of animal procedures?
Dr Kuesters: First of all, it must be said that what attracts companies is not lower welfare standards. All globally active companies, like my one, have something similar in place and in our company it is called the Charter on the Humane Care and Use of Laboratory Animals. These are binding global principles that have to be applied and which are checked. You could call them something like the internal constitution or internal bible. What really attracts companies are other factors, like access to capital for investment, the high skills of personnel, and sometimes even tradition plays an important role. In my company, the first drug to treat diabetes, which is an increasingly widespread metabolic disease, was developed in 1923 and since then the research in this big area and the production of the drugs and medical devices to administer the drugs has been in Frankfurt. This is because there is a lot of

special skill around this one disease and this cannot easily be removed and found in another place. But if it starts with one part being moved then others are likely to follow. To come back to your question, the points that are critical in attracting companies are efficient, clear and simple administrative processes in the country that we have been talking about, allowing us to do high quality work in the shortest possible time. Ms Chlebus will give you the booklet and on page three there is a table showing some figures on that. You can see that between 2001-2006 in Europe two sites have been opened and 18 have been closed, in the USA six have been opened and five closed, and in Asia 14 have been opened and one has been closed. This is quite impressive data. There are several factors involved or contributing to this. For example, one is the restructuring of companies, and this is currently underway in my own company. I have been through four mergers already. During mergers, complementary know-how and existing sites are joined, so there is always the risk that something will be closed. Another important issue is the economic crisis, especially currently, and all this means adapting a company to a changing environment. Unnecessary bureaucratic burden that does not improve animal welfare in any way, but just delays effective and efficient work, may not be decisive but it is one factor which is added when decisions have to be taken on new investments.

Q411 ***Lord Brooke of Alverthorpe:*** You think the new Directive will add to it?
Ms Chlebus: It might.
Dr Kuesters: It might. Our clear objective is to keep our research in Europe, to keep good science in Europe, our jobs in Europe and good animal studies in Europe, to work against the visible academic brain drain which has started but is at risk if things go wrong with this Directive.
Ms Chlebus: One additional point that was made by Tim Hammond in his hearing was that these changes do not happen overnight, and I would like to stress that. Sometimes you can hardly find any connection, but this multitude of different factors would result in the medium to long-term in relocation. We need to be aware that whatever decision is taken today on the administrative burden, it will be paid for only in a few years' time.

Q412 ***Lord Cameron of Dillington:*** Can I just ask a supplementary on that? You said there might be three reasons for moving research. One was the skills, the second was mergers and acquisitions, and then you put process delays. I am wondering what the steps between those three are. Those first two sound to me as though they are really important and delays are not particularly important but are just a very small factor. Can you scale them at all?
Dr Kuesters: I think the most important factor is the skills. Expertise is the core of our business. To say something on the other factors would be very difficult, but you have to keep in mind that the work with animals means just 5–10% of all the work that is done on our drugs over the long time of development, which is sometimes more than 12 years. Every day that adds to the time before we can offer a new drug to the patient really counts.
Ms Chlebus: It is a very important factor in terms of delays.

Q413 ***Lord Brooke of Alverthorpe:*** The growth of new markets as well—
Dr Kuesters: Yes.

Q414 ***Lord Brooke of Alverthorpe:*** --- is an attraction for people in deciding where to locate their new investment?
Ms Chlebus: Absolutely.
Dr Blumer: Also, the predictability of the system you are operating in is a key factor. Even if country X somewhere in the world offers you the fastest approval process ever seen, if this is a volatile country and you do not know if the law is predictable, this is an obstacle to investment. Last, but not least, animal welfare considerations are a factor and this comes in one of your next questions when we talk about re-use, as I understand it. In the company I work in, and I am sure it is the same for all the companies, if a new law forced us to obey new procedures which we clearly see as not compliant with animal welfare considerations, that might be a reason to relocate that specific kind of research because today all of us openly communicate about the numbers of animals we are using. A sharp rise in the numbers of animals we are using in our public communications would be hard to accept and also for our employees who are deeply concerned about animal welfare. Animal welfare considerations are not something randomly taken into account but really are at the core of our business considerations.

Q415 ***Lord Brooke of Alverthorpe:*** Could I just go back to the previous question about the issue of the strength of the campaigning that is undertaken in the UK by comparison with what happens in Germany. Is it possible that, in fact, the counterarguments are put more strongly by industry in Germany to the public at large than perhaps is the case in the UK?
Dr Kuesters: I would not say so. It is simply a different culture.
Dr Blumer: Can I come in on that as a philosopher? Animal welfare legislation started in the UK a long time ago.

Q416 ***Lord Brooke of Alverthorpe:*** Yes, it was a long time ago.
Dr Blumer: In 1789 there was the so-called species difference argument by Jeremy Bentham, so you have a long and rich tradition of looking at animal welfare. You have a totally different legal and philosophical system from the Germans. The German system is very stiff, not as emotional on animals as your system, and I would not necessarily say that industry or academia talk more about it, it just does not have the level of public attention that it may have in the UK.
Ms Chlebus: Certainly better communication about the value of this research would be extremely helpful, including that by the authorities. We often get the impression when it is communicated, particularly by the authorities, it is done in quite a defensive manner and on how much is being given as alternatives rather than talking about patient and consumer safety which results out of this research. Both are important and should be mentioned.

Q417 ***Earl of Arran:*** Are you saying that the downturn in the global economy is affecting scientific research and how much money is being invested? Is it definitely slowing down across the global scenario?
Ms Chlebus: Probably not yet. We would not see it immediately, but we may see it over a longer period. For the biotech companies, yes. Biotech companies that have difficulties in accessing capital have really big problems and are in difficulties today. Start-ups are definitely in danger.

Q418 ***Earl of Arran:*** Staff numbers are being reduced across scientific research to your knowledge?
Ms Chlebus: I can check and come back to you on this question.

Q419 ***Earl of Caithness:*** Most of the evidence that we have received has been very firmly of the opinion that the criteria for severity classification should be in the Directive rather than coming after. Do you agree with that? Could you please update us on what happened in the working group last week on 9 and 10 July on this discussion?
Dr Kuesters: We certainly agree because we really would like to stress that the definition of the severity classes is crucial to understand the impact of many provisions in the text. You are nodding; you know this already so I do not have to go any further. Concerning the working group meeting that took place last week, we cannot tell you the details but a colleague in my company represented EFPIA at that meeting so I can tell you something at least. By the end of next week the Commission will publish the outcome of that meeting and, as we understand, the expert working group worked within the framework set by the European Parliament proposal in amendment 161 which was Annex 7A, providing for the definition of categories and examples of the categories. The participants of the working group seem to have agreed on quite a lot of things, on the definitions, on assignment criteria, lower and upper thresholds of severity, also humane endpoints have been discussed, and we hope this will be a sound outcome and accepted in the further political process because this is important. I have to stress the point that it is important to have this in place before the final legislative text will be adopted.

Q420 ***Earl of Caithness:*** Was re-use discussed in the working group? There has been some concern with the moderate and severe procedures, that you can only have one re-use afterwards. Was that discussed? What are your thoughts on that?
Dr Kuesters: Re-use is a very important and complex issue because it is a very pragmatic way to considerably reduce the numbers of animals that we use. It mainly concerns long-living species, like dogs and primates, which is quite important, but what the Commission has proposed on the re-use so far has several highly negative effects on animal welfare. We believe it was not anticipated that this would happen in reality and it was not the intention. The Commission has proposed so far to limit the subsequent re-use to the category of mild severity. Severity is assessed prospectively and very often as a precaution a higher level of severity is assumed than the one that is experienced afterwards by the animals. This limitation would result in a significant increase in these animals and all of our member companies say this would mean a 10 to 20-fold increase, which is quite a lot. As I have said, this would increase the number of dogs and primates because these two species are the ones that are trained to cooperate. This is called PRIT—positive reinforcement training—and this does not only reduce the number of animals used but also significantly reduces the stress for them. With the Commission's proposal all of this would be discouraged, so the training and also socialisation of the animals would be discouraged which are housed in large groups with all sorts of enrichment for a long time. They are very much used to the personnel who are caring for them but this would also be discouraged, it would not be done any longer.
Ms Chlebus: The European Parliament has adopted an amendment that brings some solutions. It suggests that a subsequent study could also be moderate provided you have a veterinary green light for that. It is a case-by-case assessment rather than just a purely procedural approach. This is where I would like to reinforce the point about outputs versus processes.

Instead of having just one procedure for every case you look at these issues on a case-by-case basis.

Q421 ***Lord Cameron of Dillington:*** The Directive at the moment is saying "mild/mild" re-use. Would "moderate/mild" be good for you? Say you have taken a dog and you are putting in some sort of telemetry, injecting into a dog for retesting over a whole series, would that be satisfactory?
Ms Chlebus: From moderate to moderate.

Q422 ***Lord Cameron of Dillington:*** You want from moderate to moderate.
Dr Blumer: The key is the severity classification system you would impose. If you narrow existing systems, moderate to mild would not be acceptable because, for example, if you have to withdraw blood repeatedly at short intervals, which is what you have to do in pre-clinical toxicology, this is already considered as moderate.

Q423 ***Lord Cameron of Dillington:*** That is moderate, is it?
Dr Blumer: Yes. Even though the animals are optimally trained, it is a moderate stress level. This is the way we have to operate in pre-clinical toxicology testing.
Dr Kuesters: It all depends on the classification. We really hope that it will be something workable because it is critical, especially for animal welfare.

Q424 ***Lord Cameron of Dillington:*** Non-human primates, particularly in the UK, is a very sensitive matter, as you can imagine, on both sides of the argument. At present, the draft Directive limits the use of non-human primates to processes which are "life-threatening or debilitating" conditions, but there seems to be a degree of cloudiness over the definition of this which, in fact, again both sides object to. I am just wondering how you see this developing.
Dr Blumer: First of all, from our perspective, it is difficult to understand what the policy driver behind this was. We do understand that there is public discussion on the use of non-human primates whereas, as Magda said, our driver is good science is good policy. We do not fully understand the scientific driver behind this because obviously from a behavioural scientist and biologic point of view the non-human primate per se is not intrinsically different from the dog or the pig. The differences may be more in the physical appearance of the animal than in the true capabilities. The policy driver is really difficult to understand. Also the terms that are used in the Directive are open to wide interpretation, specifically the term "debilitating", which to my knowledge is only used in the orphan drug regulation and is not a term that has experienced sound definition by legislators. We think that the controls provided by the Commission proposal—authorisations, ethical review, harm benefit assessment and retrospective assessment—should make any additional blanket limitations redundant, especially as from the area in which we operate we do not have proof that there is any trivial science being done that uses the non-human primate. .

Q425 ***Lord Cameron of Dillington:*** So if there is no difference between a non-human primate and a pig or a dog, why do you want to use the non-human primate?
Dr Blumer: I did not say that there is no difference, but I would not necessarily say that there is a difference that justifies a very special legislative treatment. Obviously on a cellular level there is a huge difference, which is mainly the fact that the immune system of the non-human primate is much closer to the immune system of the human and this is the only species adequate in safety testing of some substances, especially the so-called monoclonal antibodies and the higher proteins, where other species, like the rodent and the dog, would not have the same—or a comparable—immune response. It is never the same immune response; they would not have an immune response comparable to the human. This is why in these areas, or the area of transplantation, the non-human primate by its biology is the most appropriate species, or often even the only appropriate species. The question is, and this is a philosophical question and not a scientific question, is there such a strong difference between a macaque and a dog that this difference justifies a very different treatment by law. I guess the majority of scientists would say that it is hard to prove. But we have to take into account that the perceived public impression is that there is a difference and this is obviously what the Commission proposal is taking into account. I am not saying that such public perception should not be taken into account, but I am stressing that the policy driver is sometimes hard to understand, especially as the terms used in this paragraph, "life-threatening and debilitating", suggest there is evidence that non-human primates at this stage are used for trivial purposes by our sector, which is not supported by the evidence.
Mr Spanhaak: If I may confirm what you say, Karin. There is some difference in perception as regards look-alike animals, such as monkeys or non-human primates, and other animals. The main driver within industry to select a non-human primate is that we do not have any other option that gives us the same capability to test for adverse effects. If we have sound reasons to think that the monkey would give us a better answer than a dog or a guinea pig or whatever,

that is the only driver within industry at the moment to select a monkey, and that should be the only driver, sound scientific evidence that you need an answer from a species which is nearer to a human being than a dog, for instance, for certain aspects.

Q426 ***Lord Cameron of Dillington:*** But it is not always successful, is it, for some of the AIDS vaccines, for example?
Ms Chlebus: It is science.
Mr Spanhaak: It can never be always successful because the best model for human beings is human beings.

Q427 ***Lord Cameron of Dillington:*** Thank you very much for that. What is your answer to the question about F2 animals and the time limit for only using the F2 animals? I think I can probably guess the answer.
Dr Blumer: If you will allow me to conclude on the first question. Our view is that the amendments proposed by the European Parliament clearly would help to solve the difficult question of defining what a debilitating disease is. We think there is no such thing as trivial use, and most of the Parliament's amendments are also supported by the recently published SCHER and Prognos reports. To come to your second question, the mandatory use of F2 primates, first of all it is important to understand that industry is fully supportive of the policy objective because here we do see the it quite clearly. The policy objective is to end taking animals from the wild to produce animals for laboratory use. We are very supportive of this objective. If this is the key objective, there are two different pathways to try to get to this. The first path is the so-called mandatory use of F2 non-human primates which, as you heard in previous evidence, has a lot of animal welfare difficulties because in the initial phase it requires significant culling of surplus F1 males, but it also has a more sophisticated problem in that the mandatory use of F2 does not end taking animals from the wild because you will always need a genetically diverse F1 generation. Unless you have established what we would call self-sustaining colonies, which are breeding communities that do not require animals taken from the wild to refresh the F1 gene pool, F2 does not solve the problem. This is especially true for a market like Europe that only accounts for 5–10% of global supply and does not have the economic power to drive that change. The other way to end taking animals from the wild would be self-sustaining colonies. This is contained in the suggestions put forward by the European Parliament that there should be a feasibility study if F2 use or self-sustaining colony use can be achieved in the timelines proposed by the Commission, and the preferred option would be so-called self-sustaining colonies where you would for example exchange male animals between breeders to sustain genetic diversity. A last point to raise is that supply does not only have purely a numerical component in terms of how many animals you need, but also has a geographical component because monkey is not monkey. A macaque from Barbados may have very a different genetic profile from a macaque from China and this may have an effect on the research protocol in which you want to use the animal. Besides securing access to an adequate number of non-human primates for European research, you also need to ensure that there is a diversity of resources from which you can import those animals into the Community. Again, this is something that needs very thorough investigation and feasibility. We do have support from reports such as SCHER and Prognos, where our key points are supported by the evidence given by these bodies.
Ms Chlebus: We are also looking at the feasibility and how this would be assessed to make sure that what would be measured would give the responses. We are looking into that and will be in a position in a few months' time to come with something sound.

Q428 ***Lord Cameron of Dillington:*** Is there a big difference on this whole question between different Member States and the approach to non-human primates? Again, is it a particularly UK problem?
Dr Blumer: It is hard to say at this stage because we do not have much data. However, we do know that some Member States have higher public awareness and public discussion.
Ms Chlebus: This research is not conducted in every country and this has to be taken into account. You would have this research in probably a handful of countries and in those countries you would have more rational legislation. In countries where you would not have this research at all it is easy to say, "We will ban it" or "We will restrict it very severely because we would never do this kind of research", and this also has to be taken into account.

Q429 ***Viscount Ullswater:*** We have sucked authorisation dry pretty well, have we not, but there are two minor points I would like to know. We have dealt with this in some considerable detail. On the basis that outputs and objectives should be harmonised rather than the process, do you think that the Directive as it stands allows enough discretion in allocating authorisation responsibilities to different levels of national authorities? If you do not, is there a way of writing that into the Directive? The second thing is taking up your point about timelines. Is there a way that should be written into the Directive that the timelines should include the ethical review process?

Ms Chlebus: The reply to both questions is yes, and then I will pass over to colleagues who work with that in practice. The question, is the discretion harmful or not at the end of the day, the answer is no. As discussed before you can have a variety of procedures, processes, but still have the same outcomes or outputs. The freedom that is given to Member States to delegate the power of delivering authorisations is not harmful to animal welfare at all, it is just a question of trust, inspections, making sure that the recording procedures work properly. On the timelines, I agree that the revised text should provide that ethical review is subject to the timelines which are set.

Q430 ***Viscount Ullswater:*** Are your concerns being taken up by the working groups? Are you expressing these things in the technical working group and are they being considered?
Ms Chlebus: In the legislative process we have reached the stage where now everything is in the hands of the Council. Yes, we are talking to the Member States. Depending on the processes in different countries we are hearing different replies, but the message has been heard and we will see whether it is translated into any text as an outcome of this process.

Q431 ***Earl of Arran:*** We have not quite sucked this one dry; there is a little bit of juice left in care and accommodation. It has been suggested by some witnesses we have had in front of us, and the ABPI, that if you have minimum standards it is going to add significantly to costs but not necessarily to animal welfare. That is the first point. Secondly, again said by the ABPI, that major companies require the same standards of care and accommodation no matter where in the world the research is carried out.
Ms Chlebus: On the first question, I think it has been slightly taken out of context. I think it was used in the context of breeding rodents and in that case technical adaptations are not necessary in economic conditions for improving welfare or there is no intent of improved welfare. That is in the context of breeding rodents and breeding rodents only. As far as the pharmaceutical industry is concerned, the new housing and care standards are being implemented already, or will shortly be implemented completely across the sector in Europe, so it should not be a problem. However, in some cases it is not just about buying new cages, it is about rebuilding some of the facilities, therefore we need appropriate time to do that, an adequate transitional period to cope with that burden. That addresses the first question. On the second question, the question implies, and correct me if I am wrong, that it would be OK to relocate research and if we applied global standards everywhere it does not matter where the research takes place, whereas I think, and this is the view of the European pharmaceutical industry, it does matter where this research takes place. Although, as demonstrated by my colleague, you have global principles, global standards applied across the companies wherever they go, our objective is to maintain research in Europe and attract as much research as possible into Europe. I understand the question, but we would like to see a slightly different logic and see how we can attract more research into Europe instead of encouraging relocation.

Q432 ***Earl of Arran:*** Are you concerned that there is considerable variation across the EU on care and accommodation in different Member States?
Ms Chlebus: The revised Appendix A of the Council of Europe Convention which sets the new housing and care standards which were adopted in 2005 is being implemented at various levels in different countries, so there should not be huge discrepancies as far as these standards are concerned. As far as the cage sizes are concerned, I think the key problem might occur in the academic world where for these adaptations you need a lot of money. If you have to build new facilities you need a lot of money. We work with the academic world and collaborate with them a lot, so it really matters to us whether or not they would be able to cope with that burden. They do not have access to the money and they also need slightly longer timelines for doing this. Where the money will come from, probably public authorities should look into that matter.

Q433 ***Chairman:*** What is the solution?
Ms Chlebus: I think in a time of economic crisis we need to look at where the money is, because that is what they need. Probably longer transitional periods would be adequate.

Q434 ***Earl of Caithness:*** The current requirements are recommendations only, whereas this is going to be mandatory.
Ms Chlebus: Yes.

Q435 ***Earl of Caithness:*** What period would you give for phasing in the mandatory?
Ms Chlebus: I could not give a reply now. The Commission have said seven years for some things, 10 years for some things and 12 years for others. It is difficult to say. I am not sure that a clear evaluation has been done on what the needs are and maybe we should start from that, to evaluate what the academic world will need in order to adapt. The impact assessment was done a few years ago when the economic situation was slightly different and this should be reassessed.

Q436 ***Chairman:*** Let us go on to something that we have not touched on at all, which is data-sharing. We know that the proposal requires Member States to share data, subject to confidentiality considerations, in the interests of avoiding unnecessary duplication of procedures. Some of the evidence that we have had is that there is little duplication in any case and there would be significant problems particularly in relation to intellectual property rights if there were a requirement to go beyond the present level of data-sharing, particularly if commercially sensitive data had to be shared. What is your general position on data-sharing? What sort of data do you think ought to be shared?
Mr Spanhaak: You have already summed it up.

Q437 ***Chairman:*** I always provide the answers to my own questions!
Mr Spanhaak: Generally, we are working with patented compounds which are unique and, therefore, there is no duplication in that sense. The process differs very significantly from the chemical sector even when you have similar compounds being investigated and this is not duplicated because small differences in chemicals in our setting may result in quite large differences with respect not only to efficacy but also safety. In that sense, there is no duplication. We are already sharing information, except commercially sensitive data, which in our view is not necessary because it does not reflect duplication. There is one particular example we identified where there could be duplication, which is the use of vehicles in experiments and studies. Because to deliver your drug you need to use a vehicle and that cannot always be water, of course, it is dependent on the compound and what you need to get your drug absorbed into the body. In that sense, there is a variety of vehicles used, and that is not unique for the compound but is a general feature which is used by several companies. Also, these vehicles have toxicity profiles, so what we have developed , and this is an industry initiative, a database where we register the toxicity profiles of the vehicles and share that amongst companies to prevent doing studies with vehicles alone just to show what the toxicity of the vehicle is. What we do not understand in the question is the policy driver here, which is what is the duplication, because we do not see that as a problem. Furthermore, we have data that we share in the sense of research projects, like the IMI project, the Framework Platform 7 project in Europe, and in various other projects, but that is not so much to prevent duplication, it is to extend our knowledge on existing models and improve models and alternatives. In that sense, as I said, we do not see the driver for this question. The only other possibility that we have identified is in vaccine batch re-testing and that is a regulatory requirement from specific Member States. That is not in the hands of industry but is in the hands of the regulatory environment to change that practice.
Ms Chlebus: This is more about mutual recognition of data rather than anything else. One point worth noting is that the provisions which have been proposed by the Commission set the right principle, that wherever you have unnecessary duplication do something about it. It does not say what you should do exactly because the solutions might diverge or could be different depending on the nature of the problem. First of all we need to understand what the problem is and, therefore, the principle provided in Article 44 by the Commission is the right one.

Q438 ***Chairman:*** What do you think about the European Parliament's amendments in this area?
Mr Spanhaak: As Magda has said, the provision as it is stated at the moment seems to be sufficient for us, especially because we are not sure what the driver is for this whole issue.
Ms Chlebus: The European Parliament's amendment is probably one of the areas where Parliament misunderstood the optimal approach. In our view, what the Parliament has tried to do is to replicate the approach to chemicals and pesticides in the field of biosciences, or to apply this across the board, but this is simply not applicable and I think Tim Hammond, during his evidence, gave a lot of examples why this would not be practical. It is the wrong approach. The principle set by the Commission is absolutely fine, but the processes that the Parliament tries to set would not be applicable in every domain. First we need to define the problem and then the appropriate solution, if there is a problem.

Q439 ***Viscount Ullswater:*** Can I ask one supplementary on that? You touched on batch testing, which is probably controlled by safety of drugs legislation rather than this Directive. It would be helpful for me particularly, and maybe the Committee, to know in your view are animals used too much for purely batch testing?
Ms Chlebus: It is not that they are used too much, but—

Q440 ***Viscount Ullswater:*** You come from global companies so your information and expertise is spread over a wide area.
Ms Chlebus: One area that has been clearly identified is unnecessary duplication and here, instead of recognising data that has been produced by the first manufacturer, Member States for public safety/public security reasons are redoing this testing. We are not calling into question the fact that especially for huge vaccination campaigns you need as much

security and safety as possible, but in some cases this is not necessary and not all countries do that. Only some countries re-do the testing. We think there is an area here where there could be some improvement. There is ongoing dialogue between national authorities in the Council of Unit, the European Pharmacopoeia, which is the body dealing with these issues, and the industry, so we hope there will be the possibility of waivers. We are not just leaving this problem on the table, we are trying to do something about it.

Q441 ***Viscount Ullswater:*** Perhaps we could hear your views on the proposed inclusion in the Directive of immature vertebrates and, of course, the whole weight of this Directive on certain live invertebrate animals. What is our view on that?
Dr Blumer: We are very consistent in our view; we always stress scientific evidence and proportionality. We do support the inclusion of species at developmental stages where sentience has been proved. However, we feel that the provisions put forward by the Commission include in terms of species and also developmental stages a vast number of animals where no proof at all of sentience exists. The most severe consequence might be that you would have to apply the same set of regulatory standards in terms of authorisation processes, ethical review, prospective and retrospective analysis to a fish egg as you would have to apply to a dog or non-human primate. We feel that this is clearly not compliant with a proportionate and realistic approach to animal welfare. In a nutshell, the worst case scenario is not that we would have to do a lot of additional statistical reporting which could be solved by fine-tuning what you have to put in the statistics, otherwise the experimental numbers would explode, but it would be in the areas of high urgency where we might be confronted with delays in production. As you may know, for example, quite a significant proportion of vaccines have been produced using fertilised chicken eggs and if you have to undergo ethical review and authorisation procedures for every egg you use for vaccine production that could significantly delay the time needed to produce new vaccines. Given the current H1N1 situation, it is absolutely obvious that in this area delays are not acceptable. Also, from an animal welfare point of view, to regulate developmental forms or species where we have no proof that they can experience pain or suffering, we do not see the value of this. From our perspective, the amendments put forward by the European Parliament are a very sensible way to address that issue.
Ms Chlebus: It could still be improved avoiding plankton in the scope of the Directives, for example.

Q442 ***Viscount Ullswater:*** How many cuttlefish, octopi, lobsters and prawns are used in experimentation?
Dr Blumer: Again, as Magda just cynically mentioned, it depends how we count these species. For example, if you think about lobster that you eat, and in my company we do not use those although there may be some academic use of those, if you go to environmental toxicology some of these species are with plankton and if you have to check the impact that your drugs or chemicals do have on seawater you may end up counting those species and the plankton. As we see it now, the law does not protect you from doing so. Another thing is fish eggs which are clearly an alternative in environmental toxicology to grown up fishes and other species to assess the safety of your compounds on drinking water. If you had to take them into the scope of the legislation I guess it is fair to say that we can assume a fish egg does not experience pain or suffering.

Q443 ***Chairman:*** I think that is about right.
Dr Kuesters: I would not say I can prove it, but there is no proof that they do.

Q444 ***Earl of Arran:*** Caviar.
Ms Chlebus: For example.

Q445 ***Lord Cameron of Dillington:*** I think I need to apologise for not getting an authorisation before I ate my egg for breakfast this morning!
Dr Blumer: It may not have been fertilised. The amendments put forward by the European Parliament are for proportionality aspects.
Viscount Ullswater: You make a very clear statement on some of the absurdities that could come up, so I think we need to take note of that. Thank you.

Q446 ***Lord Cameron of Dillington:*** Can I move on to alternative methods? Clearly the 3Rs principle is inherent to the Commission's aims and ambitions, and from what you say you very much support that. If that is true, it must be important to you also to drive the agenda of alternative methods. I was wondering how you best see that this could be done. The Commission has its proposal for national reference laboratories and, as you are aware, in the UK we have got a National Centre for the 3Rs, and there is also ECVAM, the European Centre for Validation of Alternative Methods, which seems to get some support from some and not from others. How do you see this whole agenda? In your view, what is the best method for driving it forward?
Mr Spanhaak: We certainly fully support the inclusion of the 3Rs in the research. While we would all like to see full replacement of animals in research, at present and for the foreseeable future it is simply

not realistic. However, the incentive to develop alternatives is clear: it is ethically right and commercially sensible. It is much cheaper to run an alternative than it is to support the infrastructure needed to do animal work. Most of the replacement, reduction and refinement methods are developed and scientifically validated by industry as part of optimising the research methods and improving the quality of scientific outcomes. Industry is also heavily involved in international specific 3R research projects, and that refers to the EU framework programmes, national and cross-sector platforms, the 3Rs and the EPAA, and also through the rationalisation of implementation of regulatory requirements, and in that sense we can mention the requirement for acute toxicity testing. That started as an industry initiative to investigate how acute toxicity data were used in the development of drugs. That data was shared with the UK National Centre for 3Rs. In the end, we came to the conclusion that the requirement for acute toxicity testing as it existed was redundant and the information could be derived from other data which was already produced during development, And the data could be provided later on in development because the most important issue to tackle is overdose situations where you need the information, and that can only happen later on in the development of drugs. That was a collaboration with the UK National Centre for 3Rs. We took that forward to the regulators as well and it ended up in an ICH process and was finalised in a global regulatory requirement which states that you can defer acute toxicity testing at the moment. These are clear examples where there are interactions between the various players. With respect to ECVAM and the national reference laboratories, we would say ECVAM plays a role in the revalidation of assays and the national reference laboratories could offer help Because we already have the experience that ECVAM. has limited capacity at the moment and may be hard-pushed to reach its goals. In that sense we would support national centres but it should be a focused effort, a collaboration between ECVAM and national centres, it should not divert. The same thing applies to the 3Rs institute which is more focused on providing and dissemination of information.

Q447 ***Lord Cameron of Dillington:*** You are saying that ECVAM should get more capacity and should be better supported and funded to be effective?
Mr Spanhaak: In order to support their current mission they seem to have limited capability. One way to solve that is to have these national reference laboratories or providing a higher budget for ECVAM itself.

Q448 ***Lord Cameron of Dillington:*** The national laboratories are good but they need a kind of central focus?
Mr Spanhaak: Yes.

Q449 ***Lord Cameron of Dillington:*** There is nothing wrong with ECVAM, it just needs more capacity and better finance.
Mr Spanhaak: Yes. For the pharmaceutical industry sector, each and every test that is developed does not need formal validation by ECVAM because it depends on the type of test you require.

Q450 ***Lord Cameron of Dillington:*** We have been told that a lot of the problem is dissemination of knowledge and, therefore, that could be a really important role for ECVAM, could it not?
Mr Spanhaak: Yes.
Ms Chlebus: For ECVAM, plus an efficient network of 3Rs centres. The UK's National Centre for the 3Rs is a perfect example of dissemination of information to the end users and the regulatory authorities and of good collaboration between different players. I want to add another example which demonstrates that complexity of the alternatives, which is the European Partnership for Alternative Approaches to Animal Testing, of which EFPIA is one of the active members, and a number of pharmaceutical companies as well. Actually, EPAA works on five aspects that show the lifecycle of an alternative test, which are, first, the development of alternative methods, mapping and understanding what is being done and the research on alternatives is global, it goes everywhere. The important thing is to make sure that there is no duplication, that there is complementarity and that we understand, for example, what comes out of the European funded projects, like Framework Programmes 6 and 7—it is sometimes very difficult to track back—and how best to use the knowledge that has already been developed. On the other hand, it is also about validation of alternative methods and about when formal validation is really necessary by ECVAM . We are working on streamlining the processes , including the peer review, and how select substances and so on. The next point is dissemination, to make sure that once a method has been validated it reaches both regulatory authorities, who would accept it or not in a regulatory framework, and to the end-users in the labs. If I work in a laboratory, how would I know that a new method had been developed and is suitable for what I need? There are some dissemination gaps. Finally, the regulatory acceptance, the fact that a method has been developed, disseminated and is used does not necessarily mean that all over the world regulatory authorities accept it. We may end up doing alternative testing in one country and animal testing

in another country because it would not be accepted, it is just duplication. Alternative tests are very often ex vivo tests using animal cells and tissues, so you would be using two animals de facto.

Q451 ***Earl of Caithness:*** I just want to follow up on that. Do you foresee a time when it will not be necessary to do any tests on animals?
Ms Chlebus: I think Tim Hammond gave a very good answer. We do not know, at least probably not in my lifetime, and I suppose that might be the right answer. It depends. Science could deliver something, a breakthrough technology tomorrow, and maybe we would be able to do that, but without this breakthrough technology and with the current knowledge and scientific development we do not see this will happen in the short-term, the medium-term or even in the long-term.
Mr Spanhaak: I certainly support that general principle. On certain aspects you can have alternatives in place. For certain very defined toxicities, like genotoxicity, we already have in vitro assays. For that particularly fairly defined endpoint you can have alternatives, but that means those are relatively less complex toxicities. If you are talking about liver toxicity, which may occur after two days or three months in an organism, that is not something you will be able to mimic easily in an in vitro model or any other model. It is not foreseeable in the near future that we will be able to replace that with an alternative model.
Dr Blumer: Even if you could do it in terms of safety testing, even if there was a super-computer that could mimic your body's functioning, still quite a significant proportion of animals are being used to determine disease mechanisms and gene environment interactions. This is something where, with the sheer complexity of genetic factors on the one side and environmental factors on the other side, we cannot envisage this.

Q452 ***Chairman:*** It looks as though the answer is no?
Ms Chlebus: Yes.

Q453 ***Earl of Caithness:*** If it is the case, and it has been put to me, that we will always need animal testing, particularly non-human primates, from a holistic point of view of looking at animal welfare, given the pressures in the countries from which non-human primates are coming, is it not better that we should still continue to have a steady stream of F1s coming in which protects the environment in those areas, because once you come on to F2s the logging people will go in and destroy the whole place where the animals came from?
Dr Blumer: That is a risk management question! This is the veterinarian talking, not my company. F1 has a clear downside and this means significant numbers of animals taken from the wild. The clear preferential option would be self-sustaining colonies. The risk that activists will destroy them, we have the same risks in terms of can we ensure transportation in the Community. We experienced years where it was almost impossible to transport them into the Community because, as you know, major airline companies would deny transportation. If there are violent attacks then there will be violent attacks maybe in the sourcing countries, maybe on the side of laboratories. We have to be even better in publicly communicating that this is something we have to do to ensure patient access to safe and effective therapies.

Q454 ***Lord Brooke of Alverthorpe:*** You are pretty well up-to-date with the way the latest negotiations are going from what you are saying. Overall, would you see the way the Directive is going will be of benefit to the pharmaceutical industry or do you think it will damage it? If it is the latter, what do you see as being the most important issue remaining which you would like to see changed?
Ms Chlebus: It very much depends on the final shape of the Directive. Today it is difficult to say. We have two elements which we know about. There is one element which we do not know about, which is what comes out of the Council. If the text is adopted as the Commission has written it, without any changes, that would certainly damage the industry in terms of unnecessary bureaucracy and related delays, administrative procedures, heavy procedures, and also limitations on science like non-human primates and some severe studies. Yes, that would certainly result in some damaging effects on the business. On the other hand, we have the European Parliament opinion that has improved many aspects, in particular proportionality of administrative procedures, scope and non-human primates. What is left today for resolution, certainly on the scope some improvements should be included. We also have an unresolved conflict of competence problem between the regulatory requirements for testing and approval of animal testing because these are completely different authorities dealing with those. What is required by law could potentially be banned by an animal protection authority. This is certainly something that has not been sorted out. The other issue is the international acceptance of alternative methods, and it is related to this issue of conflict of competence in a way, where a method is accepted in Europe but not accepted elsewhere, or the other way round, what happens and who decides ultimately whether a test or an alternative test can be done.

There are a number of issues related to authorisations and notification that we would like to clarify. To say that we know today what the effect of the Directive will be, it is difficult to say because we do not have the third element, which is the Council text.

Q455 ***Lord Brooke of Alverthorpe:*** But we have got a new Parliament and theoretically it is possible that the new Parliament could say: we will go back to a blank sheet of paper and start all over again. Do you see a possibility that that could arise with a new Parliament?
Ms Chlebus: Theoretically it could. I would not bet on it because we have made a lot of predictions that have not been correct previously as far as timelines are concerned or the ability of the European Parliament to deliver something in four months' time that would be reasonably research-friendly. In principle, taking into account that more than 85% of MEPs have voted in favour of that text across the whole political spectrum, that should not happen, but you never know. We will see what happens in the coming weeks. Hopefully this will not be reopened.

Q456 ***Earl of Arran:*** Your vocation is to help to alleviate human disease and human suffering. In the next decade, where do you anticipate the big breakthrough may come?
Dr Blumer: You give us a crystal ball!

Q457 ***Earl of Arran:*** What are you quite close to that is really going to help humanity?
Dr Blumer: I cannot tell you the disease area, but let me give you an example: in the past we have looked at diseases very much in terms of looking at the symptoms and trying to cure the symptoms, but now that there is novel knowledge not only on the genome but on the proteome we hope to be in a better position to understand the mechanisms of disease and redefine diseases, for example linked to the area of cancer. So far breast cancer is breast cancer is breast cancer, but now we better understand the molecular similarity (a) to colon cancer and (b) that similarly may be higher than of breast cancer to breast cancer. By understanding the molecular mechanisms of disease we hope to be able to better deliver on what are called personalised medicines, or disease pathway-orientated medicines. We hope that our therapies will be much more targeted to specific patient populations and not on the symptoms. This is a big hope. The company I am working for had a great breakthrough therapy that has now been on the market for several years in a special cancer area where it is very targeted and highly effective, and we hope there is more of this to come in the future.

Q458 ***Earl of Arran:*** So often the trouble when a great breakthrough is announced in the press is the public thinks it is available tomorrow. That is a real problem.
Dr Blumer: That is what we have seen with human embryonic stem cell research and xenotransplantation. If just one of those major breakthroughs had happened, science is a step-wise iterative process. Breakthroughs are important for better understanding, but if you have to go to the clinic there are so many hurdles you have to step over.
Chairman: Thank you very much indeed for a very, very thorough and exhaustive, at some stages exhausting, exchange. Thank you very much.

WEDNESDAY 14 OCTOBER 2009

Present	Arran, E	Livsey of Talgarth, L
	Brooke of Alverthorpe, L	Palmer, L
	Brookeborough, V	Sewel, L (Chairman)
	Caithness, E	Sharp of Guildford, B
	Cameron of Dillington, L	Ullswater, V
	Carter of Coles, L	

Memorandum by the Home Office

OBJECTIVES OF THE DIRECTIVE

Q. *What degree of harmonisation of rules governing the protection of animals in research is required to avoid distortions of the Single Market? To what extent are such distortions causing problems at present, and is the draft Directive a proportionate response to those problems?*

1. The Commission's proposal explains that the current Directive (86/609/EEC) was adopted to harmonise practices in the area of animal experimentation in the EU, but that, owing to a variety of weaknesses in its provisions, a number of Member States have established considerably more far-reaching measures in their national implementation whereas others apply only minimum rules.

2. The Commission considers that this has resulted in "a highly diversified, unequal competitive environment for industry and the research community within the EU, defeating the objective of the Directive to avoid fragmentation of the internal market".

3. They argue that this has led to economic problems affecting the internal market including *". . . competitive disadvantages for countries with high animal welfare standards resulting primarily from price differences (eg minimum requirements for housing), diverging regulatory and authorisation procedures and criteria in the Member States leading to variable delays and cost of projects, unsatisfactory (working) conditions of researchers, obstacles to horizontal mobility and increasing activist criminality. Similar problems can be identified for the breeders and suppliers of experimental animals, especially in terms of the cost of housing and care . . ."* The Commission provides no examples or costings.

4. While it is undoubtedly the case that the regulatory systems adopted by Member States vary significantly, we have no clear evidence that the UK research base—which is regarded as the most successful in the EU—has been adversely affected as a result. It does, however, create significant scope for differences in operational costs. UK practitioners have made representations about the regulatory burden arising from gold-plating and regulatory creep associated with the transposition of Directive 86/609 in the UK[1] and have sought reductions in that additional burden.

5. We are also unaware of any significant problems relating to the free movement of skilled labour arising from the current arrangements. To facilitate such movement, the UK, in common with some other EU Member States, has developed and adopted mandatory training programmes for key personnel based upon Federation of European Laboratory Animals Science Association (FELASA) recommendations. Supplementary training is generally restricted to ensuring that individuals have knowledge of specific national and local practices.

6. To remedy the problems it has identified, the Commission has concluded that strengthening the authorisation and ethical evaluation of projects would have a significant impact on leveling economical differences between Member States and would help to improve science. The Commission also believes that minimum housing and care standards would remove the current uneven competitive environment for users and breeding and supplying establishments, whilst improving animal welfare; and that standardised inspections would expose non-compliant establishments, strengthen enforcement and improve public confidence.

7. The Commission could perhaps have avoided some of the problems it has identified by enforcing the current Directive more effectively and providing some additional definitions of terms to clarify its scope. However, that opportunity appears now to have been missed and other issues arising from technical advances since 1986 would remain unresolved if the draft Directive does not proceed. On balance, we consider the

[1] The Davidson Review: Implementation of EU Legislation (November 2006).

components of the draft proposal to be broadly proportionate, although we have concerns about some of the detail. However, it is not yet clear how the text will change during the co-decision process and how this might affect its eventual impact.

International Competition

Q. *How might high(er) animal welfare standards in the EU impact upon the international competitiveness of the EU's private and public sector research base, and that of commercial establishments carrying out routine testing? Is there a risk of displacing research using animals to third countries and, if so, what would be the consequences of such a trend?*

8. We believe it is essential for Europe to set and maintain high animal welfare standards incorporating developments based on the improved understanding of welfare needs developed since the adoption of Directive 86/609. However, other economic regions are more likely to follow Europe's lead if the standards we set are practical and realistic and demonstrably lead to improved animal welfare and good science. There is already strong competition from regions outside the EU which is likely to intensify as emerging economies further develop their research base. Increasingly, the EU public and industry research base is threatened more by this external competition than by any distortions in the internal market.

9. We believe there is a real risk of displacing both private and public sector research as a result of increased cost, regulatory burden and restrictions on the type of research that can be undertaken. However, it is difficult to quantify the precise effects of a loss of research using animals and of any consequent loss of other types of associated research. Nevertheless, the use of animal testing by biopharmaceutical companies is an essential element in the development of new drugs. The UK pharmaceutical sector spends over £3.3 billion on research and development in the UK and employs some 26,000 people in R&D activities. Clearly, this investment and employment is influenced by whether the regulatory environment continues to be conducive to R&D, including animal testing. A better picture of the potential loss and its impact should be possible following completion of the public consultation launched on 8 May.

The Proposed Requirement to Restrict Research on Non-human Primates (Article 8)

Q. *Are the proposed restrictions proportionate, and what might be their impact?*

10. Under section 5(6) of the Animals (Scientific Procedures) Act 1986 (ASPA), non-human primates are already given special protection in the UK and we would support the inclusion of similar measures in the new directive. However, the limitation in Article 8 of their use to conditions having *"a substantial impact on [human] patients' day-to-day functioning being either life-threatening or debilitating"*, would stop some legitimate and important lines of research (for example, into aspects of human fertility and infertility). We would prefer a revised provision to allow use where it is essential to satisfying unmet clinical needs.

11. We have concerns about the proposed restrictions in Article 10 on the acquisition of non-human primates. In particular, we are concerned that, as the key changes need to take place at breeding centres outside the EU, no clear funding, or strategy, is proposed to meet the target and no planned EU investment to make it happen. We also have concerns that the proposal offers no commitment to review at critical points whether the target is likely to be achieved, or to change the timetable if it is not.

12. Only purpose-bred, non-human primates are used in the UK, but a number of these are the offspring of animals taken from the wild. The offspring of animals which were themselves bred in captivity (F2) are in very short supply. We, therefore, have strong reservations about the practicality of Article 10. World-wide, the availability of second generation, captive-bred Old World primates is not sufficient to sustain the UK public sector and industry research base—where they are used primarily for pharmaceutical research and development. Although it is proposed to encourage overseas breeders to produce more F2+ animals, as EU use represents only a small proportion—about 5%—of the total, it is unlikely this will be achieved within seven years or without considerable investment and ongoing costs. Some of these concerns are addressed in the legislative report adopted by the European Parliament on 5 May 2009.

Extension of the Scope of the Directive (Article 2)

Q. *Are the proposed extensions to the scope of the Directive justified, and what might be their impact?*

13. Article 2 extends cover to:

- animals bred specifically so that their tissues and organs may be used for scientific purposes;
- live non-human vertebrate animals, including independently feeding larval forms and embryonic or foetal forms from the last third of their normal development; and

— the classes of live invertebrate animals listed in Annex I (cyclostomes, cephalopods and crustacean decapods).

14. Article 2 also identifies the practices and classes of animal use to which the Directive will not apply. These are:

— non-experimental, agricultural or clinical veterinary practices and trials;

— practices undertaken for the purposes of recognised animal husbandry;

— practices undertaken for the primary purpose of marking an animal; and

— practices that are not invasive.

15. We believe the extension of cover to animals bred specifically so that their tissues and organs may be used for scientific purposes will affect about one million animals a year. Currently in the UK these animals are largely bred, kept and used at places already regulated under ASPA, and their welfare is adequately protected under general UK animal welfare legislation. We estimate that, implemented efficiently, this provision is likely to require about 250 additional project authorisations and a small number of additional establishment authorisations. This will create a significant administrative overhead without a clear welfare or scientific gain. We are, therefore, minded to oppose it.

16. Section 1(2) of the Animals (Scientific Procedures) Act 1986 already provides protection to foetal, larval or embryonic forms of vertebrate mammals, birds or reptiles, but from half way through the gestation or incubation period for the relevant species, and also provides for their protection at an earlier stage if that is warranted. Given the similarities in the provisions of the draft directive and current UK legislation in this area, we are minded to accept this element of the proposal. If adopted, it may result in some work currently licensed in the UK falling outside the scope of regulation, for example, on embryonated avian eggs, but there is unlikely to be any resulting animal welfare cost.

17. The only invertebrate form currently protected under ASPA is the common octopus (Octopus vulgaris).The extension of cover to cyclostomes, cephalopods and decapod crustaceans reflects advice provided to the Commission by the Scientific Committee of the European Food Standards Agency (EFSA). In our view, the EFSA advice, which has not been peer-reviewed, is not robust. In the absence of satisfactory peer reviewed evidence that these animals have the capacity to suffer, the provision has the potential to increase the regulatory burden significantly without achieving any animal welfare benefit. Again, we are minded to oppose it.

18. With regard to the wider implications of these proposals, the Animal Welfare Act (AWA) does not currently protect the unborn or invertebrate species and their recognition in European legislation could result in pressure to amend the AWA. We do not believe there is scientific justification for such an amendment. Any European legislation premised on sentience in invertebrates could result in pressure to introduce welfare regulations for other activities involving invertebrates, such as crustacean farming. This could have a serious negative impact on the crustacean farming industry.

19. The proposed exemption of the use of animals for veterinary clinical trials extends well beyond the position under ASPA. It would, for example, appear to exempt any surgery or sampling, or any withholding of treatment from control groups performed as an integral part of the veterinary clinical trial. Although few UK licences would be affected, it is not clear what other regulatory framework would make provision for the welfare of the animals involved, or even if such studies would be permissible under general animal welfare legislation in the UK. The Royal College of Veterinary Surgeons has made it clear that it has no regulatory framework to cover such trials.

20. There is a risk that this change could result in trials being carried out without due concern for welfare. Veterinarians would be bound by their ethical code, but no regulatory system would be in place to control such activities. There is also a risk that many veterinary clinical trials will not be carried out as they will be outside the remit of veterinarians under the Veterinary Surgeons Act, and not classified as scientific procedures. This could result in reduced progression of clinical veterinary knowledge and a long term negative impact on animal health and welfare. We are, therefore, minded to oppose this exemption unless alternative provision can be made to protect the welfare of the animals affected.

21. The proposed exemption of practices undertaken for the purpose of marking animals refers to the primary rather than the sole purpose of the procedure and sets no upper limit on the harm that can be caused. Under ASPA, the ringing, tagging or marking of an animal for the sole purpose of identification is not regulated if it causes only momentary pain, suffering, distress and no lasting harm. We propose to support this exemption but will seek to include a stipulation that the most appropriate humane method should be used.

AUTHORISATION OF PERSONS, REQUIREMENTS FOR ESTABLISHMENTS, INSPECTIONS AND PROJECT REQUIREMENTS (ARTICLES 20–43)

Q. *Are the administrative demands that the draft Directive would impose overall propotionate to its objectives?*

22. The impact of these measures will vary significantly between Member States. In some cases they will require a step change in their approach to the regulation of animal experimentation and testing.

23. Currently, the proposal does not reflect the Commission's better regulation agenda or commitments and has the potential to increase the amount of regulation significantly. We believe there is scope for the proposed Directive to be improved by applying better regulation principles. Our provisional impact assessment shows that additional UK compliance costs would be up to £130 million in the first seven years. This assumes there is no disinvestment or other reduction in science spend in the UK over the same period. In addition, there are no offsetting animal welfare or quality of science benefits.

24. The high cost items (and those with the greatest potential to damage EU/UK competitiveness) include:

- extending protection to invertebrate species that may not be capable of experiencing pain and distress;
- regulation of animals humanely killed to provide organs and tissues;
- premature disclosure and publication of findings;
- increased costs, and possible non-availability, of purpose-bred animals, including non-human primates;
- restrictions on the use of non-human primates;
- reduced provision for the responsible re-use of animals;
- poorly thought through, and costly, provisions for standards of care and accommodation and humane killing;
- the requirement for permanent ethical review bodies; and
- the establishment of national reference laboratories to assist the Commission.

Q. *Do any of the provisions relating to the authorisation of persons, the requirements for establishments, the inspection regime, or project requirements require further consideration and/or amendment and, if so, why?*

25. The roles of the animal welfare and care person and designated veterinarian set out in the proposal are similar to those of the Named Animal Care and Welfare Officer (NACWO) and Named Veterinary Surgeon (NVS) under ASPA. However, NACWOs do not currently have responsibility for identifying and rectifying compliance. This need not require additional resource, but it will change the relationship between the scientists and those who support and assist with their activities.

26. Regarding project applications, we are broadly content that the general classes of information required are similar to current UK requirements and with the ability to ensure information requirements are proportionate to the scale, complexity and sensitivity of the programme of work. However, we are concerned that implementation will be largely determined by the severity classification system which has yet to be developed and agreed.

27. We also note that the Commission has offered no rationale for the four-year maximum duration of project authorisations. A reduction from five years (as currently allowed under ASPA, and which has been shown to work well in practice) to four years will entail a significant increase in user costs and impact on regulator resources. Other minor adjustments required to current information requirements should not involve any significant increase in the regulatory burden.

28. We also have concerns about the practicality of the proposed requirements for data sharing (Article 44). These are designed to reduce unnecessary duplication of procedures. We note that the Commission's Impact Assessment provides no evidence that duplication of procedures is a significant problem in practice and where it is known to take place, for example, to enable the release of batches of some vaccines, this would still be permissible.

29. In the UK most regulatory testing is undertaken in contract research organisations, where the data belongs to the client not the laboratory, and many of their clients are not based in the EU. There are justified concerns that mandatory disclosure of client data would drive contract research out of the EU. With regard to non-regulatory testing, there are concerns that the publication of non-peer reviewed research findings would make it difficult to distinguish between reliable and unreliable findings.

30. While we strongly support measures to reduce and eliminate unnecessary duplication of animal use, we believe that the blanket approach to data sharing currently proposed will create a significant administrative burden and that a more targeted approach would be more likely to deliver the desired outcome.

Care and Accommodation (Article 32)

Q. *Are the care and accommodation standards set out in Annex IV to the Directive appropriate, and will they produce an adequate level of harmonisation across the EU?*

31. Many elements of the new proposal reflect current UK good practice and much of the recent investment in facilities and equipment in the UK has taken account of the emerging EU proposals. However, some of the the increased space requirements will require considerable investment in new infrastructure if current capacity for animal production and use is to be preserved. UK breeders estimate rodent production could drop by at least 20%, and user costs increase as a result, without investment in additional animal accommodation. The proposals would also impact on long term toxicology programmes where up to 50% more space would be required.

32. The proposal also emphasises "engineering standards" (inputs) rather then "performance standards" (outputs). It prescribes what the animals have to be provided with, rather than the quality of life they should enjoy, and removes the flexibility currently allowed in the UK to innovate or customise to make best provision for local requirements and animal welfare.

Alternative Methods

Q. *How satisfactory are the provisions on alternatives to animal testing and National Reference Laboratories (Article 46)?*

33. Article 45 requires the Commission and Member States to contribute to the development and validation of alternative approaches and to take such other steps as they consider appropriate to encourage research in this field. We agree that there needs to be a commitment to make progress with the Three Rs and support this proposal in principle. However, the focus on replacement alternatives, as opposed to inclusion of reduction and refinement, could risk marginalising the latter, and therefore be counterproductive under the proposed EU model.

34. We have sought clarification as to what is meant by "contribute" and whether the Commission will seek powers to direct or control activities at national level or require a specific financial contribution. Also, we note that although elements of the Member States' contribution in this area are set out in Article 46, the proposal does not explain what the Commission's duties or contribution will be.

35. Regarding Article 46, all UK stakeholders who have expressed an opinion agree that more needs to be done to develop and validate alternative methods. However, while we agree that Member States must play their part in this work, no reference laboratory currently exists in the UK and on the face of it this requirement will involve a significant financial cost, even though the Commission's impact assessment identifies the annual cost to each Member State as only £100,000.

36. We believe the obligation should be on Member States to assist the Commission in prioritising and placing validation studies in existing high-quality laboratories, not to provide dedicated facilities. This would be both more cost effective and more likely to achieve the required policy objective. We will pursue this line in the negotiation of the directive.

37. In addition, it is not clear what input the Commission itself will provide; who will do the essential preparatory work, manage the funding, co-ordinate studies in progress, and assess and implement the findings. It may be that one or more "virtual" centres will be needed to fulfil this role at a national or European level. Likewise, it is not explained what is to be the future role of the European Centre for the Validation of Alternative Methods (ECVAM) and its scientific advisory committee (ESAC). We believe the proposal should be revised to address these concerns.

Subsidiarity and Legal Base

Q. *Is it appropriate to regulate at the EU level—as opposed to lower tiers of government—in all of the proposed areas?*

38. In broad terms, the UK Government is content that this is an area in which it is appropriate to have Europe-wide legislation—both as a matter of principle and based on experience with the current Directive, which has shown that Member States have widely differing approaches to the regulation of animal experimentation if given freedom to devise their own measures. We believe that this divergence has been

compounded by the apparent unwillingness of the Commission to adopt a robust approach to enforcement or to clarify the meaning of key provisions.

39. The more prescriptive measures set out in the draft proposal offer the prospect of more effective harmonisation across Europe than has been achieved under current arrangements, but this may be at the expense of the success, sustainability and international competitiveness of the EU science-base if the benefits are not realised at a proportionate cost.

Q. *Is the legal base for the proposal adequate in light of the content of the Directive?*

40. The UK Government is satisfied that the legal base for the proposal is adequate. Article 95 does not require total harmonisation and Member States are free to impose stricter standards where it is felt appropriate.

26 May 2009

Letter from Lord Roper to Admiral Lord West of Spithead

PROPOSED REVISION OF THE DIRECTIVE ON THE PROTECTION OF ANIMALS USED FOR SCIENTIFIC PURPOSES

Over the past three months, we have been conducting an inquiry into the proposed revision of this Directive. We have taken evidence from a number of key interested parties, including the pharmaceutical industry, academic and research funding bodies, the National Centre for the 3Rs (NC3Rs), and organisations advocating animal welfare, the use of alternatives to animals in research, and an end to vivisection. Our intention is to conclude our inquiry and publish our report after the summer recess.

However, we know that the Swedish Presidency aims to make early progress with this dossier, and that there may well be important discussions related to the proposal during September. While we have not yet finalised our inquiry, we think that we should indicate our emerging conclusions at this stage, so that these are in the public domain before discussions under the Presidency move ahead significantly.

Our first finding, which reflects a firm consensus among our witnesses, is that a revision of the Directive is clearly needed; and that, of the changes contained in the proposal, the introduction across all Member States of a **requirement for prior authorisation** of animal procedures, including an **ethical review process,** is particularly to be welcomed. Much of our evidence has borne out the importance of the operation of this process in the UK.

There was, however, a clear divergence of views among our witnesses about the possibility that the requirement for authorisation of "mild" procedures might be modified (as a result of amendments proposed by the European Parliament) to become one of notification. We note the argument that this would significantly lower current levels of animal protection in this country. We agree that a revised Directive should not lead to this outcome, and we therefore support the authorisation requirements set out in the Commission's proposal and reject a move to require notification (rather than authorisation) for "mild" procedures. However, we would urge that those concerned should seek to ensure that the authorisation process is completed quickly.

We consider that the concerns about authorisation voiced by industry and academia may in some instances result from a lack of clarity in drafting. We therefore urge the Council to ensure that the Directive provides clearly for a smooth and timely authorisation procedure, while maintaining a high level of animal welfare. It will be important to ensure that the ethical review process is effectively dovetailed into the procedure, including specifying time-limits for that process which are consistent with the 30-day time-limit for authorisation.

We have looked at the issue of whether implementation of the proposal might drive animal-based research work out of the UK and EU to other parts of the world, but we have not found evidence that this is likely to be the case. As witnesses recognised, a good deal of activity linked to the pharmaceutical sector has been built up in recent years in China and other non-EU countries for commercial and economic reasons, and it is these factors that will continue to dominate key locational decisions. And in the case of academic research, transfer of activity abroad is also mostly driven by other reasons, notably the availability of research funding.

We accept, however, that the imposition of bureaucratic burdens that are not justified by any gain in animal welfare is undesirable in itself, and may influence the climate of opinion among those deciding on future investments. To that extent, we lend our support to calls for the procedures contained in the proposal to be fine-tuned to the scientifically demonstrated needs of animal welfare, without unnecessary elaboration. Authorisation processes must be efficient, so that scientists in both industry and academia can take on new lines of inquiry and amend current approaches without undue delay.

The proposal envisages that the maximum **term of authorisation for projects** should be four years; in the UK it is five years. We have not seen evidence that shortening the term in this way would be justified by significant animal welfare benefits. We are also not persuaded of the case for the provision in the proposal that all projects lasting 12 months or more should be subject to **annual review** (by the ethical review body). This also contrasts with the current position in the UK, where, while retrospective review is required, ethical review processes (ERPs) are allowed more flexibility in the degree of on-going scrutiny they give to projects, allowing efforts to be focused where and when the ERP feels that review is really needed.

Some of our witnesses raised the issue of the **transparency** of the authorisation process. The proposal requires (in Article 40) that non-technical summaries of authorised projects be made publicly available and that these be updated with the results of retrospective assessment. In addition, it also requires (in Article 49) the annual collection and publication of statistical information on the use of animals in procedures, including information on the actual severity of the procedures. Of these provisions, reporting data on actual severity and the results of retrospective assessments would increase the information on animal procedures made publicly available in the UK. We consider that such greater transparency may well be justified, although publication of additional information should not extend to the disclosure of the identities of individuals or establishments.

It seems clear to us that the **care and accommodation standards** in the proposal (which are the result of extensive and lengthy discussion among stakeholders) are not likely to impact unduly on the competitiveness of the pharmaceutical industry. We note that those standards have been anticipated for some time and are already being applied or worked towards in this country and elsewhere in the EU.

None the less, we understand that the standards proposed may prove more difficult for academic research establishments to meet on the timescale envisaged, and we think that there may be a need to re-consider the timescale for implementation in the light of experience. We welcome the fact that the proposal provides for this possibility, since Annex IV can be amended through Article 48 (adaptation of annexes to technical progress). Moreover, we draw particular attention to concerns that have been expressed over the practicalities of the stocking densities proposed for rodents and rabbits at breeding establishments.

Importantly, we also heard from several witnesses that key explanatory text which accompanied the standards as first elaborated by the Council of Europe guidelines has been lost in the proposal, and we agree that it should be restored.

We understand the importance of research work undertaken using **non-human primates.** While we acknowledge the arguments put to us about the special case of these animals, we consider it important that the Directive allows such work to continue as at present. We are mindful of concern voiced by some of our witnesses that the Directive as drafted is insufficiently clear in establishing the circumstances in which research work using non-human primates may be permitted. Some witnesses considered that the wording of Articles 5 and 8 would allow an increase in this type of research, while others considered that it would lead to an unacceptable decrease. We therefore stress the importance of ensuring that the text of the Directive is clear in setting out the circumstances in which research work using non-human primates may continue.

We fully endorse the aspiration that supply of non-human primates should be restricted to **F2 non-human primates,** the offspring of such animals bred in captivity. We have sympathy with the arguments by some of our witnesses that the Directive should include specified time-limits after which only F2 animal should be used. It may be that the time-limits suggested in Annex III are appropriate. However, given the degree of uncertainty related to the practicality of this suggestion, we consider it crucial that this aspect of the Directive be monitored closely, and that the feasibility of the time-limits should be investigated on a species-by-species basis. The Commission's review of the Directive must include information on progress in phasing out the use of F1 primates. On this issue as well, it is relevant that there is flexibility under Article 48 to amend the time limits.

The proposal extends the **scope** of the Directive to include several invertebrates. We would argue that the scope should be linked as closely as possible to broadly accepted evidence of sentience. It is apparent, however, that the scientific evidence on the sentience of certain species is unclear. Against this background, we are minded to agree that, while cyclostomes and cephalopods should be included, decapods should be excluded. We also take the view that independently feeding larval forms of invertebrates should be excluded.

At the same time, we are concerned that there is no provision in the Directive to amend the list of invertebrates in Annex I. We therefore consider that Article 48 should be amended to include Annex I. This would allow the Commission to take account of the new scientific evidence pertaining to sentience, either by expanding the list in Annex 1 or reducing it.

Independently feeding larval forms and embryonic or foetal forms (as from the last third of their normal development) of live non-human vertebrate animals would also be included. We are concerned that this may in some cases lead to a substantial increase in the administrative burden with no benefit. While the proposal would in fact mean a reduction in the extent to which controls applied to eggs used in vaccine production in

the UK (from half-way through development to the last third), the impact on production procedures elsewhere in the EU may well be greater. This may again beg the question of whether a potentially very significant increase in administrative burden would be matched by a corresponding benefit to animal welfare.

More generally, we consider that the provisions of the Directive should be amended to ensure that the **breeding and humane killing of animals for their tissues and organs** should not be regarded as a "project" within the terms of the Directive. While it is of course necessary that the care and welfare of these animals should be ensured, work involving them should not be subject to the authorisation processes required of projects.

We fully endorse the near-unanimous view among our witnesses that the **severity classifications** need to be clearly defined in the text of the Directive. We welcome the efforts made by the Commission towards building a consensus among stakeholders on the content of the definitions. We note that clarity on the definition of severity classifications is particularly important for implementing the proposal's provisions on re-use of animals. We also consider that the **re-use** provisions must be amended in order to avoid unintended consequences for animal welfare. Left in their current form, the provisions would be likely, in certain specific circumstances, to increase the number of animals (and degree of suffering) that would need to be used.

There is widespread support for the principle (Article 44(1)) that there should be mutual acceptance between Member States of data from tests required under Community legislation, so that, for example, vaccine batch-testing done in one EU country should not have to be repeated in another. Key to this, we consider, is that Member States implement legislation to ensure that, at the least, the use of animals for ratification of such data will be sanctioned only in exceptional circumstances and for strictly scientific reasons.

The provisions in Article 44(2) give rise to some of the more substantive concerns relating to the proposal. We are aware of the strong concerns expressed by the research community about the loss of intellectual property rights if researchers were obliged to share commercially sensitive data. We consider that obligations on **data-sharing** should apply only where there is evidence of duplication of procedures making use of animals, and we have seen little, if any, such evidence. We reject the European Parliament amendments on this issue.

We fully support the **principle of the 3Rs,** including the explicit reference to it in the proposal, but we consider that the specific proposal that national reference laboratories be set up must be re-considered. We are persuaded, on the other hand, that a system of national centres along the lines of the UK's NC3Rs might well be developed. Some witnesses have suggested that the role of the European Centre for the Validation of Alternative Methods (ECVAM) be expanded. We consider that ECVAM plays a valuable role and it may be able to assist in the important task of sharing best practice and information on the 3Rs between EU countries.

Finally, we have been struck by what we have heard from our witnesses about the inconsistency with which the 1986 Directive has been implemented; this is indeed one of the reasons why there is widespread agreement on the need for a revised Directive. We put particular stress on the need for due attention to be paid to the implementation of the revised Directive, once it has been adopted. Such are the uncertainties around the implementation of this Directive that Member States must send information on implementation of the Directive sooner than six years after the transposition date. The Commission should **review the Directive** no later than five years after it has come into force (and not ten, as proposed).

We support the European Parliament amendment which would oblige, rather than permit, the Commission to undertake controls of the infrastructure and operation of national inspections in Member States; we see this as of particular importance.

I will release this letter to the media at 2.00 pm on Monday 20 July.

17 July 2009

Letter from Lord Brett to Lord Roper

PROTECTION OF ANIMALS USED FOR SCIENTIFIC PURPOSES

I attach as an annex to this letter Council document 13784/09 (marked LIMITE) compromising a Presidency compromise text of the proposed new directive for ht protection of animals used in scientific procedures. The second annex provides commentary on key changes in the compromise text.

Document 13784/09 has been tabled for discussion at a meeting of the Council working party of veterinary experts (Animal Welfare) on 12 October 2009. The working party is attended by policy officials and veterinary and other experts representing Member States.

Further work will be required to finalise a text acceptable to the UK, but, in broad terms, we believe the regulatory framework provided in this text is workable and would allow current UK standards of welfare and animal protection to be maintained and improved. Our main concern is currently that potentially damaging

restrictions on the use of non-human primates remain in the text. We are pressing for the adoption of EP amendment 57 which seeks to remove these restrictions.

The Swedish Presidency hopes to agree a Council position by the end of 2009 to pave the way for a second reading deal early in 2010. Should this be the case, it may be necessary to seek agreement to release the proposal from scrutiny at short notice. We will, however, endeavour to provide as much advance warning as possible. We will also provide a further progress report when the timetable is clearer.

7 October 2009

Annex B

REVISION OF EU DIRECTIVE 86/609/EEC ON THE PROTECTION OF ANIMALS USED FOR SCIENTIFIC PURPOSES

KEY CHANGES IN COUNCIL DOCUMENT 13784/09

Article 2 and Annex I: Scope

Article 2 has been the subject of extensive discussion in the Council working party. The compromise text now specifies the lower threshold for pain, suffering, distress and lasting harm below which regulation will not apply. The threshold is set at pain, etc, equivalent to that caused by the [skilled] introduction of a [hypodermic] needle. This is based on a working definition used under Directive 86/609/EEC.

Article 2 now excludes embryonated avian eggs from the scope of the directive. Embryonated avian eggs are currently covered in the UK from the half-way point of normal development, but the impact on animal welfare of their exclusion would be negligible.

Invertebrate species remain within the scope of the directive. We are sceptical about their inclusion as the evidence that they have the capacity to experience pain is in our view unclear or lacking.

Article 2.6 allows Member States to maintain or adopt stricter measures in national legislation aimed at providing greater protection to animals or better care and accommodation. This is a significantly more limited provision than originally proposed by the Swedish Presidency and, subject to further discussion and clarification, is likely to be acceptable to most Member States, including the UK.

Article 6 and Annex V: Methods of Killing

Article 6 now provides greater scope for competent authorities to authorise methods not listed in Annex V provided they are at least as humane. This is welcome and reflects concerns expressed in the Council working party that Annex V was too restrictive, as originally drafted. Work is continuing in the working party to refine Annex V to remedy significant omissions and technical deficiencies.

Article 8: Non-human Primates

Article 8 now includes a definition of "debilitating clinical condition" which is intended to remedy the concerns expressed by the UK and others about the potential impact of the proposed restriction of non-human primate use to research into "life-threatening or debilitating clinical conditions in human beings". These terms are in our view restrictive and imprecise and likely to lead to confusion with regard to their proper application. Furthermore, none of the potential definitions of these terms in other legislation quoted in Recital 16 (of the Commission's proposal) is applicable in the present directive.

Although the proposed definition is helpful, we continue to support European Parliament Amendment 57, which seeks to remove the phrase "life-threatening or debilitating clinical conditions in human beings" from the text altogether. In our view the requirements for ethical evaluation set out in Article 37 of the draft proposal will be sufficient to ensure that non-human primates are not used for trivial purposes and that the numbers which are used will be kept to a minimum.

Article 10 and Annex III: Animals Bred for Use in Procedures

Article 10 now includes a requirement that the Commission should publish a feasibility study, including an animal health and welfare assessment, on the required move to the use of F2 and F2+ non-human primates within the timescales set out in Annex III. These timescales for Cynomolgus and Rhesus monkeys have been extended from seven to 10 years in this text. The assessment and study is to be published within five years of transposition. Article 10 also now specifies that Annex III should be adapted, as appropriate, in the light of study.

It is essential that the feasibility of achieving full use of F2 and F2+ animals in the specified timescales is considered carefully and that there is a mechanism to allow revision of those timescales where this is shown to be necessary. We, therefore support the revised text of Article 10, which incorporates the intention expressed in EP Amendment 60. We have also suggested incorporating the key aspects of Article 27, relating to breeding strategies, into Article 10, so that all requirements relating to this issue are set out in a single article.

Article 15 and Annex IX: Classification of Severity

The omission of the details of a severity classification system from the Commission's original text has now been remedied by the inclusion of a new Annex IX based on the work of an expert working group which met in July 2009. Although some further detailed refinements may be required, Annex IX has wide support in the working party (including from the UK).

In recent working party discussions it has been agreed that the prohibition in Article 15.2 of procedures involving pain, suffering and distress that is likely to be long-lasting and cannot be ameliorated should apply to procedures which are above the upper threshold of the severe category defined in Annex IX. The Commission concurs with this position. This has now been clarified in the text. We welcome this.

Article 16: Re-use

The compromise text now provides for the re-use of animals provided the cumulative effect experienced by the animals is not "severe". This amendment makes better provision for responsible re-use and is welcome. A derogation is also provided for exceptional circumstances, which we welcome.

Articles 21 to 24A: Authorisation of Persons and Places

This section of the proposal has been the subject of extensive discussion, reflecting concern about the bureacratic burden involved for Member States where authorisation of individuals is limited or not currently required.

Under the revised Article 21, each breeder, supplier and user (establishment) must be authorised and registered with the competent authority. The authorisation must specify:

— a person responsible for ensuring compliance with the detailed requirements placed on establishments by the Directive;

— one or more persons responsible for overseeing the welfare and care of the animals bred, kept, killed or used in the establishment; ensuring staff have access to species-specific information; and ensuring staff are adequately educated, trained and supervised; and

— a designated veterinarian.

Under Article 23A, each establishment must have sufficient, adequately educated and trained staff to:

— carry out procedures on animals;

— design procedures or projects;

— take care of animals; and

— kill animals.

Member States may, if they wish, choose to authorise these individuals.

Ensuring compliance with project authorisations will be the primary responsibility of the equivalent to our current UK project licence holder.

As they stand, these requirements are not too far removed from current UK arrangements and, subject to further discussion and refinement, we believe should provide the basis for an acceptable organisational framework.

Articles 25 and 26: Animal Welfare Bodies

The term "Animal Welfare Body" has now replaced "Permanent Ethical Review Body" in part to remove potential confusion over the role of this body in relation to ethical evaluation of projects. Provision has now been made for smaller establishments to pool resources when setting up these bodies.

Article 32 and Annex IV: Care and Accommodation

Annex IV has been substantially amended (with detailed input from the UK) to correct technical errors and omissions in the original text. Although further work is required to finalise the text, Annex IV now has support, in principle, from most Member States. Adoption of Annex IV standards will require substantial investment if current capacity is to be maintained in breeding establishments. We will be arguing for extended implementation periods to enable UK breeders and users to comply.

Article 33: Inspections

The original text of Article 33 was viewed by many Member States (but not the UK) as too prescriptive. The emphasis in this article is instead now placed on a risk-based approach and no minimum frequency of inspections is specified. The revised article will not require any changes to the current UK inspection system.

Article 35 to 43: Authorisation and Ethical Evaluation of Projects

There is general agreement in the working party that all projects should be subject to ethical evaluation and prior authorisation. There is no significant support for EP Amendment 167 which would allow projects involving mild and non-recovery procedures to be merely notified to the competent authority.

However, the Presidency has been exploring ways to accommodate current national approaches to project authorisation. As a result, the text now includes provision in Article 41A for so-called "tacit approval" of limited categories of project licence application. In addition, Article 36.2 waives the requirement to provide a non-technical summary for these projects. An earlier draft of this provision received a mixed response in the working party and we remain to be convinced that it is desirable or workable. In particular, we believe that it is important for transparency that a non-technical summary is published for all projects.

On a detailed point, we remain concerned about the implications in Article 37.4 of the requirement that ethical evaluations "shall be performed in a transparent manner and integrate the opinion of independent parties". We will be seeking clarification of what compliance with this requirement would entail.

Article 44: Avoidance of Duplication of Procedures

The requirement for data sharing in Article 44.2 of the Commission's proposal has met with significant opposition from a number of Member States and has been deleted. The single remaining requirement for mutual acceptance of data generated by procedures recognised by Community legislation is acceptable to us.

Articles 45 and 46 and Annex VIII: Alternative Approaches and "Community Reference Laboratory"

Articles 45 and 46 have been substantially revised and restructured. Article 45 places a new requirement on the Commission to set priorities for the validation of alternative approaches and the allocation of tasks to laboratories nominated by Member States. There is, however, no longer a requirement for national reference laboratories in each Member State. Article 46 creates a requirement for a Community Reference Laboratory, the duties and tasks of which are set out in a new Annex VIII. It is intended that the Community Reference Laboratory should subsume the existing European Centre for the Validation of Alternative Methods (ECVAM) and retain its name.

These revised provisions are a substantial improvement on the proposal as originally presented and provide a workable basis for the further development of alternatives.

Home Office

6 October 2009

Examination of Witnesses

Witnesses: **Lord Brett**, a Member of the House, Parliamentary Under Secretary of State, Home Office, **Dr Jon Richmond**, Head of the Home Office Animal Procedures Division and **Mr Martin Walsh**, Head of the Animals Procedures Division Policy Team, examined.

Q459 ***Chairman:*** Hello and welcome, Minister, to the Committee. I do not think that any of your predecessors have come to give evidence to this particular sub-committee; we do not have much contact with the Home Office. It is really corduroy trousers and gumboots here!
Lord Brett: When my departmental ministerial period comes to an end on Friday, I will probably claim that appearance before this Committee was a crucial factor in it! Of course, I am standing in for Meg Hillier who is on maternity leave; she returns from maternity leave next week.

Q460 ***Chairman:*** Why did she put the return off for two weeks?
Lord Brett: I could not possibly say!

Q461 ***Chairman:*** I have to go through the usual formal bit. This is a formal evidence-taking session and there will be a transcript. That will be submitted to you shortly and any slips or minor errors can be corrected. With a bit of luck, you can even turn it into grammatical English but that is often beyond us! We are being broadcast and there is an infinitesimally small probability that someone out there may be listening to our words. We have never had any evidence that such a sad creature does actually exist, but it is theoretically possible. I think that is all I need to say on the formal side of it. As I say, thank you very much, indeed, for the time you have given to us. We are coming to the end of this inquiry. We have found it a fascinating and important area to look at in terms of ensuring that we maintain both a commercial interest in pharmaceuticals and also, of course, a pure research interest as well. We have taken evidence from a wide range of interests including the animal welfare lobby, academia and the industry, and you are really the icing on the cake! I wonder, Minister, if you would begin by updating us on how things have been developing.
Lord Brett: Yes, I will, indeed. There has been a flurry of meetings but, as EU meetings go, a flurry does not mean necessarily that there has been a great deal of progress made. I wrote to Lord Roper last week providing a copy of the latest Presidency compromise text. It needs further work, but on the whole we believe that the text is now starting to take shape. It sets out a framework for regulation which has the support of the Member States and it would allow current UK standards of welfare and animal protection to be maintained and improved, which is of course a very important factor to us. It has also begun to resolve some of the detailed issues. For example, the maximum duration of project licences which was initially set at four years but has now been extended to five years, as desired by your Lordships' Committee in its emerging conclusions. A Council Working Party met to discuss the text on Monday of this week and is grinding its way through it and there will be a further meeting on Friday to continue that work. In the meantime, the Presidency is due to meet the European Parliament Rapporteur to begin informal discussions. The Presidency will report back on those discussions at the meeting on Friday of the Council Working Party. We also can report that the Swedish Presidency wants to agree a Council position at the Agriculture Council on 14 and 15 December. This week, the Working Party meetings and the meeting with the Rapporteur should give a clearer picture of where this is achievable and how quickly progress can be made. If it meets with the Committee's wishes, I would propose to submit a further written report next week setting out progress on the issues and also cross-referencing that progress with the emerging conclusions that were sent to us by Lord Roper in July in order that you can see where we are going.

Q462 ***Chairman:*** That would be very helpful, indeed. It will save us quite a bit of work as well. Thank you.
Lord Brett: That is my opening statement.

Q463 ***Chairman:*** I would like to go through a number of issues. Do you get the feeling that other Member States think that it has reached the stage where there is a document which provides a workable regulatory framework now, or are some people saying that it is miles away from reality?
Lord Brett: I think there is an emerging consensus that there is a workable document. We still have Member States with concerns over the level of prescription that is in the draft, but some of the key players, including the UK, are anxious to maintain the high standards of welfare that we have and also to maintain support for the science community. I think amongst those there is now the feeling that we are moving to something which will allow us to have a new Directive and to do no damage where damage might be feared and to improve the situation where it clearly needs to be improved. The real burden, of course, as seen by some Member States was the adoption of provisions with more prescriptive proposals, such as the staffing of establishments. There, the requirement is not changed significantly but there is now more flexibility on how to achieve it. So, it is in that area of achieving flexibility but at the same time not losing, from our point of view, the

major components of a new Directive that makes me have growing confidence that we are going to get something which is manageable and effective from our point of view. My colleagues who are at the day-to-day discussions in the Working Party might want to add to that.

Mr Walsh: It is by no means a polished document—I think no one would claim that—but certainly the basics seem to be in place and we think that most Member States are starting to feel more comfortable that they will be able to implement in a way that is not going to be too burdensome. That has been a very significant concern for a lot of the different Member States, particularly I think some of the newer Member States and some of the smaller Member States who perhaps have to do more to come up to the required standard than some of the more established Member States who already have fairly stringent procedures and processes in place. We think that by and large most Member States are now reasonably content that it is in the right sort of area, but with the need for further detailed work.

Q464 ***Chairman:*** The rationale for going ahead with a revision of the Directive was basically inconsistency in the implementation of the old one, was it not?

Lord Brett: Yes. I think I would characterise it as being a consensus on the need for a new Directive but, once arrived at that consensus, then of course all the normal national interests come to the fore and then it is the hard work of getting to something which is worth having and replacing and improving on the 1986 Directive. In that sense, the jury was out a couple of months ago and it is still subject to detail, but I think it is now coming up with a document that most people will think we can take forward. We are interested more in getting a document that is right for our interests and protects the UK rather than rushing to a document that is produced just to fit the timescale.

Q465 ***Chairman:*** One of the continuing themes that have emerged during our evidence taking is that the UK standards on animal welfare are high comparatively, and a concern to avoid a situation where those standards would be watered down and eroded. Do you see any danger of the Directive, as it emerges, threatening the present high UK standards?

Lord Brett: I do not believe so and that has been one of the things that our representatives have been very, very keen to press and to gain allies amongst those who also share our view that there is no incompatibility with good science and high animal welfare. I think that view has been supported fairly widely across Member States and, therefore, I do not think we have anything really to fear in that direction.

Q466 ***Chairman:*** On the very helpful document you gave us on the latest changes to the draft to the Directive, Article 2.6 dealing with scope says, "Member States may, by respecting the general rules laid down in the Treaty, maintain or adopt provisions aimed at ensuring more extensive . . ." and then protection of animals and so on. Is the ability to come forward with more extensive changes related to scope only?

Lord Brett: Ministerial knowledge is wide, as you know, but not always deep! I will ask my colleagues to deal with that.

Mr Walsh: The original proposal for Article 2.6 which came basically from the Presidency was very wide-ranging indeed and it really would have allowed Member States to adopt stricter measures in virtually any area of the Directive. I am not quite sure why but there was a change of heart on that. I think there may have been representations that that was going too far and possible conflicts with the base Treaty perhaps. Now, they are really aiming to make sure that it is the animal welfare and protection measures which it is going to be possible for Member States to maintain because there are Member States that have higher welfare standards than are being required in the new Directive, and I think that Sweden is one of those, so they are keen to be able to maintain those higher requirements. So, it is narrowly focused in specific areas and there will not really be a free-for-all. I think that was one of the problems with Article 2.6 as it was originally drafted in that it could have just blown a hole through harmonisation, but now it is being focused on specific limited areas.

Dr Richmond: Council Legal Services are advising us that the derogation will simply allow additional measures to be taken which cannot and will not distort the internal market. So, Member States will not have *carte blanche* to introduce additional measures; they will have to be limited to those which would not distort the internal market.

Q467 ***Chairman:*** Obviously, we have to be content with what Legal Services advise us, but are we content in terms of that enabling us to maintain standards that may be higher than elsewhere?

Mr Walsh: We are happy with the way that particular article has gone. We were concerned about the impact on harmonisation if it had been left in its earlier state, but now it does provide the scope for us to maintain our standards if we wish, which we do, but does not allow for that free-for-all that seemed to be possible as it was originally worded.

Q468 ***Chairman:*** My second and last detailed point is on notification which is 41A, the tacit approval proposal. Article 41A, the notification, tacit approval as it is now called, and linking with the ethical review

process, would that require changes to UK legislation on current administrative procedures or not?
Mr Walsh: I think the answer is "not necessarily". I think that we can adapt our procedures without any major change.
Lord Brett: In terms of the total of the text, though we cannot be detailed in the answer, we are starting work to identify the legislative implications. We do not think necessarily this area is an issue. The initial assessment is that we will not require changes to basic regulatory structure, nor should it require changes to the levels of control we exercise on animal experiments and animal welfare. At the same time, the current text could and should provide scope to review the detail of our current legislation and perhaps make some regulatory changes which would reduce the regulatory burden without doing any harm to animal welfare, but that will only come out as we see the Directive and post-Directive studies.
Mr Walsh: On 41A, I think I am right in saying that that is something that will be discussed at Friday's meeting this week. It is not by any means, as we would see it, yet firm. We think that that particular suggestion or proposal is still in flux.

Q469 ***Chairman:*** A number of people to whom we have spoken have set their face strongly against notification.
Mr Walsh: I think that notification as such is not really on the table, but the Presidency is certainly trying to find ways to provide some flexibility. They are really bending over backwards in some ways to try not to throw out some of the processes that are already in place in a number of Member States where there are different approaches to approving project applications. This tacit approval seems to be one attempt to do that, but I do not know if Jon Richmond agrees. I do not think we see this as being the final word on this; I think maybe there are further thoughts.

Q470 ***Chairman:*** Which way will you be pushing on it?
Dr Richmond: I think that we support a proportionate approach to dealing with applications, simple treatment of simple applications and more complex treatment of more complex applications. Even the tacit approval as drafted in the current text would allow Member States 60 days to look at the application before the authorisation went live. We would say that the application would still have to be ethically reviewed; it would still have to be judged to be legally sound against the requirements, and if you do both of those things it is difficult to see why you would not go the additional step and issue an authorisation.
Lord Brett: Perhaps it would be helpful if we provided a slightly more detailed note on this in our report next week to you.
Chairman: We do have worries about this and in particular the creeping-in of going from mild to moderate. I think I have done enough on that, so I will hand over to Viscount Brookeborough to look at "Bureaucracy: the UK experience". We could write a book about that, could we not?

Q471 ***Viscount Brookeborough:*** We have heard a lot of evidence about problems perceived with the United Kingdom authorisation process and that it is a great deal more complex than most other nations. In particular, with these new amendments and Article 42, there are those who are concerned at the potential for enormous delays. On Amendment 42 it says at the top, ". . . significant change to the project that may have a negative impact on animal welfare" and the next line says, "Any amendment . . ." Where there is an extension of a project with live animals, that is bound to be a negative impact, is it not, but then it comes on to any amendment at all.
Dr Richmond: We think that the way this is going will give us more flexibility than we currently have and there are a number of modifications to protocols, the way animals are used during the course of a five-year project, some of which will actually reduce the welfare cost and, at the moment, those have to be effectively agreed and amendments made. If we take the text you are looking at, we would say that that would now allow us to effectively allow projects to evolve and become more welfare-friendly without the need to return documentation for amendment.

Q472 ***Viscount Brookeborough:*** Who judges that and at what stage?
Dr Richmond: I think often it is relatively clear. If someone has a protocol which requires up to ten injections of 20 animals and they come up with a better method that means four injections of six animals, it is self-evident. There will be cases where we would expect people to consult and to take advice from the Department.

Q473 ***Viscount Brookeborough:*** We do have accusations that we gold-plate on such applications. Are you saying that there may be less gold-plating and we will conform more to the letter?
Lord Brett: I would say that there is less gold-plating. In a sense, there were some criticisms, which I think the Committee heard, about our current system which we were well aware of. In fact, we have been working with the industry to see how these can be made more simple and of course we have had a Better Regulation group which has been studying this and we are hoping that will see improvements in processes. The next major development will be the

launch of a new project licence application form later this month which will require less detailed information from applicants and should reduce the need for trivial amendments and also reduce the scope for technical infringements. We think we are working with the grain of what we all want to see. We are aware that gold-plating has taken place—the noble Lord Davidson had things to say about that—and in the implementation of any new Directive we will certainly be anxious to avoid any element of gold-plating.

Q474 ***Viscount Brookeborough:*** In your Better Regulation in the animal scientific procedures, during the year, three main workstreams have been pursued. How far are these already making a difference?
Dr Richmond: We have amended the personal licence form to make applications simpler and that is being used, but some places still prefer to retain their in-house coding lists for their internal management purposes. The certificate designation form is being increasingly used as places seek amendment or come on-stream. The changes that we have made to the project licence application form, the launch is due shortly, but we have already in the last 18 months been giving people advice on how to write more maintenance applications and texts and, if you look at our Division and Inspectorate Report from last year, you will see that the number of amendments is already falling as a result of that advice being given and acted upon.

Q475 ***Viscount Brookeborough:*** Lastly, looking at the animal procedures themselves, in the statistics the number of procedures has gone up by 14%. Of course, this is a headline figure but it is not a popular one in the public domain. What do you think that this actually means within the industry? Is it that we are just doing more and achieving more?
Lord Brett: One answer, and I would not put it forward as the only answer, is that it shows that the UK's biological science is in a healthy state. There is more scientific activity and more funding for science. So, in a sense, it is part of success. It is certainly not a failure of regulation in our view but we are in the Home Office taking our duty to minimise animal suffering and the use of animals very, very seriously and there has not been, and will not be of course, any lowering of standards. That is my immediate response to your question.

Q476 ***Chairman:*** I would like to ask you a basic summary question. When you put all the changes together, what you are doing departmentally and what the Directive will do, what impact will all that have on the time that it takes to process a project licence and a personal licence?
Lord Brett: Hopefully simplifying the procedures will help in terms of time. My colleague spoke about 60 days which is now the emerging figure within the Directive. We could have lived with a shorter period than that and therefore would not find the Directive in itself onerous, but my colleagues may have more detailed information.
Mr Walsh: I think that we see the Directive as an opportunity for a further step forward in terms of improving our processes, efficiency and so on. There will be some flexibilities in there that we can make use of without damaging animal welfare or the control that we apply. So, when we come to analyse the detail of how to transpose, we will be looking for opportunities to improve the way we regulate and the framework that seems to be emerging from the discussions seems to provide a good deal of scope for us to do that, so we are quite optimistic.

Q477 ***Chairman:*** Can you give us any figures at all?
Dr Richmond: I can give you the current figures and we can try and extrapolate from that. Currently for project licences, the average processing time within the Department is 27 days and over 85% are in and out within 35 days.

Q478 ***Chairman:*** Are they working days?
Dr Richmond: They are what we call "clock" days; they are working days when the Home Office is not waiting for the applicant to supply additional information or explanation. We are working with a paper-based system at the moment and we would hope that when we move to an IT-based system we can actually cut four or five days off those times simply by changing the back office processes and make further savings once we have a more simplified application system under the new Directive.

Q479 ***Chairman:*** The criticism—and again you will have seen this—that we have heard is that increasingly it is more attractive to bung a researcher on a plane and send them to the States to go and do the procedure than go through the whole business of going through our internal licensing.
Mr Walsh: I do not think we have any evidence to support that suggestion. We have looked for it but I am not sure that we have come up with anything to substantiate it.

Q480 ***Lord Palmer:*** Dr Richmond, when do you hope that this simplified procedure will come into play?
Dr Richmond: We are already simplifying as far as we can within the current legal framework. We hope to have the IT system up and running, although we have still to secure the finances to complete the project by 12 to 15 months from now, and we would be dependent on revising the legislation in line with a

Directive which allowed us to take a more proportionate response in dealing with applications to put the finishing touches to them.

Chairman: Let us move on to non-human primates and here there is a little bit of difference in our thinking.

Q481 ***Lord Cameron of Dillington:*** I think that probably most of the electorate would believe there was something different about carrying out experiments on non-human primates compared to, say, rodents and so on, and I think they would be pretty horrified to know that experimentation on non-human primates went up in 2008. Did the response to your consultation confirm that and why are you taking a line that, in spite of the 3Rs, seems to be justifying increased use of experiments on non-human primates?

Lord Brett: First of all, we really should be giving special protection to non-human primates and I understand entirely the public sentiment and identify with it. The current UK requirement is of course that they can only be used and should only be used when there are no other animals suitable for the scientific programme involved, but where we do not support the proposal is in the draft Directive to restrict primate use to research into "life-threatening and debilitating conditions in man". We believe that the terms are too imprecise and are likely to lead to confusion with regard to their proper interpretation, but we are also concerned that the definition of "debilitating conditions" as quoted in the present text could be equally problematic and could lead to the prohibition of legitimate uses not included in the list of examples. We believe that the robust ethical evaluation project is the best way of ensuring that primates are not used where it is not essential and the ethical evaluation project, which is very central to our operation, is now a key part of the draft Directive. Therefore, we are strongly in support of the European Parliament position which is to seek to delete references to "life-threatening and debilitation conditions". We believe that by removing that it will do nothing whatever to change the situation in reality. Of course, the current Directive has been in existence 20-plus years and the new Directive is likely also to have a lifespan of that duration. We do not know where research will be going. Our position is perhaps not to be as restrictive on the use in terms of areas of research but to be as restrictive as possible on the use where it is unnecessary or where it would be harmful, and I think that is the position. In terms of the consultation, as might have been expected, I think there is broad support of our current position from within the science community, but obviously the animal welfare community wishes the use of non-human primates to be as restricted as possible. My colleagues have been involved in the detailed discussions on that.

Dr Richmond: I do not think anyone in the UK science base ever seeks to use non-human primates when there is another research tool that will give them the same scientific outcome and as the regulator we will only authorise primate use when the objective is sufficiently important and there is no alternative. The issue with the text which is being discussed in Europe is that the terms "life-threatening and debilitating" are already established in Community legislation. Under normal conditions I know what these terms mean but, in Community legislation they restricted to a very small set of current pharmaceutical research and development, not the entire pharmaceutical research and development programmes as they are just now.

Q482 ***Lord Cameron of Dillington:*** Given your way, as it were, would you envisage that experiments on non-human primates would carry on going up because there still seems to be a huge amount of experimentation in this country?

Lord Brett: I am not sure that the term "huge" is correct. The numbers tend to fluctuate year on year. I suppose one could say that, given that there is more biotech pharmaceutical research, primate use is likely to increase though of course they are effectively only used where we need species with similar immune systems to humans. I said, if the science base expands in the way it has in previous decades, then there will be uses that we have not required to cure diseases that happen to come along. Therefore, I believe that it will be too restrictive not to accept that there might possibly be, and probably will be, an increase in use, but we need to control that as tightly as we can and get the balance right between animal welfare and the need for us to continue both in terms of what is a very, very valuable industry and one in which we are world leaders and also, of course, for the human good. I think that, putting those things together, we think we have the balance about right.

Q483 ***Lord Cameron of Dillington:*** May I move on to the use of F2 animals. Do you think that the Directive should set a deadline? Do you think that would be a useful procedure because it was pretty effective in terms of the Cosmetics Directive?

Lord Brett: I think that signalling a destination is fine. Timing the journey is the difficult part. In principle, we believe that we should move to the use of F2 animals and that is already happening in the UK, but a key point is that we have to establish the feasibility of making F2 use mandatory before we lock ourselves into a timescale and that feasibility study, in our view, should consider issues such as the health status of the animals and the welfare standards at breeding centres. We currently set high welfare

standards and we are very reluctant to accept animals from colonies with lower standards just because they are F2 animals. We think that there is general support within Member States for a feasibility study from the research community and also there is pressure for an early mandatory requirement for F2 animals from other groups as well. I think, again, the balance is to check the feasibility and to establish that we are not setting ourselves impossible timescales which will fail and then not only receive public criticism but also will probably not be doing any great favours to either animal welfare or indeed to science and the pharmaceutical industries which are so important to us.

Q484 ***Chairman:*** I would like to come back on this. You have been making the point about UK use of non-human primates and the power of the ethical review system. Of course, we are not just looking at a UK system, we are looking at a European system, so we have to be looking beyond the UK experience and seeing how it fits in the context of trying to get a European-wide regulatory framework. Would your reluctance to have the reference to "life-threatening and debilitating" in the Directive be lessened if the words in Recital 16 were actually included in the Directive, because that means that their use should only be allowed for the preservation of the respective non-human primate species or when the work, including xenotransplanation, is carried out in relation to life-threatening conditions in humans or in relation to cases having a substantial impact on persons' day-to-day functioning, ie debilitating conditions, such as, and then you get the list, "infectious diseases, diabetes, allergy, asthma, dementia, hearing or visual disorder, dyslexia, addiction, obesity or infertility"? Would that incorporation not give a very strong degree of comfort?

Lord Brett: It might well do, but the realpolitik of this being a joint endeavour between the European Parliament and the Presidency of the Commission and Member States means that what is going to emerge has to pass muster with both. It is the European Parliament's very strong view that the removal of this would actually improve the Directive rather than diminish it, a view which we share because effectively it would be the most likely outcome that would achieve what we want, but if that were not to the case then I think that other language would have to be put in place. More prescriptive does not necessarily mean more effective. We believe that having it taken out completely would not impact on how we operate and need not have a deleterious effect on the Directive and its application in other Member States. Again, my colleagues are at the coalface of the discussions.

Mr Walsh: One thing is that we have concerns about lists because of what might not be on the list that we might then come to later and have a problem with. So, just on that simple level, we have a difficulty with that. It is not inconceivable, I suppose, that someone could come up with a definition that everybody was happy with, but I do not think that anybody has achieved it quite yet and perhaps in the timescales we are talking about for agreeing the Directive it may not be possible, so we would prefer to keep it simple. There will still be a clear restriction on the use of non-human primates and I think that all Member States who use them—and that is a smaller group within the 27—agree that use should be kept to essential purposes only. Our position is that we have successfully achieved that through our current version of ethical evaluation and that is to some extent being exported into this new Directive and other Member States will carry out similar sort of ethical evaluations, and we think that that is the way to make sure that non-human primates are not used for what might be termed as trivial purposes. That is our approach.

Dr Richmond: The flavour of the recital is fine; the wording is not quite right but the wording in the Article is different again. For example, improved contraception would not fit either of those texts; it is not infertility, it is not life-threatening and it is not debilitating. Also, if you go to see your general practitioner and he prescribes a medicine, it will have been tested, almost certainly, on non-human primates in order to get authority for the clinical trials that preceded the demonstration of safety in the marketing authority. I suspect that most people who go to see their general practitioners and have something prescribed probably do not have conditions that you would generally believe to be life-threatening or debilitating.

Chairman: Let us move to care and accommodation standards.

Q485 ***Lord Palmer:*** I have a quick question on care and accommodation standards. On our site visit to Guy's back in May, I think that we were all fantastically impressed at the pristine condition that everything we saw was actually being kept in. In that the UK is recognised for its high levels of welfare, could we not have expected breeders and indeed the users to have anticipated the higher standards of care and accommodation that are shortly going to be implemented?

Lord Brett: I think the answer is that many in the UK have already done so, but the requirements in the revised Council of Europe Guidelines, which Annex IV of the draft Directive reflects, have been available and so that is what people have been able to look to. However, the big difference is of course that Annex IV has a mandatory requirement and sets deadlines

for implementation. I do not think that was necessarily expected and therefore people will not gear themselves up to that mandatory requirement, and we think that will have a significant impact on breeders who will have to make a significant investment in turn if they are to maintain current production capacities. We are supporting changes to the implementation deadline so that we can ensure that those costs can be set over a reasonable timescale.

Q486 ***Lord Palmer:*** What do you think a reasonable timescale is?
Lord Brett: That depends on the discussions that are taking place.
Dr Richmond: I think the issue is that the draft Directive is turning what was a guidance document which set aspirational high standards into a minimum standards document. We have used the guidelines document to expect the standards which it sets out but to accept alternative provision where sufficiently good arrangements are in place and animal welfare is demonstrably of a high standard. The main area of concern seems to be that there is a period of time between when animals are bred for scientific use and issued for scientific use. There is a small period of time between those two. If we move from guidance to mandatory minima, production and holding capacity will fall by about 30% in the UK. We would say that there is no welfare problem for the animals currently being held to the alternative provisions. It is not as if we would be spending money and getting better welfare and better science. We would say that the arguments are currently that we would be spending additional money to maintain capacity but with no improvement in animal welfare as a result.

Q487 ***Chairman:*** What is the evidence base like? How robust is the evidence base when it comes to animal care and accommodation? Can you really say there is strong evidence that increasing the size of the cage by X centimetres has a measurable impact on rat happiness?
Dr Richmond: Can I show my hand? I was actually Chairman of the Council of Europe Working Party which developed these as guidelines and Chairman of the multilateral meeting which approved them as guidelines. There is no evidence that bigger is necessarily better and the guidelines were produced around either what was recognised to be good practice or aspirational best practice. We know that you can have good welfare at slightly lower standards. The most important part of the guidance is not the tables, it is the text. The text tells you what you have to achieve rather than how you have to achieve it. The problem with the proposal as it is developing for the new Directive is that it is giving you the inputs and not the outputs, "You shall provide cages of this size", not, "You shall be able to demonstrate high standards of animal welfare". We think it is a pity that the proposal has not taken on board more of the text and allowed best provision to be made for local needs.
Chairman: Thank you. We turn to level playing-fields.

Q488 ***Lord Brooke of Alverthorpe:*** We had evidence from the pharmaceutical industry and the breeders complaining that, whilst they were happy to embrace the 1986 Directive and they had in many areas gone beyond the 1986 Directive, they were very unhappy that it had not been uniformly applied throughout the rest of the Union. One of the issues which have concerned us during the course of this inquiry is to ensure that we get good standards but also that we get good practice on a uniform basis throughout Europe. We are somewhat disappointed to see that some of the original recommendations on the scale of inspections may have been watered down and I wonder whether you feel that this is going to help or hinder the objective of ensuring that we have a harmonised approach on this. Secondly, one of the issues which arose previously was the extent to which the Commission itself could try to ensure that countries were applying the Directive. Are you content with the current arrangements within the Directive there or do you feel that it should be strengthened and, if so, in what way?
Lord Brett: On balance, there will be improved and increased harmonisation in some key areas. As I have said, all projects will require authorisation and, importantly from our point of view, all will be subject to ethical evaluation before they are approved. There are also going to be common minimum care and accommodation standards and we think that those are significant advances for a level playing-field whereas, as Lord Brooke has just said, there is less harmonisation likely in other areas. Authorisation of individuals carrying out procedures on animals is now to be optional in the current text. This has been a central element of the Commission proposal and, as has been said, the arrangements for inspections have now been amended and are no longer set to a minimum frequency of inspection. It will now be for national decision. This was a point strongly argued by a number of Member States and I think a key point is that if it is not going to be done to a timescale, et cetera, then we look to the European Commission to monitor implementation. I have to say anybody who looked at the monitoring of the current Directive can only be extremely disappointed. There is provision for the control of Member State inspections and the text also places the usual reporting requirements on Member States. Those controls on Member State inspections will look at the

infrastructure and operation of national inspectors in Member States. What is not clear is how often the controls will be carried out and how they will be triggered. In our view, the Commission's record of monitoring has not been good, as I have said, and, for that reason, we are pressing very hard to try and ensure that in the new regime that will follow the Directive they do have a positive attitude to their responsibilities to inspect. This is obviously a view shared by some Member States but possibly with less enthusiasm by others. I think that it is in our interests as a country and also in the interests of an effective Directive that we press the Commission as strongly as possible that it takes on a clear role of carrying out these responsibilities given under the Directive and we are not at all sanguine, given their previous record, that this is going to be the case unless there is very considerable pressure put upon them.
Dr Richmond: There is one subtlety in the text to which I would draw your attention. In the two adjacent Articles, "Member States shall inspect" and, in the next Article, "The Commission may inspect". It would appear that the Commission will have discretion as to whether or not it does indeed seek oversight or choose to exercise national inspection rules.

Q489 ***Lord Brooke of Alverthorpe:*** Is it not possible from what you have just said that we may end up in the same position as we were with the 1986 Directive in five years' time?
Lord Brett: I think that is why it is important at this stage, that the UK and others press the argument by pointing to the amount of dissatisfaction that emerged over the years with the previous Directive and how that might have been avoided had there been closer monitoring by the Commission itself and to challenge the argument that, in some way, because it says "may", it means that they can simply ignore it. All EU negotiations depend on the number of allies that one can bring into the column. I have to say that in my experience of both EU negotiations and more extensively in UN negotiations it is actually the bilaterals outside committee in gathering together those like-minded groups which is equally important to ensuring that the Commission takes a more proactive line than perhaps the text would allow it to take, but then you have to recognise there are other groups with a similar but opposite view.

Q490 ***Chairman:*** I think that what we are all grappling with is this: the justification for having a new Directive was the inconsistent application of the old Directive, and yet the door is still being left open to inconsistency.
Lord Brett: As you say, the door is left open; it is substantially less open than before only because of the prerequisite we have now in terms of the ethical base and approval systems. Yes, this is something where we would rather see a more robust text than exists and, if we cannot get a more robust text, then we have to try and put pressure on the Commission to ensure that it fulfils a role it has but is not mandatory in the text.

Q491 ***Earl of Caithness:*** Have the Commission given any indication that they do want to undertake this role?
Lord Brett: I think that the discussion is not yet complete.
Dr Richmond: It is still subject to discussion. The European Parliament has offered a more stringent amendment which would require the Commission to do so. The Commission stands by its original proposal, but this is one of the Articles which we were discussing in more detail within the Council Working Party on Monday and certainly I think the United Kingdom would expect the Commission to exercise proper oversight, otherwise we will not get the benefits of harmonisation.

Q492 ***Chairman:*** Absolutely.
Dr Richmond: The Commission has also been clear that it would expect a new Directive, in terms of Commission resources, to be resource-neutral. So, it is difficult to see how the Commission can up its game and do it at no resource cost as well.
Lord Brett: I think that much will depend on those informal discussions between the Commission and the Rapporteur of the Parliament because clearly in a number of amendments the Parliament put down, there will be those to which the Parliament is rather more attached than others and one hopes that this is one of those to which there is somewhat greater attachment than there is to some others. We certainly have seen that the Parliament has a strong position on this and there is no reason why it should resile from it easily.

Q493 ***Chairman:*** You will be familiar with our letter on 17 July to Lord West when we said, "We support the European Parliament amendment which will oblige, rather than permit, the Commission to undertake controls of the infrastructure and operation of national inspections in Member States. We see this as of particular importance". That was in the letter on our emerging conclusions and I do not see us changing our view.
Lord Brett: I see no reason why you should. One of the strengths we have in negotiations is where we have, for example on animal welfare, very much a concordat between science that sees high animal welfare standards being complementary to good science and efficient science. Here, I think, if we are talking about harmonisation then we have to hold feet to the fire for those for whom harmonisation is a

theory but in practice are not going to seek to do too much about it. The more allies we can have in that task the better, but we are dealing with 27 sovereign Member States with varying interests. Our colleagues in the negotiations have a difficult but not impossible task.

Q494 ***Earl of Caithness:*** A point of detail. In Article 33(2), where the appropriate portion is made, are you happy with the wording "an appropriate proportion of inspections should be carried out"? Should it not be a figure over 50% of inspections should be carried out unannounced because an appropriate proportion for Britain will be very high and an appropriate proportion for some other country is going to be very low?
Lord Brett: Perhaps my colleagues could say how that emerged.
Dr Richmond: This has emerged through the Council discussions where more than one Member State has objections to specifying precise frequencies or proportions. We are generally satisfied that with the risk-based approach and a proportion unannounced we can maintain current UK standards. I do not suggest that all Member States will operate inspection schemes in the same way, but I think it will allow us the flexibility we need to have the correct degree of oversight to ensure that there is compliance, standards are met and best practices are being communicated and picked up across the UK.
Earl of Caithness: I am not worried about the UK because we will gold-plate this, but what about the other Member States who are not doing the inspections, and now they only have to do an appropriate proportion?

Q495 ***Chairman:*** Is an appropriate proportion zero in some cases?
Dr Richmond: You might think so and I think that some of the arguments that we heard from other Member State was to have the numbers taken out of the draft. Some of them thought that even one or two per year might be a bit on the high side.

Q496 ***Chairman:*** We are back to inconsistency again, are we not?
Lord Brett: We are back to the original consensus that we all agree that we need a new Directive and then none of us agree precisely what it is that new Directive should cover and I think this area has shown where the divisions are probably at their greatest, but we have to arrive at a compromise text acceptable to everyone.

Q497 ***Lord Brooke of Alverthorpe:*** Would we perhaps find that some of the work done at European level might be better accepted by the public at large if, when we came to implementing the new Directive, at least the existing Directive had been fully implemented before we moved on?
Lord Brett: It is chicken and egg. We may nearly not have needed this egg had the previous chicken been monitored properly over the better part of a quarter of a century.
Lord Brooke of Alverthorpe: Perhaps you will keep us posted with developments on these discussions.
Chairman: Let us turn to international competitiveness.

Q498 ***Viscount Ullswater:*** By way of background, we have already had a bit of a discussion about bureaucracy and the time and cost of authorisation in the UK perhaps as against the USA and maybe China. Obviously there is concern about displacement of research as a result of perhaps increased cost and bureaucracy regulatory burdens imposed by this Directive. In our emerging conclusions in the letter to Lord West, we have said that we felt that the imposition of bureaucratic burdens that are not justified by any gain in animal welfare are undesirable in themselves and I was quite worried about what Dr Richmond said about the care and accommodation standards now being imposed by the Directive because, I think in your own words, it did not necessarily improve the animal welfare standards that we were trying to achieve through the Directive.
Dr Richmond: That is the point I was making.

Q499 ***Viscount Ullswater:*** I am glad you agree with me because there are two questions that I really need to pose. Did you yourselves, in your consultations, get hard evidence of this sort of situation and are you still concerned that the compromise text will affect international competitiveness? Certainly the Biosciences Federation feel it does.
Lord Brett: First of all, the consultation confirmed our estimate of the economic importance of the biomedical sector. They also acknowledge that there is a risk that research will be displaced, but I have to say that anecdotal evidence on this is not hard evidence as such, and that is possibly because it is actually quite difficult to find a clear delineation of the reason why investment goes somewhere else. It is probably a whole range of things. I have been told, for example, in previous experience that investment went to China rather than India because the Chinese could give planning permission and provide sites and do everything very speedily and that was the key because the cost issues were pretty much in balance. It is not easy to find why investment decisions are made; there is a whole series of factors. There is a perception that there is a risk. So we are prepared to accept, because the industry believes it and anecdotally has some evidence, that there is "a risk", but I think it is not one that we can actually positively

measure and are able to counteract that risk other than trying to avoid gold- plating—and we are down to cost which I think the better regulation approach is trying to do—and of course in terms of the Directive to try and ensure that it does get to that level playing- field.

Q500 ***Earl of Caithness:*** In our letter that you mentioned, we recommended that Annex I, which referred to invertebrates, should be amendable under Article 48. I see that the new Annex IX is amendable but Annex I is still not there. Is this something that you are working on and, indeed, are pressing for?
Dr Richmond: This has been raised at almost every Council meeting and the Commission and the Council Legal Services themselves are insistent that this forms part of the scope of a new Directive and anything which forms part of the scope of a new Directive shall not be amended by comitology. So, we are being told that there are technical reasons why that is included in the scope and why it cannot be subsequently amended. At the last Council meeting, we had a discussion as to whether or not, if the list is going to be sufficiently small and it is indeed part of the scope, then why is it not in the Article rather than a separate technical annex and we hope to hear more about that when we return to Brussels on Friday.

Q501 ***Earl of Caithness:*** So you are still pressing?
Dr Richmond: We are still pressing but the Commission shows no sign of changing and the Council's Legal Services are telling us that the Commission's interpretation is correct.
Lord Brett: That will be part of the report that we deliver to you next week.

Q502 ***Viscount Ullswater:*** I would like to ask a supplementary on that. Are you content that in the scope, in Article 2(a) and (b), they are correct about invertebrates particularly?
Dr Richmond: We have looked not only at the evidence base used by the Commission but we have previously reviewed this for our own purposes and Defra previously worked in a similar area in the preparation for the Animal Welfare Act. Our view is that the evidence for including decapods is too weak to justify that. We believe that the evidence for cephalopods is restricted to one or two species, not the entire class of animals, and that, if cephalopods were to be included, it should not be the class, it should be the one or two species for which we have evidence, but even the evidence for those is not conclusive.

Q503 ***Viscount Ullswater:*** So, are you seeking then to amend the scope of Article 2?
Mr Walsh: Yes. This comes up every time that Article is on the table and we keep pressing.

Q504 ***Chairman:*** I am wondering whether the decapods issue has any read-over to how you cook lobsters! Thank you very much for your time and your evidence. All the information you have given us has been very helpful. I would like to say one thing. I think that we are all united in trying to maintain that there are high, appropriate standards in terms of animal welfare when you come to the use of animals in scientific procedures. But it is no good putting material in the new Directive which has the avowed intent of establishing high standards if implementation is not there. There must be consistency on implementation. It is better to have slightly lower standards as long as you have the consistency of implementation. I think that that it is hard to overstate the importance of that issue.
Lord Brett: That is a view with which we would concur. What we have within the Presidency has come with very high standards and they are as anxious as we would be to have no situation which lowered our standards. Equally, the whole purpose of this Directive is to seek to move to harmonisation and it would be undermined considerably if Member States avoided the very harmonisation that they all signed up to have a new Directive to achieve.

Q505 ***Chairman:*** Remember the difference between the French "*en principe*" and the British "in principle". They are very different concepts.
Lord Brett: Indeed.
Chairman: Thank you.

Letter to Lord Roper from Meg Hillier MP

PROTECTION OF ANIMALS USED FOR SCIENTIFIC PURPOSES

In his evidence to Sub-Committee D on 14 October 2009 in connection with its inquiry into the proposed new European Directive on the protection of animals used in scientific procedures, Lord Brett undertook to provide a further note summarising progress on the issues identified in your emerging conclusions letter of 17 July 2009 to Lord West. I attach that note as an annex to this letter.

Overall, the picture is a mixed one. Some issues have been successfully resolved, for example, the proposed maximum duration of project authorisations has been extended from four years to five, as suggested by the Committee. Many others have made good progress but need further work before the details can be finalised. A much smaller number have not yet made satisfactory progress. As Lord Brett explained to the Committee,

the most notable of these relates to the use of primates in scientific procedures, where we do not yet have agreement on a text which is clear in setting out the circumstances in which such work can continue. We agree with the Committee that clarity on this issue is absolutely essential.

With regard to the further negotiating process, after last week's Council working party meetings, consideration of outstanding issues will now pass to attachés, who are due to meet on 6 November 2009. It remains the Swedish Presidency's aim to agree a Council first reading position at the December Agriculture Council.

20 October 2009

PROPOSED REVISION OF THE DIRECTIVE ON THE PROTECTION OF ANIMALS USED FOR SCIENTIFIC PURPOSES

HOUSE OF LORDS EUROPEAN UNION COMMITTEE SUB-COMMITTEE D (ENVIRONMENT AND AGRICULTURE)

EMERGING CONCLUSIONS—UPDATE

Conclusion	*Article(s) in current Presidency text or EP amendment*	*Current position*
1. The introduction across all Member States of a requirement for **prior authorisation of animal procedures,** including an **ethical review process,** is particularly to be welcomed.	Article 35 (authorisation of projects) Article 37 (ethical evaluation)	Member States accept the need for prior ethical evaluation and authorisation of projects and both are provided for in the current compromise text. Some details of the approval process remain to be agreed, with one Member State keen to make provision for approval by default if maximum processing times are not met (see also 3, below).
2. We reject a move to require **notification (rather than authorisation)** for "mild" procedures.	EP amendment 167 to Article 35.1	The EP amendment proposing "notification" for some projects has not been adopted in the current text.
3. However, we would urge . . . that the authorisation process is completed quickly [and] that the Directive provides . . . for a **smooth and timely authorisation procedure**	Article 43 [New Article 40] (authorisation decisions)	The text now proposes a maximum of 60 days for project authorisation with an additional 30 days allowable in more complex cases. We, and the Commission, believe that shorter timescales would better protect competitiveness.
4. **Authorisation processes** must be efficient so that scientists … can take on new lines of inquiry and amend current approaches without undue delay	Article 42 (Amendment and renewal of project licences)	No time limits are currently set for authorisation of amendments or renewal of licences. Also all amendments must be subject to further ethical evaluation.
5. We have seen no evidence that shortening the **term [of project authorisations]** to four years] would be justified by significant animal welfare benefits	Article 41.3 (Granting of project authorisations)	Resolved. Maximum duration now extended to five years.

Conclusion	*Article(s) in current Presidency text or EP amendment*	*Current position*
6. We are also not persuaded that all projects lasting 12 months or more should be subject to **annual review**	Article 26.1(d) (Tasks of animal welfare body)	Resolved. Requirement deleted.
7. . . . Reporting data on actual severity and the results of retrospective assessments would increase the information on animal procedures made publicly available . . . We consider that such greater **transparency** may well be justified, although . . . identities of individuals or establishments should not [be published].	Article 38 (Retrospective assessment) Article 40 (41)(Non-technical project summaries)	Retrospective assessment is mandatory for projects with procedures using non-human primates and projects classified as severe and optional for mild, or non-recovery procedures. Non-technical summaries are to be updated with the results of retrospective assessments. Retrospective reviews are likely to be carried out by the users and establishments.
8. . . . the **care and accommodation standards** in the proposal . . . are not likely to impact on the competitiveness of the pharmaceutical industry.	Article 32 (care and accommodation) and Annex IV	We broadly agree, but there is potential for some purpose bred animals to cost more.
9. . . . the **[care and accommodation]** standards . . . may prove difficult for academic . . . establishments to meet over the timescale envisaged . . . . . we think that there may be a need to re-consider the **timescale for implementation** in the light of experience. We welcome . . . that the proposal provides for this . . . through Article 48 . . .	Annex IV and Article 48	We agree that it is important that appropriate timescales are set. Some timescales have been extended in the current text, but the final position remains to be agreed.
10. . . . we draw particular attention to concerns . . . expressed over the practicalities of the **stocking densities** proposed for rodents and rabbits at breeding establishments.	Annex IV	Not yet resolved. The UK is seeking changes to Annex IV to mitigate the impact on breeders which would otherwise reduce capacity and increase costs, but produce no animal welfare gains.
11. . . . we agree that [the key explanatory text from the **Council of Europe guidelines**] should be restored.	Annex IV	No progress. The Commission and Council Legal Services advise that annexes to directives must be "enforceable" and that the inclusion of explanatory text is no longer allowable. However, the full text of the Council of Europe document will retain guideline status by virtue of Commission Recommendation 2007/526/EC.

Conclusion	*Article(s) in current Presidency text or EP amendment*	*Current position*
12. We . . . stress the importance of ensuring that the text of the Directive is clear in setting out the circumstances in which research work using **non-human primates** may continue.	Articles 5 (purposes of procedures) and 8 (non-human primates) and European Parliament Amendment 57	We agree that clarity is required. However, we consider that the consequence of restriction of such research to "life-threatening and debilitating conditions in humans" is not clear as these terms are imprecise and open to misinterpretation; and where they are already used in Community legislation they refer to only a small subset of pharmaceutical products. We also have concerns about the proposed definition of debilitating conditions in the current Presidency text which has the potential inadvertently to exclude legitimate uses of non-human primates. We support EP amendment 57 which deletes reference to "life-threatening and debilitating conditions in humans".
13. Given the degree of uncertainty related to the practicality of [restricting the use of non-human primates to **F2 animals**] . . . it is crucial that this . . . is monitored closely and that the feasibility of the time-limits should be investigated on a species-by-species basis. The Commission's review of the Directive must include information on progress in phasing out the use of F1 animals.	Article 10 (Animals bred for use in procedures) and EP amendment 60	Resolved. EP amendment 60, which provides for a feasibility study and animal health and welfare assessment, has been adopted in the compromise text.
14. We are minded to agree that while cyclostomes and cephalopods should be included [within the **scope** of the Directive] decapods should be excluded.	Article 2 (Scope) and Annex I	Cyclostomes are properly classified as vertebrates and within scope. No additional evidence relating to potential sentience has been produced or considered. Cephalopods continue to be included and are likely to remain so. No final decision has been made on decapods.

Conclusion	*Article(s) in current Presidency text or EP amendment*	*Current position*
15. . . . we are concerned that there is no provision in the Directive toamend the **list of invertebrates** in Annex I. We . . . consider that Article 48 should be amended to include Annex I.	Article 48	No progress possible. Commission and Council Legal Services agree that issues affecting the scope of Directives cannot be revised via comitology. Only "non-essential" elements can be revised through that process.
16. We are concerned that [the inclusion of **independently feeding larval forms and embryonic and foetal forms** of non-human vertebrates] may in some cases lead to a substantial increase in administrative burden with no benefit.	Article 2 (Scope)	Free-living or reproducing larval forms and foetal forms of mammals as from the last third of the normal development remain within scope. This will increase the administrative burden in the UK, but produce no animal welfare benefits. Embryonic forms of birds have been deleted from the current text as have larval forms of invertebrates.
17. . . . the **breeding and humane killing of animals for their tissues and organs** should not be regarded as a "project" within the terms of the Directive [and] should not be subject to the authorisation processes required of projects.	Article 3 (Scope)	Resolved. Killing for tissues using an approved method in Annex V will not be classified as a procedure or a project, but some related inconsistencies in the text have yet to be fully resolved.
18. . . . the **severity classifications** need to be clearly defined in the text of the Directive.	Article 15 (Classification of severity of procedures) and Annex IX	Resolved. The new Annex IX defines severity classifications. There are, however, potentially significant unresolved issues relating to the status of an "upper threshold" and whether and on what terms it might be exceeded.
19. . . . the **re-use** provisions should be amended to avoid unintended consequences for animal welfare.	Article 16 (Re-use)	Some progress has been made, but the framework for re-use has not yet been finalised.
20. There is widespread support for the principle that there should be **mutual acceptance** between Member States of data from test required under Community legislation.	Article 44.1 (Avoidance of duplication of procedures)	The current text includes this requirement.

Conclusion	*Article(s) in current Presidency text or EP amendment*	*Current position*
21. We consider that obligations on **data-sharing** should apply only where there is evidence of duplication of procedures. We reject the [EP] amendments on this issue.	Article 44.2 (Avoidance of duplication of procedures)	The data sharing proposal has been deleted from compromise text.
22. We fully support the **principle of the 3Rs**, including the explicit reference to it in the proposal.	Article 4 (the 3Rs)	Article 4 requires the application of the 3Rs and the division of responsibilities between the Commission and Member States has been clarified.
23. We consider that the . . . proposal that **national reference laboratories** be set up must be reconsidered.	Article 46 (Community Reference Laboratory) and Annex VIII	Resolved. The requirement for national reference laboratories has been replaced with a proposal for a "Community Reference Laboratory" with duties and functions set out in a new Annex VIII.
24. We consider **ECVAM** . . . may be able to assist in . . . sharing best practice and information on the 3Rs between EU countries.	Article 46 and Annex VIII	This is included in the responsibilities set out in Annex VIII
25. We put particular stress on the need for due attention to be paid to the **implementation of the revised Directive**, once it has been adopted . . . Member States must send information on implementation . . . sooner than six years after the transposition date.	Article 49 (Reporting)	Unresolved. Remains at six years.
26. The Commission should **review the Directive** no later than five years after it has come into force (and not 10, as proposed).	Article 53 (review)	Unresolved. Remains at 10 years
27. We support the [EP] amendment which would oblige, rather than permit, the Commission to undertake **controls of the infrastructure and operation of national inspections** in Member States; we see this as of particular importance.	EP Amendments 186 and 176 to Article 34 (Controls of national inspections)	The EP amendment has not been adopted. The Commission is believed to prefer an approach under which their checks would be risk-based or where they have been made aware of a problem or deficiency.

20 October 2009

Written Evidence

Memorandum by Animal Aid

1. Objectives of the Directive

1. There should be enforced across the Union minimum standards of animal protection together with a requirement to develop and implement non-animal methods. However, because of varying standards of competence and efficiency, the playing field can never be completely levelled out. Equally, Member States should be encouraged to go beyond the bare minimum set out in the final Directive with regard to animal protection and replacement measures. After all, the second strategic objective of the revision process—in addition to creating a level playing field—is to "strengthen the protection of animals used in scientific procedures in line with the Protocol on Animal Welfare".

2. In terms of a proportionate response, it must always be borne in mind that giving licence to research establishments to conduct painful and lethal experiments is a grave step. In response, the EU must set sufficiently robust standards that reflect this reality.

2. International Competition

3. It is often argued by pro animal research interests that biomedical research departments will go to countries with lower standards, rather than deal with extra welfare costs and red tape. There is no credible evidence that this will happen. In fact, despite comparatively high animal protection standards in Britain, compared with many other EU Member States, the pharmaceutical industry has put up a strong performance for many years. And it should be remembered that public confidence in the pharmaceutical/biomedical industry is being seriously tested with a succession of scandals and investigations (eg the June 2006 publication by Consumers International of *Drugs, Doctors and Dinners)*. Confidence is likely to be tested further if powerful businesses threaten to flee to other jurisdictions to avoid proper limitations on what they can do to animals in the course of, for instance, poisoning them during toxicity tests. In a post-credit crunch world, public confidence is likely to become increasingly important.

4. The case is often made by pro animal research interests that a vigorous programme to develop and implement non-animal testing methods, and also to provide additional protection for animals who continue to be used, is at odds with profitable, efficient and productive biomedical research. The opposite is the case. By way of illustration: Three powerful US federal agencies have recently committed themselves to a development programme that the director of one of them—the National Institutes of Health (NIH)—has said marks the beginning of the end of animal use for toxicity testing. As part of that federal project, the NIH has been carrying out tests using high-speed robots that can screen 200,000 chemical compounds in two days. That amount of testing would take a researcher using traditional animal "models" not two days but 12 years working eight hours a day, seven days a week—and the end results still could not be trusted.

5. Why would researchers, whether working for government safety testing agencies or for pharmaceutical companies, want to forego new economic efficiencies and cling to systems that are slow, unreliable, expensive and hugely divisive morally? The answer is: they ultimately won't—even though inertia and a deeply embedded conservatism currently hold many in the sector back. It is essential that the new Directive reflects progressive attitudes and developments. Britain can give an important lead in this regard.

3. The Proposed Requirement to Restrict Research on Non-human Primates

6. The original Commission Draft proposed certain restrictions on the capture of wild-caught primates, also on the use of their immediate offspring and subsequent generations of captive bred primates. We felt that those proposals did not go far enough in that a key yardstick for obtaining project approval was whether the proposed procedure related to "life threatening or debilitating" conditions in human patients. We felt that this test was too loose in that any number of human ailments debilitate. The Commission's proposals were weakened substantially by the EU's Agricultural Committee, whose amendments were subsequently carried in a Plenary vote. This is despite MEPs having voted last year to phase out all primate experiments. On 5 May, they voted to delay indefinitely a proposal by the Commission to phase out the capture of wild-caught monkeys for breeding purposes. And MEPs backed an amendment permitting primate use for "basic" or curiosity-driven research, as well as for experiments relating to "life-threatening or debilitating" human conditions.

7. With regard to whether far greater restrictions on primate capture and use are "proportionate", that question cannot be answered except with reference to whether or not primate research delivers what it is intended to deliver—namely, reliable toxicity data and the elucidation of human disease processes and potential remedies. The evidence points to the primate model as having conspicuously failed to meet these objectives. Often, the price for human patients of such a failure is devastating. Examples include the many AIDS vaccines that protected monkeys from the disease but failed to protect people. There is also the trialling of TGN1412—an immunotherapy drug that was pre-tested in monkeys who remained well, despite being given doses up to 500 times greater than those subsequently administered to the human trial volunteers, who suffered near-fatal multiple organ failure.

8. All primate use should be considered on a case-by-case basis, with a view to implementing a programme of replacements. 80% of people in the EU oppose the use of primates.

4. Extension of the Scope of the Directive

9. The proposal offered by the Commission (subsequently diluted by the Parliament) was modest and reasonable, and deserves the support of the British authorities. The Commission's proposal is as follows: "It is necessary to include specific invertebrate species within the scope of this Directive, as there is scientific evidence of the potential ability of such species to experience pain, suffering, distress and lasting harm". That proposal is wholly "proportionate".

10. The Commission's original proposals to extend equivalent protection to embryonic and foetal forms (and, again, subsequently weakened by Parliament) are equally deserving of Britain's support. There has been dismissive talk of, for example, the "ludicrousness" of extending protection to "prawns so small that the eye cannot see them". However, the choice becomes clearer when one considers animals such as cats, mice, dogs and primates, and contemplates them being surgically mutilated and poisoned without restraint. The authorities must be prepared to back protection for late term animals.

5. & 6. Authorisation of Persons, Requirements for Establishments, Inspections and Project Requirements

11. The decision by the Parliament to require authorisation from a competent central authority only for primate experiments and for procedures classified as "moderate" or "severe", is a seriously retrograde step. At current rates, some 4.3 million experiments would go ahead "on the nod". Even if local ethical review bodies objected to what was proposed, they would have no power to stop it. It cannot be right to remove so many procedures from proper central authority scrutiny and, thereby, effectively exclude them from the cost-benefit test, and from an assessment as to whether non-animal replacements could be used. This proposal, in short, undercuts the whole revision process with its core objective of improving protection for animals.

12. The inspection regime must be as robust as possible, and it is right and appropriate that the Commission itself should investigate on a regular basis adherence by Member States to the requirements of the Directive. Where Member States fall short, the Commission should have the powers to ensure problems are remedied and sanctions applied.

8. Alternative Methods

13. We were encouraged to see that MEPs voted to increase resources for the development of replacements and also called for an expansion of the scope of ECVAM. However, they simultaneously removed the mechanisms for ensuring that the drive for replacements would yield meaningful results. They did this by eliminating the need for authorisation on millions of animal tests (and, therefore, rendering those activities near invisible as far as central scrutiny is concerned) and they removed, in most instances, the need for retrospective reviews. Such reviews potentially answer all sorts of important questions about the validity of animal use, the purpose to which those animals were put and the number of animals used.

14. While the UK's NC3Rs Centre is doing an amount of useful replacement work, the scale of it is meagre. The best example is to be found in Germany, where the search for replacements has been prioritised by the government since 1980, and where, to date, more than 70 million Euros has been invested in the pursuit of that objective. The Commission currently envisages alternatives research costing each Member State about 100,000 Euros. This is far short of what is needed.

9. SUBSIDIARITY AND LEGAL BASE

15. It is essential to regulate at the EU level, not only for the sake of the much-vaunted level playing field but also to ensure cruel and morally corrupt practices are not allowed to take place within the Union.

18 May 2009

Memorandum by the Animal Procedures Committee

1. *What degree of harmonisation of rules governing the protection of animals in research is required to avoid distortions of the Single Market? To what extent are such distortions causing problems at present, and is the draft Directive a proportionate response to those problems?*

There are currently potential causes of distortion within the Single Market due to variations in national laws regulating the care and use of animals in research and testing.

Harmonisation of the regulation of animal experimentation to a good standard, including training, the authorisation process and ethical review, is necessary.

2. *How might high(er) animal welfare standards in the EU impact upon the international competitiveness of the EU's private and public sector research base, and that of commercial establishments carrying out routine testing? Is there a risk of displacing research using animals to third countries and, if so, what would be the consequences of such a trend?*

We welcome high welfare standards because good science and good animal welfare usually go hand in hand

The Directive should reflect the EU's Better Regulation agenda, which is aimed at reducing administrative burden and ensuring a proportionate approach to legislation.

Some APC members believe that some of the provisions in the proposal would merely increase bureaucracy and therefore costs. Others believe that the provisions reflect the need for proper regulation of animal care and use.

Concerns that unjustified increases in bureaucracy could diminish international competitiveness, for example by acting as an incentive to move work to non EU countries, are held by some members.

It has been suggested that limiting primate research to that which could ameliorate "life-threatening or debilitating" conditions may lead to some work being done in non EU countries. However, the term "debilitating" is open to interpretation, so the implications of this proposal are not clear.

3. *Are the proposed restrictions [on non-human primate use] proportionate, and what might be their impact?*

Most APC members hold the view that primate use should be subject to the same authorisation process as the use of any other species, without restrictions on purpose. However, one member believes that restrictions on primate use are justified on animal welfare and ethical grounds.

The need to change to F2+ primates is not in dispute due to the pressing animal welfare and scientific issues involved.

The requirement to have a strategy to increase the supply of F2+ animals to the EU is likely to increase the costs of undertaking primate research.

Balancing the financial costs to primate users against the welfare implications of trapping from the wild, we agree that the Directive should include a strategy for changing to F2+ primates.

The role of the National Animal Welfare and Ethics Committee should include advising the Competent Authority on the suitability of overseas primate suppliers.

The proposed study on the feasibility of changing to F2+ primates should be completed within the proposed timescale of 18 months, so that realistic targets for the changeover to using only F2+ animals can be set.

4. *Are the proposed extensions to the scope of the Directive justified, and what might be their impact?*

It is difficult to set out definitive criteria that can be used to judge whether or not species of animal are capable of suffering.

It appears that the mammalian fetus may not become sentient until following birth, once breathing has commenced.

The precautionary principle should be applied and procedures on the developing mammalian and avian fetus should be regulated. The APC supports the current proposal for the final third of the development period, as there has to be a "cut off point" in practice.

An Annex to the Directive could list species-specific developmental stages of vertebrate that have been demonstrated to be capable of suffering.

Procedures on Cyclostomes, or Agnatha, should be regulated.

Research on species of cephalopod and decapod crustaceans has concluded that at least some species may be able to experience pain.

If some cephalopod and decapod species are included in the new Directive, an option to reduce paperwork could be to regulate their care and use but not require statistics on procedures to be submitted centrally.

Regulating research on invertebrate larvae may be unrealistic at present.

5. *Are the administrative demands that the draft Directive would impose overall proportionate to its objectives?*

The APC has concerns relating to three Articles and one Section of the proposal, which we discuss in paragraphs 5.2, 5.3, 5.4 and 5.5:

- Authorisation and oversight of breeding and supplying establishments (Article 21);
- Suspension and withdrawal of authorisation for minor technical infringements (Article 22);
- Granting of project authorisation (Article 41), in which the duration of project authorisation is reduced to four years; and
- Requirements for projects (Section 4), ie whether the degree of control should be adjusted in relation to the potential harm to the animals.

6. *Do any of the provisions relating to the authorisation of persons, the requirements for establishments, the inspection regime, or project requirements require further consideration and/or amendment and, if so, why?*

The APC believes that several Articles require further consideration, which is discussed in paragraphs 6.2, 6.3 and 6.4:

- Authorisation of persons (Article 20), which should be more prescriptive with respect to ensuring that persons are appropriately trained and competent and how this should be documented.
- Tasks of the permanent ethical review body and ethical evaluation (Articles 26 and 37), with respect to statistical experimental design, interpretation of studies and reviewing scientific progress.
- Amendment, renewal and withdrawal of a project authorisation (Article 42). Some APC members feel that it should be possible for mild and moderate project amendments, which do not increase the severity classification, to only require notification to the Competent Authority. Other members take the view that all levels of severity should be subject to the same scrutiny throughout the licensing process, including amendments.

7. *Are the care and accommodation standards set out in Annex IV to the Directive appropriate, and will they produce an adequate level of harmonisation across the EU?*

The care and accommodation principles in Annex IV are largely appropriate, if somewhat inexplicit and lacking detail in some aspects.

Annex IV is taken from specific guidance given as Appendix A to Council of Europe Convention ETS 123, but it is an abridged version in which much important explanatory text is missing.

Annex IV should incorporate both the text and tables from Appendix A.

Annex IV does not acknowledge the potential need for different housing standards for animals under procedure and it is inconsistent in that it does not recommend air conditions for any species other than reptiles and amphibians.

The current Annex IV leaves scope for a lack of harmonisation if some Member States, such as the UK, continue to apply specified guidance whilst others merely interpret principles.

8. *How satisfactory are the provisions on alternatives to animal testing and National Reference Laboratories (Article 46)?*

It is not clear from the proposals how the Commission and Member States are to be encouraged to contribute to the development of such alternatives.

The concept of National Reference Laboratories is flawed. An alternative approach is needed in which research can be better coordinated and focused on areas of greatest need.

The role of ECVAM should be reviewed and expanded beyond the validation of alternatives to regulatory toxicity testing.

9. *Is it appropriate to regulate at the EU level—as opposed to lower tiers of government—in all of the proposed areas? Is the legal base for the proposal adequate in light of the content of the Directive?*

Regulation at the EU level could provide properly harmonised standards and a "level playing field" across all Member States, which would seem to be desirable.

Member States should be able to implement higher standards than the Directive if they wish to do so.

Evidence submitted by the Animal Procedures Committee

Introduction

The APC agrees that Directive 86/609/EEC is in need of revision, in order to accommodate progress in scientific techniques, the Three Rs (replacement, reduction and refinement) and understanding of animal behaviour.

We recognise that a degree of harmonisation of the regulation of animal care and use is essential to ensure that the objectives of the internal market are met and that animal use is avoided and replaced wherever possible throughout the EU. It is also critically important in maintaining consistently good standards of research animal welfare within and between Member States. At present, this is not achieved due to variations in national laws.

The UK Animals (Scientific Procedures) Act 1986 (ASPA) is widely regarded as promoting good standards of animal care and use and the APC believes that the standards within the ASPA should not be weakened or compromised in any way as a result of the Directive revision.

Views of the APC on Directive 86/609

The APC has regard both to the legitimate requirements of science and industry and to the protection of animals against avoidable suffering and unnecessary use in scientific procedures. This is an especially difficult balance with respect to drafting international legislation and we could not always achieve a consensus view when discussing the questions below. In these cases, we have set out the differing viewpoints and we hope that this will be of use to the Environment and Agriculture Sub-committee.

The APC notes that there are some ambiguities in the wording of the current Commission proposal, leading to a lack of clarity in certain areas. We have not highlighted all of these, as we understand that the Home Office consultation will be covering more specific issues such as the precise wording of the draft. However, we have mentioned inconclusive wording where it is relevant to our answers to the questions in the Call for Evidence.

1. *What degree of harmonisation of rules governing the protection of animals in research is required to avoid distortions of the Single Market? To what extent are such distortions causing problems at present, and is the draft Directive a proportionate response to those problems?*

1.1 A good law regulating the care and use of animals in research and testing should serve the purpose of facilitating more consistent and valid scientific data, as well as ensuring acceptable standards of animal welfare and addressing public concerns. The way in which animals are reared, transported, handled, housed and cared for has a direct effect on their physiology, such that poor practice can result in significant physiological and behavioural responses that could affect research data quality. Furthermore, conducting procedures without ensuring that any pain, suffering or distress is minimised can also lead to physiological responses that may confound results (we can supply references on request).

1.2 Discrepancies in the conduct of animal experiments and in the quality of housing and care could therefore result in variations in the quality and validity of scientific data and results within and between Member States. However, there is no evidence that studies conducted in the EU yield unreliable results. In addition, differing

standards of ethical review and decision making regarding necessity and justification will lead to variations in the competitiveness of science at a national level.

1.3 Current potential causes of distortion within the Single Market include variations in the rigour of authorisation of procedures, animal accommodation requirements, training and licensing of individuals, projects and premises and the development of alternatives. We do not know the extent to which the Single Market may be distorted at present. However, it is clear that harmonisation of the regulation of animal care and use to a good standard, including training, the authorisation process and ethical review, is necessary. Harmonisation should also ensure mobility of scientists and projects between Member States and negate the distortions in the cost base of animal research for different countries.

1.4 Views within the APC differ with respect to whether the proposal as currently drafted is a proportionate response to improving harmonisation. One member believes that it is appropriately prescriptive so as to facilitate an appropriate level of harmonisation, with the flexibility to incorporate new knowledge about animal behaviour, physiology and welfare into national legislation. Furthermore, the housing and care guidelines were agreed (at the Council of Europe) with full input from all stakeholders, including academia and industry, as was the advice to the Commission on the authorisation process. Another member considers that the proposal is overly prescriptive in the areas of authorisation and care and accommodation and that it includes some provisions that would bring very little animal welfare benefit, but would increase the costs to researchers.

1.5 Notwithstanding these different viewpoints, a certain level of prescription is desirable from the UK point of view. This is because it would prevent other Member States from interpreting loose principles in order to be more competitive and still comply with the same Directive, albeit with standards of science and animal welfare that would fall below those in the UK.

2. *How might high(er) animal welfare standards in the EU impact upon the international competitiveness of the EU's private and public sector research base, and that of commercial establishments carrying out routine testing? Is there a risk of displacing research using animals to third countries and, if so, what would be the consequences of such a trend?*

2.1 Both the bioscience community and animal welfare organisations welcome high welfare standards because good science and good animal welfare usually go hand in hand. The EU should be at the forefront in promoting best practice in animal welfare where there is sound scientific evidence of benefit. This in turn should provide a stimulus to non EU countries to raise their welfare standards.

2.2 The Directive should reflect the EU's Better Regulation agenda, which is aimed at reducing administrative burden and ensuring a proportionate approach to legislation. Some APC members hold the view that some of the provisions in the proposal would merely increase bureaucracy with little or no enhancement of animal welfare. Examples include inclusion of invertebrates within the scope, the proposed authorisation process, limitations to certain types of research and the requirements for housing and care (these issues are addressed later in this document). Others disagree and believe that the provisions are at an appropriate level, reflecting the need for proper regulation of animal care and use and recognition of public concerns.

2.3 Concerns that unjustified increases in bureaucracy could increase research costs and diminish international competitiveness are held by some members. There is already a trend for industry to develop new facilities in the Far East and they believe that further escalation of costs could speed this long term relocation, since cost is one of the drivers of work to non EU countries. Conditions of animal care and use in some of these countries may not be up to European standards and will clearly be out of the control of the EU. There is thus clearly a need to take these issues into account to an appropriate extent, although they should not force the relaxation of EU regulations to unacceptable levels.

2.4 Proposals to limit research that can be undertaken in non-human primates to that which could ameliorate "life-threatening or debilitating" conditions may lead to some fundamental studies being done in non EU countries. Commonly cited examples are research into memory disorders, attention deficits, neurostimulation and vision. However, the term "debilitating" is open to interpretation as it literally means "weakening" or "incapacitating". On that basis, it is not clear whether or to what extent the current wording of the proposal would have an impact on primate research in the EU. The APC believes that this Article is not meaningful as currently drafted.

3. *Are the proposed restrictions [on non-human primate use] proportionate, and what might be their impact?*

3.1 Members of the APC hold a range of views regarding the various current issues within primate research and testing. These include the acceptability of primate use *per se*; whether and how there should be a strategy to replace primate experiments; and how realistic and desirable it might be to set timescales for moving to the use of F2+ animals. The views set out below in answer to this question are the majority view of the APC, but they are not unanimous.

3.2 *Purposes of primate use*

The majority of the APC members hold the view that primate use should be subject to the same scrutiny with respect to necessity and justification, and the same harm-benefit assessment, as the use of any other species. That is, there should be no restrictions on the permitted purposes of primate use. Instead, there should be sufficiently robust authorisation requirements and ethical reviews to ensure that primate experiments are appropriately challenged as a "built in" part of the process, taking into account the cognitive abilities of these animals and possible links between these and their ability to suffer. However, one member believes that restrictions on primate use are justified on animal welfare and ethical grounds and wholly proportionate to the level at which primates can suffer and the public concerns regarding the acquisition and use of these animals.

3.3 *Great Ape use*

The draft proposal is pragmatically worded. Even if Great Ape experiments were banned, any scenario requiring their use would probably be exceptionally serious and urgent, such that these animals would be used regardless of the Directive and national laws. We hope that the likelihood of this would be extremely small.

3.4 *Strategy for breeding and supplying establishments to change to F2+*

The need to change to F2+ primates is not in dispute. A number of authoritative reports have stated that moving to F2+ is desirable due to the pressing animal welfare, health and scientific concerns, such as the reports by SCAHAW[1] and the APC Primates Sub-committee.[2] Trapping wild primates can cause significant distress, suffering and physical injury. There are also a number of scientific implications, eg using animals only one generation away from the wild would be unthinkable in other species such as rats or mice for scientific reasons.

3.5 We note that the EU is a relatively small user of primates on a global scale, and that breeding establishments of non-human primates are mostly located outside the EU. The requirement to have a strategy to increase supply of F2+ animals to the EU, which is not a major customer of these suppliers, is likely to increase the costs of undertaking this type of research in the EU. This is because F2+ animals are more expensive and the cost is passed on to the customer requesting them, which has led to a two tier price structure at some breeding centres.

3.6 Notwithstanding this, the APC Primates Sub-committee suggested that breeding centres accepted to supply primates to the UK should have a strategy in place for moving to F2+ animals:

> "The UK should require any centre that traps from the wild to have a clearly defined strategy to decrease reliance upon wild populations and move to the supply of F2 animals only (for example by gradually decreasing their trapping quota and retaining a significant and increasing proportion of first generation offspring for breeding second-generation stock). The overall progress towards this goal for centres generally should be kept under review by the PSC".[2]

3.7 Balancing the financial costs to primate users against the welfare implications of trapping from the wild, we agree that the Directive should include a strategy for "increasing the proportion of animals that are the offspring of non-human primates that have been bred in captivity". We recommend that the role of the NAWEC should include advising the Competent Authority on the suitability of overseas primate suppliers and monitoring progress towards supplying F2+ animals only.

3.8 Timescale for change to F2+ primates

We do not understand how timescales can be set for the various species without first obtaining the results of the proposed feasibility study. It is thus essential that the feasibility study should be completed within the proposed timescale of 18 months. The switch to F2+ should then be accomplished within whichever time periods are recommended by the study, even if these differ from the estimates in the original draft.

[1] European Commission (EC) Scientific Committee on Animal Health and Animal Welfare (SCAHAW) (2002) *The Welfare of Non-human primates Used in Research.* EC: Brussels,

[2] APC Primates Sub-committee (2006) *Acceptance of Overseas Centres Supplying Non-human Primates to UK Laboratories*. APC: http://www.apc.gov.uk/reference/primate-sources-report.pdf

4. *Are the proposed extensions to the scope of the Directive justified, and what might be their impact?*

4.1 It is difficult to set out definitive criteria that can be used to judge whether or not species of animal are capable of suffering. Suggested criteria for the ability to experience pain include a suitable central nervous system and receptors; avoidance learning; protective motor reactions such as limping or rubbing; physiological changes; evidence of reduced pain responses with analgesia; and high cognitive ability and sentience.[3] Most vertebrates have been demonstrated to fulfil these criteria and so have many invertebrates, suggesting that either these invertebrates can experience pain or that at least some of the criteria are erroneous or insufficient.[4]

4.2 This means that, to an extent, all legislation that aims to protect animals operates according to a "benefit of the doubt" principle. The key question is how far legislation should go in applying this concept, given the desire to spend resources wisely yet not risk causing avoidable suffering. It is also important to consider and try to weigh the economic, scientific and moral consequences of not protecting species that are capable of experiencing suffering on the one hand, as opposed to including those that cannot suffer on the other.

4.3 We considered the proposed additions to the scope with respect to (i) developmental stages of vertebrate species, (ii) invertebrates and (iii) developmental stages of invertebrates. There will inevitably be an impact if procedures are regulated when they were previously not regulated. However, the APC is not in a position to estimate what this might be in each case.

4.4 Developmental stages of vertebrates

To summarise current research on fetal development and sentience, it appears that the mammalian fetus moves between different sleep phases and may not become sentient until following birth, once breathing has commenced. Reasons for this include oxygen in the blood not reaching requisite levels for higher brain function and the presence of hormones that suppress consciousness.[5,6] However, there are concerns that there may still be transient episodes of awareness and that experimental procedures may arouse the fetus to a temporary state of sentience.[7] There are also concerns that painful stimuli to the fetus might adversely affect welfare after birth, even if the fetus did not consciously perceive pain at the time of stimulation, but no direct studies have tested this.[8] If an experimental manipulation is predicted to cause suffering after birth and the animal is to survive after birth as part of the experiment, then the procedure should obviously be licensed.

4.4.1 The domestic fowl fetus reaches a stage of development at which it is capable of a cerebral state resembling awareness after day 17, which is 80% of the incubation period. It is probably in a sleep-like state for most if not all of the time during the rest of the incubation period, but there is particular uncertainty about the period between internal "pipping" and hatching, when the fetus gains access to atmospheric air.[6]

4.4.2 Taking this current knowledge into account, the APC believes that the precautionary principle should be applied and procedures on the developing mammalian and avian fetus should be regulated. We also apply the precautionary principle because this research has only been conducted on a limited number of species. The proposed period for regulation of the final third of gestation or incubation is arbitrary and not based on any empirical evidence, but then the same is true of the current UK ASPA, which licenses procedures conducted after halfway through development. The APC supports the current proposal for the final third for pragmatic reasons, as there has to be a "cut off point". The half way point works well in the UK so other Member States should be able to comply with a less rigorous limit (NB procedures on the fetus are not published in the annual UK statistics on animal use or centrally recorded; the same approach could be used in the Directive.)

4.4.3 The draft Directive applies to other vertebrates (ie fish, amphibia and reptiles) from the time when they are feeding independently. This is the same as the current UK ASPA and is presumably a precautionary measure in recognition of the fact that these larvae are responding to their environment in a way that suggests sentience. This system of regulation also works in the UK.

4.4.4 An Annex to the Directive could list species-specific developmental stages that have been demonstrated to be capable of suffering, to be revised as appropriate when new knowledge becomes available.

[3] Elwood R W, Barr S & Patterson L (in press) Pain and stress in crustaceans? *Appl Anim Behav Sci.*
[4] Sherwin C M (2001) Can invertebrates suffer? Or how robust is argument-by-analogy? *Anim Welf* 10: S103–S118.
[5] Mellor D J & Diesch T J (2006) Onset of sentience: The potential for suffering in fetal and newborn farm animals. *Appl Anim Behav Sci.* 100: 48–57.
[6] Mellor D J & Diesch T J (2007) Birth and hatching: Key events in the onset of awareness in the lamb and chick. *NZ Vet J* 55: 51–60.
[7] European Food Safety Authority Animal Health and Welfare Panel (2005) *Aspects of the Biology and Welfare of Animals Used for Experimental and Other Scientific Purposes*. http://www.efsa.europa.eu/
[8] Mellor D J, Diesch T J, Gunn A L & Bennet L (2005) The importance of "awareness" for understanding fetal pain. *Brain Res Rev* 49: 455–471.

4.5 Invertebrates

The draft proposal suggests regulating procedures on Cyclostomes (Agnatha), or lampreys and hagfish, referring to them as invertebrates. It is not clear whether this is taxonomically correct. There is a view that, on the basis of morphological and physiological characteristics, lampreys are true vertebrates and hagfish are a sister group of the Vertebrata. However, the Natural History Museum places Agnatha in the Subphylum Vertebrata. The proposal is therefore unclear from a taxonomic point of view and it might have been better to propose regulating procedures on the Craniata, ie all animals having a skull. The APC believes that procedures on Cyclostomes or Agnatha should be regulated in any case.

4.5.1 A number of studies and reviews of recent research on species of cephalopod and decapod crustaceans have concluded that at least some species fulfil many of the key criteria that are generally accepted as necessary for animals to experience pain, as set out above.[9,10,11] Researchers into cognition and pain in these species have concluded that either these animals can experience pain or the criteria for determining this are wrong—which would cast doubt upon the ability of many other non-human animals to suffer.[10] If decapod crustacea and cephalopods are to be given the benefit of the doubt, then scientific procedures on them should be regulated.

4.5.2 This would clearly require resources and presents an ethical dilemma. For example, invertebrates are used in environmental safety studies, including as "replacements" for higher species such as fish and mammals. Including cephalopods and decapods in the Directive will add bureaucratic costs in terms of counting and reporting and could detract from their use in developing alternatives. However, if these animals are capable of suffering, the extent to which they can be regarded as alternatives becomes debatable.

4.5.3 If some cephalopod and decapod species are included in the new Directive, an option to address concerns about counting these animals could be to regulate their care and use but not require statistics on procedures to be submitted centrally, as with procedures on the fetus in the UK. The suggested Annex to the Directive above could also list invertebrate species whose use should be regulated, once there is evidence of sentience.

4.6 Developmental stages of invertebrates

The draft Directive applies to independently feeding larval forms of invertebrate. However, decapod and cephalopod larvae begin feeding soon after hatching and the stage at which the potential for suffering begins is not known. Assuming that research on these animals is to be regulated, it would be in principle neither logical nor desirable from a welfare aspect for regulation to begin at the time when metamorphosis is completed. We are unable to suggest a meaningful "cut-off" point due to lack of scientific evidence and it may be that regulating research on invertebrate larvae would not be realistic at present.

5. *Are the administrative demands that the draft Directive would impose overall proportionate to its objectives?*

5.1 The APC has concerns relating to three Articles and one Section of the proposal.

5.2 Article 21 *(Authorisation of establishments)*

The commission's proposed authorisation and oversight of breeding and supplying establishments, unless qualified, could extend to animal types not purposely bred for laboratory use. The likely increased resource costs of including these animals within the scope of the Directive would not be proportionate to the benefits of doing so, assuming that Member States had other effective national animal protection legislation in place. This may or may not be the case in individual Member States.

5.3 Article 22 *(Suspension and withdrawal of authorisation)*

Suspension and withdrawal of authorisation for minor technical infringements of non-compliance allows no flexibility and would require an establishment to stop all work, requiring animals to be killed. This would be a disproportionate response and with no mechanism for appeal it is unreasonable. It would also be a very strong disincentive to self-reporting, to the detriment of animal welfare. Defining different "levels" of infringement in relation to their impact on animal welfare, and proportionate responses to these, could be a constructive solution (eg see Home Office Inspectorate Annual Reports).[12]

[9] Elwood R W, Barr S & Patterson L (in press) Pain and stress in crustaceans? *Appl Anim Behav Sci.*
[10] Sherwin C M (2001) Can invertebrates suffer? Or how robust is argument-by-analogy? *Anim Welf* 10: S103–S118.
[11] Mather JA (2008) Cephalopod consciousness: Behavioural evidence. *Cons Cogn* 17: 37–48.
[12] http://scienceandresearch.homeoffice.gov.uk/animal-research/publications-and-reference/publications/reports-and-reviews/

5.4 Article 41 (*Granting of project authorisation*)

The proposal suggests that project authorisations shall be granted for a period not exceeding four years. The vast majority of project licences in the UK run for five years; reducing the duration would place a burden on both PERBs and inspectors without providing any obvious gains in animal welfare.

5.5 Section 4: Articles 35 to 43 (*Requirements for projects*)

Some members hold the view that the Directive does not apply proportionality in that the degree of control is not adjusted in relation to the potential harm to the animals. An example is animals humanely killed for tissues. This work would require all the levels of authorisation, ethical assessment and evaluation, and approval as invasive studies on living animals. This is very different to a severe study involving dogs, for instance. Another example is the need for minor amendments to projects, which do not change the severity limit, to have to be subjected to the same process as new licences. Some members believe that this is not appropriate and that levels of authorisation should be proportionate to severity (see also para 6.3.2 below).

6. *Do any of the provisions relating to the authorisation of persons, the requirements for establishments, the inspection regime, or project requirements require further consideration and/or amendment and, if so, why?*

6.1 The APC believes that several Articles require further consideration, as set out below.

6.2 Article 20 *(Authorisation of persons)*

This article should be more prescriptive with respect to ensuring that persons are appropriately trained and competent. It should require that procedures be in place to ensure that prospective licensees are supervised during training until they are able to demonstrate competence through testing and assessment. Demonstrated competence and authorisation should be for an agreed fixed period of time, in respect of specific procedures, and it should be documented. Proper documentation will enable auditing to monitor compliance.

6.2.1 Maintenance of a personal documented training competence record covering designated procedures would avoid the need for applicants to demonstrate competence by practical testing at licence renewal. Member States should recognise and mutually accept authorised documented training competence to conduct designated procedures. A common EU training framework, together with the requirement for continuing education would facilitate this. These provisions would also be in keeping with the spirit of harmonisation and the free movement of skilled persons.

6.3 Article 26 and 37 *(Tasks of permanent ethical review body and Ethical evaluation)*

The APC recommends that the local Permanent Ethical Review Body (PERB) in user establishments should either include a person with expertise in statistics, or be able to access that expertise when required. Expert statistical input at the ethical evaluation stage (Article 37) is also essential, but may be too late to avoid mistakes and unnecessary animal use. It is essential that user establishments utilise appropriate statistical input at the design stage of animal studies, optimise studies before running them routinely and monitor their performance, which all helps with the implementation of the Three Rs.

6.3.1 The PERB should form an integral part of the authorisation process. The scientific progress of all projects should be reported to the local ethical review body, in addition to the other tasks set out in Article 26(1). This process is distinct from ethical evaluation (Article 37) or retrospective assessment (Article 38) by the Competent Authority.

6.3.2 Furthermore, it is not clear how ethical assessment and ethical evaluation will work together, especially where the role of the Competent Authority has been delegated to another body. Some APC members believe that, in accordance with general regulatory principles, the extent of control should be proportional to the harm caused by the procedures and the potential welfare gains of regulation. The level of bureaucracy and burden of costs should be minimised when harms are least, allowing the Competent Authority to concentrate on projects where the harms are greater. Other members believe that all projects should be subject to the same level of regulation and ethical review, with extra scrutiny paid to projects involving procedures that may cause substantial suffering. In either case, proper classification of severity is essential.

6.3.3 If scientific monitoring and reporting of project progress are effective, then formal retrospective review of each project every year by the Competent Authority would add little value to animal welfare. Any formal project review and/or subsequent amendment(s) to procedures by the Competent Authority should be at appropriate times and intervals, depending on the nature of the project. This could be initiated by the PERB.

6.4 Article 42 *(Amendment, renewal and withdrawal of a project authorisation)*

Some APC members felt that it should be possible for mild and moderate project amendments that do not increase the severity classification to be given by the local PERB and only require notification to the Competent Authority. This process would deliver efficiencies, as the local PERB would already be monitoring projects (see above). The PERB should operate within set boundaries and report to the Competent Authority to ensure consistency in its judgements.

6.4.1 Other members did not agree, taking the view that all levels of severity should be subject to the same scrutiny throughout the licensing process, including amendments. There were concerns that there could be a series of amendments, each of which did not appear to alter severity but that ultimately resulted in increasing severity. The local perception of severity levels might drift over time within an institution, without external input by way of comparison. Also, numbers of animals could potentially be increased without affecting the severity level to each one, but this would increase the overall harms to animals of the project.

7. *Are the care and accommodation standards set out in Annex IV to the Directive appropriate, and will they produce an adequate level of harmonisation across the EU?*

7.1 The care and accommodation standards in Annex IV are largely appropriate, if somewhat inexplicit and lacking detail in some aspects. Guidance on the requirements of an increased range of species over the present UK Codes of Practice (CoPs) is welcome, as are other inclusions such as the explicit guidance on adjusted lighting levels for albino animals. The guidance was taken from Appendix A to Council of Europe Convention ETS 123, which was constructed over some 12 years, taking evidence-based advice from a wide range of individuals and organisations with expertise and experience in animal care. However, Annex IV to the draft Directive is an abridged version of Appendix A in which much of the explanatory text is missing.

7.2 As a result, Annex IV is less detailed than the current UK CoPs. A further concern is that it combines guidance for the accommodation of animals under procedure with those for breeding and/or supply. This reflects the fact that the Annex was designed to fulfil the behavioural and physiological requirements of the species in question. The problem lies in that the proposed guidance, as abstracted from Appendix A, fails to take account of the difference in accommodation sometimes needed when animals are under long-term procedures. Pigeons, for example, are often used individually in daily behavioural tests of learning and memory, but under the proposed guidance would have to be accommodated in large communal stock cages where the inability to feed the birds individually would frustrate the running of the experiment. The potential need for different standards for animals under procedure should at least be acknowledged in Annex IV, and it should include a means of applying specified variations that are justified on scientific or animal welfare grounds.

7.3 Much of the advice provided in Appendix A was aimed at preventing basic errors of husbandry and the full text provided encouragement towards good practice, with advisory qualifications. It is a great pity from the point of view of animal welfare that so much of this text was removed when producing Annex IV. It would have been preferable for Annex IV to incorporate both the text and tables from Appendix A.

7.4 Facilities should have the option to adopt additional provisions demonstrated to improve welfare, with advice from the PERB. Reinstating the full text, plus tables, would provide a basic understanding of animals' welfare requirements and how to fulfil them in a flexible way. It would also re-establish the links to the important supplementary information in "Part B" to the species-specific guidelines.

7.5 Annex IV is not prescriptive on air conditions for any species other than reptiles and amphibians, merely stating that temperature and humidity should be "adapted to species housed" and that "the air in the room shall be renewed at frequent intervals". Whilst these are sound principles, this approach leaves their application open to widely differing interpretations by Member States, which raises risk in an area critical to animal welfare. It is engineering tasks that are being legislated on here, and it seems appropriate to set engineering standards for them.

7.6 The current Annex IV does therefore leave scope for a lack of EU harmonisation if some Member States, such as the UK, continue to apply specified standards whilst others merely interpret principles. It seems unlikely that Member States with existing well-developed and explicit guidelines would wish to lower standards, whilst in others the likely increased financial burden associated with Annex IV could well be an incentive to adopting low-cost interpretations, to the detriment of harmonisation and animal welfare.

8. *How satisfactory are the provisions on alternatives to animal testing and National Reference Laboratories (Article 46)?*

8.1 Both welfare groups and the animal user community welcome provisions to speed the development and implementation of alternative approaches that yield the same information, or equivalent information, as that obtained in procedures using animals. However, it is not clear how the Commission and Member States are to be encouraged to contribute to the development of such alternatives. Clearly the UK has taken a major step forward in the establishment of its National Centre for the 3Rs, which we believe is delivering meaningful benefits to animal welfare. Its structure and operation is a model envied by a number of countries, including the US. The NC3Rs does not have its own laboratories for the validation of alternative methods, but instead funds high-quality research in universities and industry and works with the scientific community to deliver alternatives in priority areas.

8.2 The establishment of National Reference Laboratories is a flawed concept. More needs to be done to develop and validate alternative methods, but a proliferation of national laboratories is counter productive. It is essential that a laboratory (or centre such as the NC3Rs) has sufficient expertise and infrastructure as well as adequate funding. It is also essential that research is coordinated and focused on areas of greatest need. A "hub and spokes" approach is one way to achieve this, in which a number of satellite organisations could be linked in terms of their coordinated activities to meet agreed objectives.

8.3 The future of ECVAM and its advisory committee (ESAC) is unclear. Its role should be reviewed and its preoccupation with the validation of alternatives to regulatory toxicity testing should be reviewed. Currently, toxicity testing is responsible for approximately 15% of animal use. There should be increased focus on developing alternatives to the other 85%.

8.4 The role of the Commission in the development of alternatives is also unclear. Its formation a few years ago of the European Partnership for Alternative Approaches (EPAA) with DG Environment was a step forward. Unfortunately, it again focused on regulatory toxicity testing.

9. *Is it appropriate to regulate at the EU level—as opposed to lower tiers of government—in all of the proposed areas? Is the legal base for the proposal adequate in light of the content of the Directive?*

9.1 Regulation at the EU level could provide properly harmonised standards and a "level playing field" across all Member States, which would seem to be desirable. It is essential from an animal welfare and scientific aspect that the standards in the Directive are high. It is also important that Member States are able to implement higher standards than the Directive if they wish to do so.

21 May 2009

Memorandum by Huntingdon Life Sciences

With regard to the above consultation I write to confirm that Huntingdon Life Sciences joins with the UK co-ordinated Bioscience Sector response to the consultation with regard to points of principle concerns within the draft Directive and alternative proposals.

As an organisation we have no specific concerns over and above those represented by the coalition.

18 May 2009

Memorandum by King's College, London

1. Objectives of the Directive.

Harmonisation of rules governing this activity across the EU is a worthwhile aim, but if the new Directive allows individual Member countries to apply more stringent rules, then it may not be achievable. Much of the current distortion has arisen because of this inconsistency of regulation at country level and it is not clear why this would not happen again.

The other objectives of the Directive (improved animal welfare, better application of the 3R's) are also worthwhile.

2. International Competition

Research is a world-wide activity. If EU rules on the use of animals in research become too restrictive, then work will indeed be displaced to other countries where regulations are less stringent. This could have unintended negative consequences for animal welfare and the quality of scientific data obtained, and also adversely affect the competitiveness of research in the EU. One particular example of concern in the draft Directive is the controls on the use of primates (see below).

Requirements to restrict research on non-human primates.

As drafted, the Directive appears not to allow any fundamental research using primates. This would most certainly mean that work of this sort would be displaced outside the EU.

The restriction on the sourcing of primates, so that only second generation captive bred animals may be used, is practical for some species (eg common marmoset), but unproven for other species, and may turn out to be impractical. This could have a major impact on the ability to do pre-clinical research for certain diseases such as Parkinson's disease in the UK, with the possibility that this may drive this area of research to countries outside the EU where experiments are less regulated and welfare may be compromised. There is already evidence that movement of primate research outside the EU is happening (see, for example http://www.scidev.net/en/south-east-asia/features/primate-research-moves-to-china.html). The amendment suggested in the Parish report, which suggests that a feasibility study will be carried out to ascertain if this proposal is practical, seems essential.

The proposed ban on the use of Great Apes is unlikely to have any material effect: a similar administrative control on their use in the UK has been in force for many years and has not had to be overruled for any reason.

Extension of the scope of the Directive

Extension of all the provisions of the Directive to animals bred for collection of organs and tissues for scientific purposes would add a significant administrative burden for little if any gain in animal welfare. The increase administrative and economic burden may in turn reduce practical education opportunities for biomedical scientists, areas where there are established skills shortages. The Parish report proposes that only the provisions affecting animal accommodation and husbandry should apply, and this is a welcome improvement.

Any extension of the scope to invertebrates, and larval/embryonic/foetal forms of vertebrates should be based on scientific evidence of the sentience of these animals, not applied as a blanket ruling.

Authorisations

There are a number of concerns here:

(a) Authorisation of staff who may humanely kill animals within an establishment. This could add significantly to the number of staff requiring authorisation. The Directive suggests there could be exceptions for emergencies, but a more sensible option might be to require such staff to be trained and competent rather than "authorised".

(b) The draft Directive proposes that there are three categories of people who require authorisation, and that they should have appropriate education and training, and have demonstrated the requisite competence. It is not clear how competence would be demonstrated in order to gain authorisation, before actually being given authorisation.

(c) The process for authorising projects is quite unclear:

  (a) Each establishment will be required to set up a permanent ethical review body. Review of projects does not appear in the list of tasks for this body, so it is our interpretation that ethical review of project applications is only undertaken by the competent authority. However, Article 6, para. 2 states that, for projects involving procedures "up to mild", "a reduced project proposal covering only the ethical evaluation and elements listed in Article 41(2)" may be submitted. This is confusing—who does this ethical evaluation that is submitted to the competent authority in this instance? Also, there is an apparent assumption that the applicant will be able to judge that the procedures are "up to mild". What if, having seen them, the competent authority disagrees?

  (b) Article 39 refers to the establishment keeping records of ethical evaluation. Again, this is confusing versus the list of tasks of the establishment ethical review body.

  (c) The draft states that the "user establishment" shall submit applications for project authorisation. While the establishment should be aware of applications being made, it would be far preferable for the person who will be responsible for the particular project to make the application, as they

will be best placed to provide the information covered in Annexe VII. This would also make it clear who was responsible for the conduct of the work, and any deviations from the plan. Individual responsibility if far better than corporate responsibility in this situation.

(d) Article 41 (5) states that the user establishment shall keep records of all project authorisations . . . and submit them to the authority on request. Surely the competent authority will have its own records of the projects that it has authorised?

(e) Article 43 implies that, if the authority does not respond to the applicant in 30 days, and the project is for "up to mild" procedures, then the authorisation should be presumed to have been granted. Again, there is an assumption that the applicant has made a judgement about the severity of procedures that the competent authority agrees with, which seems dangerous.

Care and accommodation

The care and accommodation standards have been converted from guidance, by substituting "shall" for "should". This makes them rigid and inflexible, and less useful than the document from which they derive. Article 32(3) then states that member states may make exceptions for animal welfare reasons, and one can see that many exceptions will be necessary. It is likely that the end effect will be neither the benefit of good but flexible guidelines, nor the benefit of true standardisation in care across the EU. The Council of Europe guidance from which the standards have been derived is a far better document.

Alternative Methods

The requirement for each member state to have a national reference laboratory for the validation of alternative seems narrow and probably duplicative. The NC3Rs in the UK seems a better model—this centre helps support development and validation of alternatives in other laboratories by provision of funding, and also helps promote and disseminate progress in the field.

Subsidiarity and legal base

No comment.

21 May 2009

Memorandum by The Laboratory Animal Breeders Association

The Laboratory Animals Breeders Association of the United Kingdom is submitting evidence focussed on those areas of the proposed revision to Directive 86/609 where its members have observed the most significant impact on their current operations and therefore the future competitiveness of their businesses.

Summary

Our members recognise the need to regulate the use of animals for scientific purposes in the European Union. A small number of specialist commercial breeders of laboratory animals supply the overwhelming proportion of the total number of animals used for scientific purposes both in the UK and other EU countries and are regarded as "critical suppliers" by many customers. Our capabilities commonly extend into key service areas utilising a unique combination of innovation, technical know-how and experience. Laboratory animal breeders and the biomedical research community are interdependent and an impact on competitiveness for the breeder sector has consequences for the academic, biotech, contract research and pharmaceutical sectors.

Our overall assessment is that the proposed regulations will bring additional costs and negatively impact our international competitiveness (Section I below). We assert that disproportionate mechanisms, specifically mandatory and highly detailed engineering standards for housing of stock animals in Annex IV, are being applied to achieve harmonisation and this has not been properly evaluated by impact assessment. The standards in Annex IV for space allocation for stock rodents significantly exceed the enforced UK standards set out in the Codes of Practice which already provide acceptable animal welfare. Flexibility and efficiency in achieving welfare standards will be lost and we will be obliged to divert the entire capital expenditure of our businesses to facility space for rodent and rabbit species for several years to come by enhancing the current UK standards. This will in turn bring additional costs to the whole research sector. Our analysis of the Commission's impact assessment on housing and care (Section II below) indicates it has underestimated the costs while the benefits to animal welfare have been greatly overstated yet these supposed benefits are not even supported by scientific evidence. The Commission has only set out one single policy option for housing and care standards in its impact assessment leading to the housing standards in Annex IV implemented by Article 32 being mandatory yet these are drawn from Council of Europe Convention ETS 123 which titles them as

"guidelines"; likewise the Commission originally published this Convention as a "recommendation" in 2007/526/EC.

This regulation will create an uncertain investment climate in Europe for the commercial breeding of animals for scientific purposes and ultimately could compromise welfare by promoting relocation of activities outside the EU and a fragmentation of our efficient breeding colonies.

SECTION I

Evidence on "specific issues" indicated in the Call for Evidence

1. Objectives of the Directive: harmonisation and proportionality

   (a) We believe that some harmonisation of the framework of the regulations pertaining to the use of animals for scientific purposes is desirable to avoid distortions of the Single Market. Areas where harmonisation has the potential to avoid distortions in the market of relevance to our members include regulation of what sources of animals are permitted for scientific research and which species of animals must be purpose bred for use in scientific purposes. We understand the overall burden of regulation should be similar throughout the market if distortions are to be avoided; however, as detailed below, it appears to us that the Commission is ready to sacrifice competitiveness for an extreme degree of harmonisation that does more to serve intellectual satisfaction of policy than the practical implementation of that policy in a dynamic market and challenging economic environment. We believe the very reasonable policy objectives cited by the Commission can be achieved with a lighter touch of regulation while still serving the needs of animal welfare.

   (b) In the proposed Directive, the level of detail in some areas proposed for harmonisation goes far beyond what is required. The key example of this of direct relevance to our members is in Annex IV referred to in Article 32 which would set down as mandatory very precise "engineering standards" as they relate to the housing space allowances for all animal species likely to be used in scientific research. These engineering standards relating to cage sizes are not supported by scientific references, neither in the expert reports prepared for the Council of Europe revision to ETS 123 which recommended them as guidelines, nor in the Annex of references in the Commission's impact assessment. This is in contrast with the more meaningful "performance standards" set out in the general section of Annex IV which promote sound practices in animal care underpinned by scientific references. Although these detailed standards will permit more harmonisation, this is very much at the expense of competitiveness and will result in our obligation to undertake very significant costs when the economic climate is so adverse.

   (c) Our view is that to cite mandatory housing space allowances for all classes and species of laboratory animals is a disproportionate response to avoid a distortion of the Single Market. The market is a very complex and there are many factors which influence the costs of operations, the revenue operations generate and therefore the profitability of the business. Of particular relevance is the cost of transportation of small laboratory animals such as rodents as this can be a significant component of the cost to the end user, and of course, this is a factor that is independent of the cost to produce and house the animal until its despatch.

   (d) Cages sizes and stocking densities are not the exclusive determinant of fairness of competition and there is no evaluation in the Commission's own impact assessment of the diverse range of other operational factors and market forces. The Commission's impact assessment has been distorted by the assumption that cage sizes are an overwhelming factor in determining business competitiveness within the EU in this particular market.

2. International competition: competitiveness

   (a) Higher welfare standards involving more generous space allowances imply higher costs and in this regard there will be a negative impact on the competitiveness of our industry. The current proposals would require our members to commit our entire capital expenditure for several years to come to expand current facility space while at the same time accepting the legislation is aimed at reducing the market for these very same animals. Our investment would result in increased costs which will have to be absorbed by the biomedical research sector and would be made at a time when there is a very unfavourable economic environment.

   (b) Of particular relevance to our members are the mandatory space allowances specified in Annex IV of the proposed Directive as these are generally much more generous than those mandated as minima in third countries. Likewise the space allowances for stock rodents and rabbits are significantly more

than those required under the current UK Codes of Practice issued under Animals (Scientific Procedures) Act. As stock animals at breeders are supplied to all users for scientific purposes, any additional costs will inevitably be absorbed in both the private and public sector; likewise incremental upward adjustment of space allowances will increase the costs to house animals and therefore diminish the available investment in other areas.

(c) As stated above, the regulation being considered aims to reduce the market for laboratory animals while requiring further investment in facility space. This creates an uncertain investment climate and is compounded by a diminution of our international competitiveness which could lead to private sector investment being made outside the EU. This could have the consequence of further diminishing the market for our members in the EU and neither aids nor favours long term capital investment decisions.

3. Care and accommodation (Art. 32): standards producing harmonisation

(a) Article 32 of the proposed revision to the Directive makes Annex IV mandatory and this highlights regulatory creep by adoption of recommendations and guidelines as normative standards. In this regard it should be noted that Annex IV is derived from the Council of Europe Convention ETS 123 Appendix A titled as guideline; likewise the Commission originally published this same Convention as a "recommendation" in 2007/526/EC. The expert reports which form the basis of the species specific provisions used for ETS 123 Appendix A are pertinent as best practice was used to inform the guidelines, usually upgraded from current UK standards, when scientific evidence or references were lacking. Indeed the report from the expert group for rodents and rabbits is explicit in Section II.1.1 ". . . the exact numeric values for minimum cage sizes and heights as well as for maximum stocking densities can never be scientifically evaluated and "proved". Working out minimum requirements with respect to animal welfare and to supposed well-being of laboratory animals is a political question".

(b) Mandating the standards in ETS 123 Appendix A will certainly assure harmonisation but only on the assumption each EU country implements, inspects and enforces in a similar manner. However, harmonising by upgrading to such high standards which lack scientific evidence implies significant actual cost with a compromise to competitiveness.

Section II

Evidence on "additional issues" to those indicated in the Call for Evidence: Analysis of the Commission's Impact assessment on for EU Directive 86/609 and the proposed revisions relating to Article 32 and Annex IV

1. The full impact assessment for this proposed Directive published by European Commission (Commission Staff Working Paper SEC(2008) 2410/2, Impact Assessment) is flawed in several key respects due to the incomplete and inconsistent data analysed. There are several arguments for why the impact assessment justifying the chosen option to adopt Council of Europe Convention ETS123 as a minimum standard is not valid. Key elements from the impact assessment are discussed in the paragraphs which follow.

(a) We believe the assessments are not robust due to the limitations highlighted on page 8 of the full impact assessment regarding the contracted survey to gather the data: "The results of this survey were by far not as complete, detailed and fact-based as expected because many respondents were not able to provide new facts and figures on the use of animals for scientific purposes in their establishment or country. As only relatively limited data was available, the contractor (Prognos) developed a model about benefits and costs, and derived qualitative hypotheses from it about possible impacts of the respective options".

(b) Although a percentage of establishments is quoted on page 48 of the impact assessment as complying with the new standards in CoE ETS 123 Appendix A, this figure is specified as a "preliminary finding" and therefore cannot be relied upon given the diversity of respondents and non-respondents to the survey. The full survey data have never been published. In fact the sampling through the survey is likely to be biased towards those users who are more likely to be in full compliance and does not take account of how a small number of breeders supply the overwhelming majority of animals to user establishments.

(c) Our members found the questions in this key survey in 2006 to be ambiguous and open to interpretation. We would assert other respondents would share our view. This no doubt has lead to a great deal of extrapolation by the contractor (Prognos) which has not assisted the Commission to produce an objective impact assessment.

2. Three main documents have been published and are available on the DG ENV website: http://ec.europa.eu/environment/chemicals/lab_animals/ia_en.htm

(a) Commission Staff Working Paper SEC(2008) 2410/2, Impact Assessment.

(b) Commission Staff Working Paper SEC(2008) 2411/2, Summary of the Impact Assessment.

(c) Prognos Report June 2007, "draft summary", Study on the impacts of different options for the Revision of the Directive 86/609 on the protection of laboratory animals.

3. The only option considered for "housing and care standards" (page 36 of the impact assessment) was to require "as a minimum standard compliance with the revised Appendix A of Council of Europe Convention ETS 123".

(a) This option ignores that Appendix A of ETS 123 is clearly titled as "Guidelines for the accommodation and care of animals" and its formulation was never intended as minimum normative standards given the diversity of systems in use.

(b) It is also of note that Commission Recommendation of 18 June 2007 is "on guidelines for the accommodation and care of animals used for experimental and other scientific purposes (2007/526/EC)" and recommends "Member States should pay regard to the guidelines set out in the Annex to this Recommendation".

4. The impact of the proposed regulation is significantly understated (page 70 of impact assessment): the benefit in terms of animal welfare is overstated and not supported by scientific evidence while the monetarised costs are understated and incomplete. Therefore the impact of the chosen option (page 85 of impact assessment) is not properly assessed. Also given a very significant burden of costs will fall on a small proportion of all establishments, no attempt has been made to consider this.

(a) The species-specific sections to Appendix A are based on proposals by expert groups but the experts make clear that scientific evidence was often not available. Section 4.5.1 specifies the space allowances as being "suggested minimum animal enclosure sizes" and these are included in the species specific sections. Section II.1.1 of the rodent and rabbit expert working group report states " . . . the exact numeric values for minimum cage sizes and heights as well as for maximum stocking densities can never be scientifically evaluated and "proved". Working out minimum requirements with respect to animal welfare and to supposed well-being of laboratory animals is a political question".

(b) It is strongly asserted in the Impact Assessment on page 48 that animal welfare will be enhanced and the major changes are related to cage sizes. However the scientific evidence for these specific enclosure sizes is not referenced in the expert working group report for rodents and rabbits and is not included in the Annex to the Impact Assessment though references are included to justify the other more general standards (pages 92 – 93).

(c) There is no monetarisation for the upgrading of small animal facilities and for the capital expenditure that would be required; this is a significant impact as the costs will contribute to the users costs. For this reason the costs of implementation are significantly underestimated (pages 70, 71, 77). The omission of capital expenditure also means that the impact on those small number of breeders providing the vast majority of animals has not been evaluated and this cost for breeding facilities is extremely high in relative terms to user facilities given this is the focus of their work. Furthermore there is no acknowledgement that the capital expenditure which will be demanded must be considered as being relevant when considering the transitional period and that the operational changes required will demand re-equipping and construction of new facilities to breed and supply the same number of animals.

(d) The impact of the chosen options (pages 70, 85) are not properly assessed given that a very significant burden of costs will fall directly on a very small proportion of all establishments given the impact on breeding establishments. Therefore the burden of the cost will be directly absorbed in a disproportionate manner by breeders before these costs can be absorbed more generally in the market place through increased pricing. How markets respond to an increase in pricing is a major factor in determining whether a level playing field is retained.

5. The policy objective of reducing unfair competition and distortion of the internal market (page 29) is focussed on costs for breeders due to housing standards and fails to acknowledge that the market and market forces are a great deal more complex

(a) Cages sizes and stocking densities are not the exclusive determinant of fairness of competition and there is no evaluation in the impact assessment of the diverse range of other operational factors and market forces. The impact assessment has been distorted by the assumption that cage sizes are an overwhelming factor in determining business competitiveness within the EU.

(b) The imposition of minimum enclosure sizes imposes a burden which diminishes competitiveness with respect to third counties and this indirectly could diminish animal welfare by creating a disincentive to continue to invest in European versus US or Asian operations for global companies.

6. The policy objective of a significant improvement in animal welfare cites minimum criteria for housing and care but the benefit to animal welfare is not supported by scientific evidence

(a) It is strongly asserted in the Impact Assessment on page 48 that animal welfare will be enhanced though the major changes are related to cage sizes. However the scientific evidence for these specific enclosure sizes is not referenced in the expert working group report for rodents and rabbits and is not included in the Annex to the Impact Assessment though references are included to justify the other more general standards (pages 92–93).

7. There is no policy objective (page 29) relating to competitiveness and the risk of allowing activities such as breeding and supply to be conducted from third countries which do not fall under the scope of this proposal to revise the Directive

(a) The imposition of minimum enclosure sizes imposes a burden which diminishes competitiveness with respect to third counties and this indirectly could diminish animal welfare by creating a disincentive to continue to invest in European versus US or Asian operations for global companies.

8. The impact assessment has not considered the standards which are currently inspected and enforced in other countries and whether those standards meet the requirements for high quality animal welfare.

(a) A strict and detailed Code of Practice has existed in the UK from 1986 with reduced stocking densities in relation to those proposed in the revised Appendix A of ETS 123. The UK stock holding floor space allowances have never been cited as being inadequate or directly leading to compromises in animal welfare.

(b) The UK has had a strict regulatory inspection regime that has included the breeding facilities for all species within its scope and the UK has been continuously self-sufficient in breeding and supplying animals from within its borders. This significant use of animals combined with a strict inspection and monitoring regime has not been considered in the impact assessment and is significant practical evidence supporting appropriate standards in animal welfare.

9. There is a contradictory assertion for which there is no evidence regarding the transitional period which would be required by breeders given the facilities are continuously used and close to full capacity.

(a) The assessment on page 48 of the analysis of impact relating to the housing and care standards is incomplete in its consideration of the translational period which would be required; specifically there is no evidence put forward to contradict the information cited in this paragraph from Prognos report that a 10 year transitional period is required to indicate the conclusion ". . . breeding establishments can be expected to be able to cope with the new requirements earlier".

20 May 2009

Memorandum by The Mauritian Cyno Breeders Association (CBA) and Noveprim

The Mauritian Cyno Breeders Association (CBA) is a registered association regrouping all the Cynomolgus monkey breeders in Mauritius.

The CBA wishes to express its views on the proposed revision of the european directives for the supply and use of NHPs in scientific procedures, and mainly the restriction for the use of second off-spring generations (F2).

Mauritius exports over 4,000 macaques to the EU every year. The production of F2 in Mauritius, as requested in articles 9 and 27 of the directive, if imposed, will generate a number of long term consequences which we wish to bring to your consideration.

1. CONSERVATION ASPECTS—CONTROL OF ALIEN SPECIES AND IMPACT ON INDIGENOUS FAUNA AND FLORA

The macaque is not indigenous to Mauritius and is considered by the National Conservation Authorities to be a nuisance to the environment: indigenous rare birds (destruction of nests and eggs), endemic trees (destruction of slow maturing fruits) and crops (sugar cane and vegetable crops). To date the Mauritian authorities have been encouraging breeders to trap from the wild as a means of controlling the population of macaques. For many years now a number of foreign NGO's have also been spending large amounts of money for conservation of indigenous species in Mauritius.

Well managed trapping of monkeys for breeding purposes does not raise serious animal welfare concerns in the light of current breeding and animal care practices. The Cynomolgus macaque is known to be highly adaptable to captive conditions when used for breeding purposes.

An increase in the wild macaque population in Mauritius would have a serious impact on agriculture and indigenous fauna and flora, and this may lead to control by culling or hunting.

2. PROBLEMS RELATED TO BREEDING OF F1 MACAQUES FOR F2 PRODUCTION

We believe that very few breeding centres in the world have the experience of F2 generation and their physiological performance.

In Mauritius, a program to increase F2 production has resulted in health and productivity problems, such as:

- Higher incidence of obesity.
- Earlier onset of Type II Diabetes.
- Premature ageing.
- Higher rate of infanticide/aggression by F1 males.
- An increase of abandoned babies, malnutrition and generally improper infant care from F1 breeders.

F2 production is thus much slower than anticipated because:

- Of lower reproductive rate of the females.
- Breeders have to be replaced at an earlier age than anticipated because of premature ageing.

Breeding from F1 females will increase inbreeding, especially in Mauritius where the original wild colony came from a few individuals only. We cannot forecast the effect of inbreeding with F1 breeders on the long term. Several problems have been experienced with small Mauritian F1 colonies and it is too early to know whether these will be manageable on a larger scale.

3. WELFARE ISSUES

The advantages of F2 as regards animal welfare are doubtful:

A significant increase in the number of animals to be kept in captivity will be necessary to produce the same number of offspring.

In most of the cases, experimental protocols require both genders in equal proportion. Because a significant number of females need to be set apart to replace retired breeder females, there will be a surplus of males which cannot be absorbed by research laboratories. These excess unsaleable males will need to be euthanised.

4. LEAD TIME AND AVAILABILITY

A fast transition to F2 breeding will have a serious impact on availability of animals for research over the following years.

It would take several years to produce F2 offspring in the same quantity as the F1 offspring presently produced and exported.

As stated above, a program to increase production of F2 animals generated several breeding and management problems and this has lead to a pessimistic forecast as regards sole production of F2.

From our experience it appears that the young feral female is a better mother to its first offspring. The first baby from a captive F1 breeder is seldom viable. The F1 breeder therefore has to be sustained for at least five years before being productive.

At present the demand for F2 offspring is insignificant and mainly confined to the UK. F2 offspring produced in Mauritius are presently sold together with the F1 without distinction. Demand for F1 animals cannot presently be fulfilled, making it difficult for breeders to keep significant numbers of F1 offspring and mature them for breeding.

F2 production leads to lower availability of F1 females for research and thus reduces the availability of older, mature animals.

In order to meet requirements, with F2 animals only, the total number of captive animals for breeding purposes would have to be at least doubled. This means that there will be a serious shortage of monkeys for research for several years while the number of F1 breeders is being increased.

5. Financial Consequences

As the breeding colonies will have to be extended to generate sufficient F2 animals for the EU, the price of monkeys in EU will increase seriously as a result of increased costs.

Should Mauritian breeders have to move to F2 breeding, the substantial cost increases would be passed on the users in the EU. These costs increases may result in primate research leaving the EU, with negative effects on pharmaceutical and biotechnology research.

Higher costs are due to:

— F1 females being kept longer before they can produce offspring: the first saleable offspring requires six to seven years lead time from the date when the F1 female is selected.

— F1 females kept for breeding reduce the number of saleable females and further, the male that would be sold as a pair becomes unsaleable, ie a 50% loss of income.

6. Quality of the Mauritian Industry

The members of the CBA in Mauritius have become world reputed breeders and suppliers of high quality Cynomolgus monkeys. The main reasons why laboratories buy Mauritian macaques are:

— Mauritius macaques have the unique advantage of being naturally SPF, and are sought after for health and safety reasons as they do not carry the Herpes virus simiae, which can be fatal to humans. This is important to reputed laboratories committed to the protection of their employees. Mauritian macaques are also naturally free from SRV, SIV, STLV, rabies and a number of other contaminants.

— Mauritian breeders have put the accent on quality, most of them are AAALAC accredited today and follow European animal welfare and care recommendations.

— Mauritian breeders have long established supplier relationships with reputed European biomedical laboratories.

7. Our Position

There is no commercial interest to produce F2 animals; the only interest is the knowledge of the technique required for F2 production.

The alternatives available to Mauritian breeders are:

— Turn to other markets which will continue to use F1 animals.

— Maintain small F1 breeders' colonies which have little economic impact on the company.

— Increase the price of saleable animals to compensate for unusable males.

The Association strongly believes that moving to closed F2 producing colonies will have a detrimental consequence on the research community, both in terms of price and animal quality.

The consequences on the Mauritius eco-system will also be serious in that rare birds and plants, already on the verge of extinction, will have to face an increasing number of predators.

We thank you for your consideration.

6 May 2009

OPINION OF NOVEPRIM ON THE USE OF PRIMATES OF F2 GENERATION IN RESEARCH

The objective of this document is to demonstrate the consequence of the transition to F2 generation for the use of primates in research, from a Mauritian breeding perspective. This opinion is supplementary to the letter from CBA addressed to the House of Lords on 06 May 2009 (see CBA letter annexed).

1. Status

Every year, approximately 4,000 Mauritian macaques (Macaca fascicularis) are exported to the EU Laboratories. 60% are supplied by Noveprim.

Our housing structures, sanitation and health care programs are regularly assessed in order to be in strict conformity with EU and international standards. The different systems we use to ensure high quality include: ISO 9001 and British Home Office certification since 1998, AAALAC accreditation in 2006, and the Noveprim Ethics Committee complying with the US norms created in 2006.

2. Financial Implications

We believe that the financial implications relating to the production of F2 has not been taken into account in the Impact Assessment in reviewing directive 86/609.

The transition from the breeding of F1 to F2 generation means that we must build new accommodation facilities, keep and look after young animals for a longer period of time; more so that we cannot dispose of them.

The cost of the whole project would include:

— Structural and operational investments estimated at Euros 50 millions for the entire Mauritian breeding industry, which represents two years revenue.

— A reduction of the number of animals available for laboratory research.

— A 50% increase on the price of one macaque compared to the price of a macaque of the previous generation.

These significant investments are concomitant to a substantial decrease in the revenue and there is no guarantee on return.

If the laboratories decide to take the responsibility of the expected investment, the purchase of one macaque would cost them approximately 10,000 Euros at a certain time, and this equates to three times more than the present price. It is highly improbable that the laboratories would support this venture.

It is therefore highly unlikely that, without financial assistance, the breeders would commit themselves to a strategic venture which is so complex (the know-how of F2 macaque breeding is still very poor), so costly and uncertain. They would prefer to explore other markets.

Moreover, big pharmaceuticals companies and research institutions have already embarked on a process of relocation outside the European Union and they have requested us to export our monkeys to these destinations. The revised EU directive would encourage the research centres to access these markets and more so as the regulations enforced on animal welfare and sourcing are much more flexible in these jurisdictions. These countries are numerous, both in Asia and in the USA.[13]

3. Other Salient Features

3.1 *Genetics*

The production of F2 animals in Mauritius will not contribute anything in the genetic homogeneity, in as much as only very few animals were imported to the island from Indonesia, 400 years ago. Since then, nonhuman primates have not been imported from elsewhere and the Mauritian colony has not been exposed to other genetics mix. Therefore, its genetic variability is extremely low. This peculiarity coupled with the excellent health status of Mauritian macaques is not to be found in any other population of the same species and this is highly valued by researchers.

[13] European demand for macaques in research is estimated to be less than 15% of the worldwide demand.

3.2 *Conservation*

The existence of macaques in Mauritius has disastrous effects on the endemic fauna and flora and on agriculture (see enclosed report of Dr Greenwood, 2008). The only means for effective control over savage macaques is capturing them for breeding purposes. If these practices stopped, the government would have to find alternative ways to control the population of wild macaques. The production of F2 will not thus end the practice of capturing wild macaques in Mauritius.

With regards to this aspect and the previous one, we are convinced that Mauritius should be considered as an exception.

3.3 *Ethics and animal welfare*

Noveprim observes the highest standards of care for the welfare of animals. Its Ethics Committee complies with rigorous US norms and guarantees the welfare of animals in all protocols relating to the breeding processes.

We invite your attention to the following negative impacts that shifting to F2 will have on animal welfare:

— Keeping a higher population of animals in captivity for a longer period of time.

— Euthanasia of the undesirable surplus male population while the F1 females are put in the breeding process. This will affect few thousands of animals per year in Mauritius.

4. Conclusion

We are of the opinion that the obligation of using F2 macaques in the new directive would inevitably have as primary consequence the de-location of the research institutions from the European Union, and relocation of same in countries where the law affords a greater flexibility. As a direct consequence, the main objective of animal welfare will be compromised.

The logic behind the F2 project is to protect the species and genetic homogeneity, and yet, this is simply not applicable to Mauritius.

From a scientific perspective the disparity that would occur in terms of research between the European Union and the rest of the world would be enormous.

For the reasons given above, we are confident that the F2 project would not be unilaterally imposed upon the European research community.

Kindly note that we are even prepared to discuss this subject with your experts and we will be pleased to provide additional information.

5 May, 2009

CONSERVATION AND THE LONG-TAILED MACAQUE IN MAURITIUS

Background

This report has been generated from my findings on a short study visit to Mauritius in July 2007. I was able to discuss the important aspects of both the conservation status of the Long-tailed macaque population in Mauritius, and the adverse effects that population may have on endemic Mauritian habitat and wildlife, with a range of stakeholders. These included two of the major primate breeding and export companies, colleagues at Mauritian Wildlife with whom I have worked on Mauritian fauna conservation for 14 years, officials of the Forestry Service and the National Parks and Conservation Service (NPCS) and their minister, the Minister for Agriculture.

Introduction

Primates are not a part of the endemic Mauritian fauna. The sole representative found there is the long-tailed macaque (*Macaca fascicularis*), which was introduced by Portugese traders in the 16th or 17th century from its natural range in South East Asia. The range of the species, which is the most successful primate in that region, covers most of peninsular and insular SE Asia, from Burma, Thailand, Malaysia and Indonesia to Indochina. It is not found in mainland China *per se*. The species has been introduced deliberately to a number of other islands, including Papua, Palau and Hong Kong, with a view to establishing controlled populations as sources for research animals, but in none of these areas has it been as successful as in Mauritius. In Papua, however, although the population is only about 60 animals it is already regarded as a severe invasive threat to biodiversity.

The IUCN conservation status of its various named subspecies, with one exception, is Low Risk/Near Threatened and the CITES listing is Appendix II. There is no clear estimate of the world population, but Malaysia alone claims a population of 740,000 animals. The world total is likely to be in excess of 2 million. The main conservation threat to the species in its native range is probably habitat destruction for biofuels. Most host countries afford it some degree of protection but Malaysia has recently lifted a ban on capture and export.

Biology

The long-tailed macaque is an arboreal, largely frugivorous, monkey living in varying sized groups, depending on habitat. Diet also may depend to some extent on habitat, with crabs and other sea creatures being more important in mangrove forests. Habitat includes almost any kind of available forest, and the monkey does well in degraded plantation regrowth from where it can forage on agricultural crops, to which it is an important source of damage throughout its range. Macaque populations are capable of high reproductive rates when not at full carrying capacity, with rates of 0.1 to 0.9 young per fertile female per year being recorded in *M.fascicularis.*

Mauritius Population

There have been two historical estimates of the Mauritian population of the long- tailed macaque, one in 1986 and another in 1994, and both arrived at similar estimates of 25–35,000 and 40,000 respectively. These were arrived at by establishing home range and troop size, or by estimating the density in one area of habitat and then multiplying up by the available habitat on the island. There is no evidence that either the population or the available habitat have changed substantially in the last 20 years, and guestimates offered to me by the two major trapping companies agreed with a stable population of around 40–50,000 animals. Trapping activity by these two companies has persisted since 1985 and 1990 and both reported a consistently sustainable take, based on the sex and age distribution over limited areas of land. Current annual removal rates are estimated to be around 12%. It is likely that the population remains at or near maximum carrying capacity for the available forest areas, although there are signs that secondary forest regrowth is increasing and this might accelerate with gradual withdrawal of sugar cane production from more marginal land. Current available monkey habitat covers about 20% of the island's land area.

There is a captive population of 18–20,000 animals spread between the three main breeding farms, all of which derive from the original feral population and subsequent captive reproduction.

Genetic studies of the Mauritian population suggest a limited founder population and a lack of genetic variability in areas such as the MHC complex, which actually increases the attractiveness of the animals for research. There is no indication that genetic homogeneity is adversely affecting the population.

A very similar situation obtains with the vervet monkey (*Chiorocebus aethiops sabacus*) on the Caribbean island of St Kitts, although the captive population is much smaller and some 5000 animals a year are harvested from a population estimated, similarly, at 40–50,000.

Captive Colonies on Mauritius

The long-tailed macaque has been harvested and bred in captivity on Mauritius in a controlled way since 1985 to supply the laboratory animal market in Europe, Japan and the USA. There are three main suppliers with colonies of 6,800, 2,500, and 9,000 animals, and a fourth trapping organisation has recently been licensed. The market was originally supplied with wild-caught animals, but now there is little demand for these (they cannot be supplied into the UK, for example) and the vast majority of exported animals are captive-bred on Mauritius. Feral animal capture is now limited to the requirement for breeding replacements and for urgent pest control when requested. The annual take of females is about 4,000 between the three companies and none of these is exported. This provides for an approximate 10% replacement rate of breeders plus expansion, helped by a further 10% of captive-bred females which are retained annually. Males, of course, are caught as well in about a 60:40 ratio, but few of these are required for breeding replacements as the usual colony group ratio is 2–3 males to 30–45 females. One company still exports about 1,000 captured males per year, although this is a declining trade. Mother culls very young or old males, and keeps or releases the rest. One company felt that they were at maximum trapping effort, as many areas of degraded forest are too dense for trapping, and animals become trap shy.

Total annual take is around 6,000 animals. This is probably sustainable at the higher level of population estimates, and one company did suggest that the average age of trapped animals was decreasing slightly, which might suggest either that the population was growing, or that older animals were gradually being trapped out. General indications are that the population is stable or possibly still increasing as new habitat becomes

available, but accurate information is badly needed. Animals are trapped in relatively local areas, and results may not reflect the island-wide situation. Trapping success is affected by season and particularly by cyclones.

Worldwide demand for this species is about 50,000 animals per year (although it was estimated at 100–200,000 in 2001), with a particularly high demand for two-year-old animals of even sex ratio. Mauritius currently supplies 8–10,000 of this trade from captive-bred stock and Mauritian animals command a premium because of their natural freedom from most major primate viruses. There is a 20% price premium for captive-bred over feral animals. The remainder of the world demand is supplied from South-East Asia (see below).

Trade Elsewhere

The other major trade source of long-tailed macaques is China. Some animals are bred in colonies established from wild stock by the Chinese in range states, such as Cambodia and Vietnam, but there are reportedly many wild caught animals going directly into the trade, and China holds some 47,000 animals in breeding colonies which have originated from outside China. There is also a possibility of Malaysia reentering the trade with wild-caught animals. The level of take in the natural range is completely unknown, and no attempt has been made to assess its sustainability.

Conservation of the Long-tailed Macaque in Mauritius

There is no evidence that the Mauritian population is in decline, nor does it appear to suffer numerically from the current rate of trapping. In the future, unless the trade is adversely affected by external factors, this is unlikely to change, although there may be occasional higher pressure if, for example, new licencees attempt to build up new colonies. If anything, trapping rates will probably fall as the demand for wild-caught monkeys continues to fall, and captive-bred output continues to increase. Government, conservation and agricultural interests are currently more concerned about the effects of any possible increase than decrease in monkeys. Consequently, there is an urgent need to establish studies into the population size, biology and behaviour of the monkeys on the island. This would allow the development of a management plan agreeable to all parties.

In worldwide terms, the conservation of the Mauritius population is not currently of any importance, although it may become so if the Asian population is devastated for any reason. The Mauritian population does not have established sub-specific status, and derives from a low founder base.

Adverse Effects of Monkeys in Mauritius

Agriculture and the public.

The scale of agricultural damage by monkeys on Mauritius is considerable, and is likely to increase as more small to medium scale fruit and vegetable production begins to replace sugar cane plantations. Sugar cane damage has been estimated at £1–2 million (10–20 million rupees) a year, and on some estate plots can reach 1 million rupees alone. Much of the damage is caused by large troops of monkeys uprooting and damaging young sugar plants, as well as by actual consumption. This is largely confined to the edge of plots but, as the cane fields currently extend right to the edge of existing woodland, this can be considerable. Small-scale production is almost impossible because of monkey damage, and whole small farms have been destroyed overnight in some cases. In these cases there is concern that small farmers will regard the neighbouring forest as a haven for monkeys and seek to cut it back from their property.

Even more attractive to the monkeys are fruit and vegetable plots and, in this case, whole plots are regularly destroyed, again with far more damage than consumption. Although the monkey has not yet become an urban pest species as it is in parts of Asia, suburban plots and gardens can be hard hit, and the government traps and destroys a number of monkeys following suburban complaints. Raids always increase in the dry season (July-September) and this is also the only period when trapping to eliminate damage is effective, otherwise the monkeys just have too much food available to risk entering a trap. Although there is no direct reporting or compensation scheme in place which might allow monkey damage to be quantified, industry estimates are probably quite accurate. As the breeding and export companies are partly owned by big sugar estates, the response to trapping in terms of damage reduction could probably be determined quite easily. More data are clearly needed.

Direct public injury by the monkeys, unlike in Asia, is rare in Mauritius but anecdotally increasing, especially as government has successfully encouraged wider visitor access to protected forest areas where monkeys flourish, and where public rest and picnic sites have been established.

Environment and native species

Plants—the indigenous plant population of Mauritius includes many extremely rare endemic species of tree and others which are critical to the re-establishment and renovation of native forest, which currently occupies 1% of its original range on the island. Much of the existing native forest is heavily degraded by overgrowth of invasive alien species. Attempts are being made to restore forest by weeding out aliens from managed plots, thereby allowing native tree regeneration. There are seven mainland protected plots, covering 200 ha which are fenced to keep out deer and feral pigs, but monkey-proof fences are prohibitively expensive.

Monkeys damage the forest in several ways: by uprooting seedlings, by wastefully damaging and eating the fruit of native trees before it is ripe enough for the seeds to germinate (unlike trees in native primate habitat Mauritian endemic trees have not evolved defence mechanisms against monkeys), by breaking branches of mature trees and uprooting seedlings, and by spreading the seeds of invasive shrubs (such as Guava) through their faeces.

Wildlife—Mauritius is home to some extremely endangered and iconic bird species, as well as important reptiles, and these birds are the subject of intensive restoration projects. The birds are intensively monitored, especially during their breeding season, so incidents of monkey damage are recorded quite frequently, and some experimental work has been done. There is no quantification of the damage, and other alien species are also involved (rats, mynah birds), but monkeys certainly damage the nests and take the eggs and nestlings of Pink pigeons, passerines and even Echo parakeets.

Experimental work has shown that the feral monkeys show egg-orientation, and this is not seen in captive animals. It appears therefore to be a learned cultural behaviour in Mauritius.

While the kestrel and the parakeet are not at such risk, as the kestrel can defend its nest and the parakeet nests are largely protected against climbers, the pigeon and the small passerines are extremely vulnerable and there are many field records of observed predation, and many others where the signs indicate monkey predation. The damage to pigeons, in particular, includes tail feather loss in adults, removal of eggs and squabs, causing of nest desertion by general harassment, and stealing from feeding hoppers. Passerines, such as Mauritius fodies, suffer complete nest destruction and have been driven to nesting in non-native Japanese cedar trees which monkeys find hard to climb.

Any conservation efforts towards the exclusion or reduction of non-indigenous competing birds is likely to make the situation worse. In the National Park Bioculture, which has the trapping concession, is usually requested to trap out small areas where reintroductions or translocations are taking place, but with the smaller passerines mammal predation pressure is so high that all current releases have to take place on rat/monkey free off-shore islands.

Conservation benefits of the monkey trade

The government has established an "export tax" on the industry of 75US$ per animal, and this was seen from the very beginning as a hypothecated tax. A committee within the Department of Agriculture oversees the distribution of this money, which is paid into the National Parks and Conservation Service Conservation Fund at the current rate of around 600,000$ per year, being additional to NPCS core funding. NPCS uses the money towards its species and habitat work, and also funds some aspects of the work of Mauritian Wildlife Foundation. Unfortunately, unused money from the find is returned to the Treasury on an annual basis for general government spending. Any reduction in NPCS core funding or activities such that it cannot fully use the available funds may lead to serious amounts of conservation money being lost.

The major monkey supply companies also do conservation work, led by Bioculture which funds extensive field conservation and habitat preservation in both Mauritius and Madagascar directly from monkey-related profit

The degree to which monkey harvesting at its present scale assists conservation of Mauritian indigenous wildlife is very hard to quantify, but all interested parties are agreed that the process is at least keeping the monkey population from outgrowing the available resources and is thereby preventing an explosion of competition in the forest. Targeted harvesting, along with other predator control methods, is certainly beneficial in the short term to allow newly created satellite populations of reintroduced birds to become established.

Conclusions

There is no evidence that the monkey trade, insofar as it involves harvesting of wild macaques on Mauritius, materially affects the conservation status of the long-tailed macaque, either worldwide or locally. The local population has no conservation value to the species as a whole and is indeed an introduced alien, which in many situations would be a target for eradication. In the absence of any direct population survey data, trapping data have to be relied upon. These in general indicate at least a stable population over a considerable period of trapping effort.

There is no desire in Mauritius to eradicate the monkeys. They are seen as an established part of the fauna and are important to the predominant Hindu religion. The export trade for medical research seems to be generally accepted as beneficial for the economy and for mankind in general. On the other hand, there is clear and substantial conservation and agricultural damage from the monkeys, so there will always be pressure if not to reduce their numbers then at least to prevent them increasing. There is also an increasing but as yet limited risk of negative public interaction with monkeys as people venture more into the forest for recreation.

There are many and complex competing issues involving the long-tailed macaque on Mauritius and, in my view, all of these could be in some way clarified, if not solved, by a proper population survey of the species, as well as by direct research to quantify the plant and wildlife damage it causes. This should be a priority for government, the wildlife organisations and, above all, the industry. But the harvesting of monkeys for breeding and export is not a conservation issue *per se.*

Acknowledgements

For organising my visit and arranging meetings, as well as for direct input on the conservation issues, Vikash Tatayah and colleagues at the Mauritian Wildlife Foundation.

For information on monkey damage to plants and animals Jason Maiham and the MWAF Echo parakeet field team, the MWAF Pink Pigeon field team, and Mr V Tezoo, acting Conservator of Forests. Mr. Puttoo, Head of NPCS explained much of the background to the protected area problems.

Mrs Begun, Minister of Agriculture, and Carl Jones, Scientific Director of MWAF, kindly provided more general background and historical information.

For hosting me at their farms and explaining the complete picture of the monkey trapping and export processes, and for providing numerical data from their records, Owen Griffiths and Mary Ann Stanley of Bioculture and Bruno Julienne and Noelle Garnege of Novoprim.

Finally, for initiating the study and financing the visit, Professor Tim Morris and GlaxoSmithKline.

Recommended Reading

Bertram B 1994. Monkeys in Mauritius: potential for humane control. Commissioned report to RSPCA.

Cawthon Lang K A 2006. Primate Factsheets: Long-tailed macaque (*Macaca fascicularis*). Taxonomy, morphology and ecology: http://pin.primate.wisc.edu/factsheets/entry/long-tailedmacaque.

Cheke A S 1987. An ecological history of the Mascarene Islands with particular reference to extinctions and introductions of land vertebrates. In Studies of Mascarene Island Birds. Ed A W Diamond, CUP.

Ervin F and Palmer R 2003. Primates for 2Pt century biomedicine: the St Kitts vervet (*Chlorocebus aethiops*). In International Perspectives: the Future of Non-Human Primate Resources. ILAR, National Academies Press, pp 49–53.

Kemp N J & Burnett J B 2003. Final Report: a biodiversity assessment and recommendations for risk management of Long-tailed Macaques (*Macaca fascicularis*) in New Guinea. Indo-Pacific Conservation Alliance, Washington DC.

Kondo M et al 1993. Population genetics of crab-eating macaques (*Macaca fascicularis*) on the island of Mauritius. Amer J Primatology. 29:167–182.

Mungroo Y & Tezoo V 1999. Control of Invasive Species in Mauritius. In Invasive Species in Eastern Africa: Proceedings of a Workshop held at ICIPE, eds. E E Lyons & S E Miller.

Staford R J 1991. Status and ecology of the Mauritius fody Foudia rubra and Mauritius olive white-eye Zosterops chloronothos: two Mauritian passerines in danger. *Dodo* 27:113–139.

Stanley M A 2003. The breeding of naturally occurring B virus-free cynomolgus monkeys (*Macaca fascicularis*) on the island of Mauritius. In International Perspectives: the Future of Non-Human Primate Resources. ILAR, National Academies Press, pp 46–48.

Sussman R W & Tattersall I 1986. Distribution, abundance and putative ecological strategy of *Macaca fascicularis* on the island of Mauritius, southwestern Indian Ocean. Folia Primatologia 46: 28–43.

March 2008

Memorandum by The Open University

I am submitting an institutional response on behalf of The Open University to the above "call for evidence" from the House of Lords European Union Committee, Sub-Committee D (Environment and Agriculture) dated 23 April 2009.

The Open University wholeheartedly supports the collective response document from the Bioscience Sector submitted by Dr Simon Festing as it addresses all the key points and provides evidence for or against each. It also represents the views of a number of organisations from academia, industry, small to medium enterprise businesses, charities and other research funders in the UK all of which will be directly affected by the revision of the Directive.

20 May 2009

Memorandum by Professor John M Pearce, FRS

I should be grateful if the Committee could consider the following evidence relating to Objective 7 (Article 32) of the Directive concerning Care and Accommodation.

1. Background

A number of universities in the UK and Europe, including my own, use domestic pigeons to understand the nature of animal intelligence. The proposed guidelines for housing this species are likely to make this research extremely hard to conduct.

For over 60 years, pigeons have proved to be an ideal model for studying aspects of animal intelligence. The methods for this research generally involve training and testing a bird in a chamber similar to the one in the figure on Page 3, before it has received its daily food ration (ie when it is relatively hungry). The bird is then shown a series of images on a television screen. Pecking on the Perspex panel will result in the delivery of food in the presence of some images, but not others. Eventually the bird will respond rapidly in the presence of images that signal food, and slowly during image that signal the absence of food. An experiment will typically involve between 16 and 32 birds, and it may last for several months. Variations of this technique have been used to study the fundamental mechanisms of learning, memory, reasoning, and perception.

The success of the technique depends upon the level of motivation for food being the same from day to day. It also depends upon the animal entering the test chamber in a calm state (an anxious bird would be unlikely to reveal its full intelligence, instead it would cower in a corner of the test chamber). Both of these aims are currently met by housing the birds in pairs in individual cages. In this way, they can be fed a carefully measured amount of food on a day to day basis. They can also be captured with a minimum of distress before each experimental session. After the session, the birds may be allowed to exercise in a flight room before being returned to their home cage until the next session of training.

2. The Problem

The guidelines propose that pigeons must be housed in groups in cages with a floor area of 2 square metres or more, and with a height of 2 metres or more. For my experiments, groups of 12–16 birds would be housed in a single large cage. Housing pigeons in this way will make it very difficult to conduct the above research for two reasons.

— It will be extremely hard to ensure that each bird receives its specified amount of food on those days when the birds are not tested and they must be fed by a technician (weekends, holidays etc). Indeed, feeding them in this way will lead to certain birds receiving little or no food at all. Quite apart from the inevitable suffering of some animals, it will be impossible to maintain an accurate level of food motivation for the experiment.

— For the experiment to be successful it is essential for each bird to be tested at the same time each day and, as just noted, for it not to be agitated. It is impossible to see how this can be achieved when the experimenter will be required to select for testing one bird from more than a dozen that are flying freely in a relatively large cage. Birds are identified by rings on their legs, which can only be read once the bird has been caught. Thus the experimenter will have to select birds at random, catch them with a net, and then determine whether the correct bird has been chosen. This treatment will cause stress to the entire group of birds, and result in the experimental subject, when captured, being in an agitated state when it is placed in the test chamber.

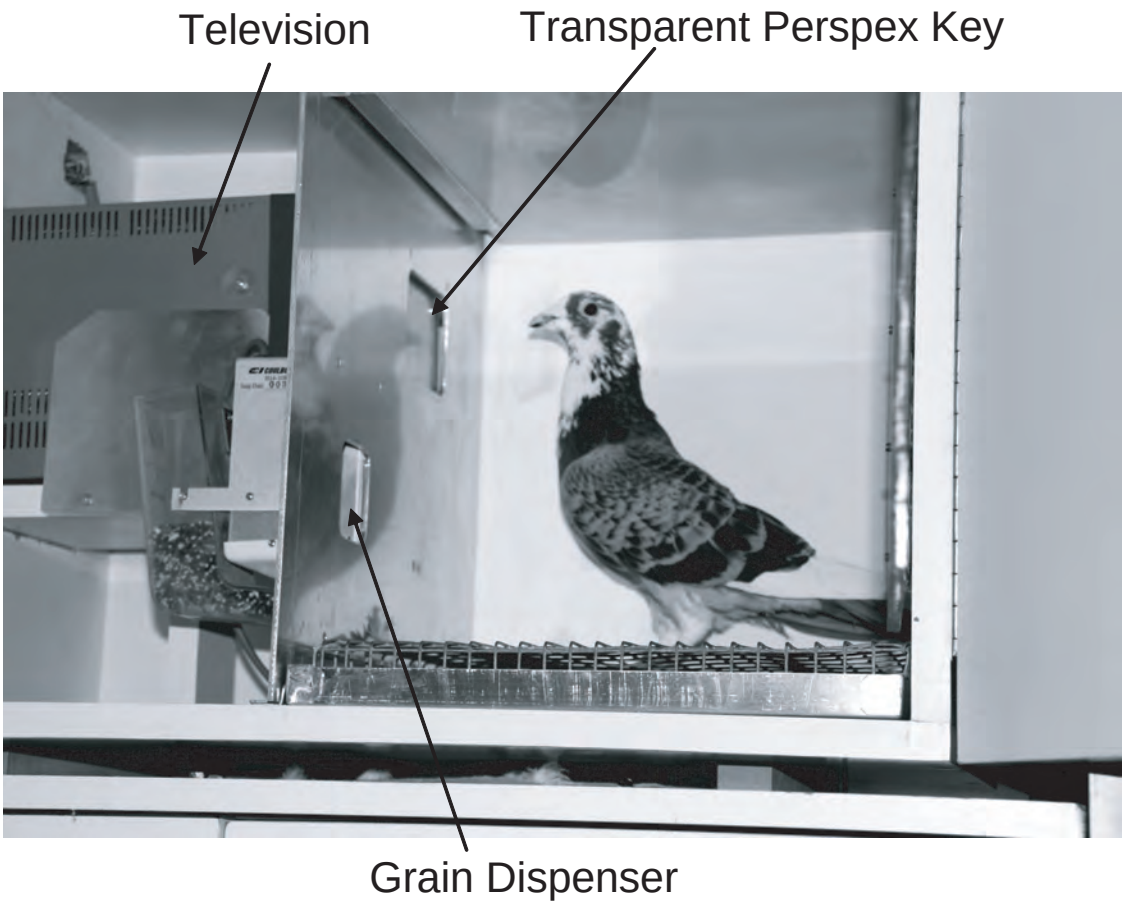
Taken together, these problems are so serious that it is hard to see how research of the kind described above can be conducted. I have already attempted to house birds in the manner proposed in the guidelines for my experiments. In addition to the problems just identified, we also discovered that some of the birds attacked quite viciously other members of the group.

3. A Proposal

I propose that the guidelines are modified so that in cases where the housing regimes prescribed in Annex IV would frustrate the objective of an authorized project or lead to an increased risk of animal welfare problems, alternative housing of agreed dimensions could be deemed acceptable. The authorisation could either be made on a case-by-case basis by the competent authority, or be defined in Annex IV specifically for behavioural testing of the kind I have described. When not participating in the experiment, birds would be housed in conditions in keeping with the proposed guidelines where this would benefit animal welfare.

4. Why the Study of Pigeon Intelligence is Important

Researchers investigate the intelligence of animals with the intention of understanding the neural mechanisms of intelligence in humans. Humans are able to learn, remember, form concepts, and reason, and these abilities are believed to be based on non-linguistic processes that can be found in animals. To study these basic processes it is necessary to use an animal that is sensitive to complex visual material that that can be used to test to the full its intellectual abilities. Primates are ideal in this respect, but are unsuitable for other reasons. Pigeons, surprisingly, make an excellent alternative. They have a well developed visual system which allows them to be used in sophisticated experiments that are able to explore the limits of their intelligence. These limits are quite impressive. For instance, in a study of how pigeons group objects into categories, it has been shown that they can be trained to tell the difference between painting by Picasso and Monet, even when they are eventually tested with pictures they have never seen before by these artists. The poorer sensory capacities of common laboratory mammals make them far from ideal for conducting this line of research and there is currently no alternative to the pigeon if progress is to be made in understanding the full extent of the intellectual capacities of animals. Future research with this species will be of upmost importance if we are to reach a full understanding of animal intelligence, and thereby appreciate the origins, mechanisms and neural basis of our own intelligence.



Apparatus used to study a variety of aspects of pigeon intelligence

May 2009

Memorandum by Uncaged

INTRODUCTORY REMARK

1. In this submission we have been selective in the questions addressed and focus on areas where we have particular expertise. Our analysis mainly draws on evidence from organisations generally supportive of animal experimentation.

OBJECTIVES OF THE DIRECTIVE

2. Insights from political science indicate that a high degree of harmonisation may be required to avoid problems arising from single market distortions. The UK animal research policy framework formally requires regulatory decisions involving expertise and discretionary, subjective judgements. This reflects the difficult ethical and scientific issues that arise from animal research proposals. The draft Directive, through its proposal for a harm-benefit assessment of animal experiments and consideration of alternative methods, is intending to incorporate similar requirements to the UK.

3. The lack of transparency and highly politicised nature of animal research policy means that it is difficult for animal protection stakeholders to obtain empirical evidence, and difficult to check the veracity of statements from animal research interest groups.

4. However, we estimate that current problems from uneven regulation are probably greater in the areas of animal welfare, scientific and public/societal, and less in economics. The weakness of the 1986 Directive means that in many member states there may be relatively poor animal welfare caused by the conduct of painful experiments that are scientifically unjustified or unnecessary. Animal harm and suffering may be further exacerbated by poor housing and husbandry standards in countries with low levels of social oversight.

5. Information published by the UK Government about the work of the Animals Scientific Procedures Inspectorate[14] demonstrates the significant role that independent scrutiny plays in improving animal welfare, science, and public legitimacy by:

— preventing proposed animal experiments that are scientifically dubious or for trivial purposes;

— preventing animal experiments where less severe or non-animal alternatives are available;

— ensuring the use appropriate analgesia and anaesthesia;

— reducing animal suffering by employing less severe methods and requiring the experiments to cease before severe suffering occurs; and

— reducing the number of animals used.

6. Hence, it can be seen that the absence of such independent scrutiny in many member states is currently causing significant problems in these areas. It also demonstrates why self-regulation is ethically, scientifically and politically unacceptable. However, the Commission's proposal for ethical evaluation, including a harm-benefit analysis, by member state governments (Articles 35-37) may not be sufficiently detailed to overcome animal welfare, scientific and legitimacy problems.

7. This is because the complex nature of this policy area means that the broader the formal text of any statute, the greater the scope for a range of discretionary judgements[15] that may be inconsistent across different member states due to Inspectorates' variable relationships with different stakeholder groups, or variations in the resources or expertise required for Inspectorates to effectively scrutinise animal research proposals.

8. Although the Commission's proposal went a significant way towards addressing these problems, important ambiguities remain that tend to encourage uneven regulation. In particular, the absence of guidance on the operation of the proposed harm-benefit assessment promotes uneven regulation. In this vein, the UK Government has stated: "It is recognised that research into life-threatening disease may necessitate a degree of severity which might be difficult to justify in other research".[16] But unless meaningful guidance for the conduct of the harm-benefit assessment is included in the Directive, it is inevitable that in some cases, animals will be subjected to severe pain for trivial purposes. The Directive as amended by the European Parliament on 5 May greatly exacerbates these problems by weakening the Commission's original proposals for independent harm-benefit based authorisation.

9. The question of whether economic problems arise from uneven regulation is difficult to assess because of conflicting evidence. Pro-animal research groups representing the pharmaceutical industry (among other animal research groups) repeatedly claim that they are committed to minimising animal suffering in order to ensure high quality science.[17]

10. This assertion brings into question the claim that animal welfare standards vary from country to country, as it is unclear why such companies or any academic animal researchers would voluntarily employ lower standards if it undermines the scientific validity of the research. If there are economic problems due to relatively weak regulation in certain countries, then the cost savings in those countries are likely to be short-term and limited to the organisation responsible. Moreover, such savings will be outweighed by longer term economic losses because poor quality science will lead to ineffective and potentially unsafe products and the pursuit of lines of research which turn out to be blind alleys. These considerations are also relevant to the risk of displacing animal research to third countries.

International Competition

11. The available empirical evidence indicates that any putative higher animal welfare standards in the EU would assist the effectiveness and competitiveness of the EU's private and public sector base. Countries with higher regulatory standards, such as the UK and Switzerland, outperform laissez-faire regimes such as the USA in terms of inward R&D investment and export earnings.[18]

[14] Eg, see the 2004 Annual Report at http://scienceandresearch.homeoffice.gov.uk/animal-research/publications-and-reference/publications/reports-and-reviews/annual-report?view=Standard&pubID=428513

[15] Hill, M (1997) *The Policy Process in the Modern State.* Hemel Hempstead: Prentice Hall/Harvester Wheatsheaf.

[16] Guidance on the Operation of the Animals (Scientific Procedures) Act 1986 (1990): 9.

[17] http://www.understandinganimalresearch.org.uk/about_research/animal_welfare_and_the_three_rs

[18] See Animal Defenders International's Technical Briefing: "Competitiveness of European Science and Industry (will animal protection drive research out of the EU?)".

12. The financial services industry's belief in minimal regulation actually had the effect of wrecking that sector and damaging society rather than ensuring sustainable prosperity. Similarly, industry's claims that more independent scrutiny and welfare regulations will undermine competitiveness and animal welfare by shifting research to third countries needs to be understood as a dogmatic reaction to the prospect of regulation, rather than a responsible reflection of what is in the long term interests of the public, the economy and animal protection.

13. Just as governments need to intervene to assist the energy industry in developing low-carbon energy, so the Commission's Proposal represented an attempt to introduce public accountability and ethical concerns into the animal research industry to help minimise animal research and boost investment in and uptake of alternative methods which offer demonstrable advantages over unreliable animal tests. In the long run, this can help give EU industry a competitive edge through leadership in more ethical and reliable testing methods.

14. Animal research regulation is a relatively minor consideration for drug companies and CROs when deciding where to locate business.[19] Thus the scale of any displacement of animal research to third countries is likely to be insignificant. Experimental protocols and procedures employed by international research groups in third countries should be no more severe than in the UK and Europe. To the extent that any displaced research involves greater suffering due to poor housing and husbandry, then such research will be at a competitive disadvantage compared to research in the EU because of the unreliability of the results.

15. Improved regulation of animal research in the EU should not be viewed in isolation. More humane attitudes and practices in the EU facilitate similar progress in third countries through international communication between scientists and regulatory bodies.[20] To that end, the European Commission's Joint Research Centre, together with its counterparts in the US, Canada and Japan, have signed a new agreement aimed at reducing the number of animal experiments undertaken in labs worldwide. .

16. It is also significant that the animal welfare NGOs—ie those with a genuine interest in animal welfare—dismiss animal research interest groups' predictions of greater animal suffering due to the displacement of animal research to third countries. The position of the animal research lobby on this matter is inconsistent and lacks credibility, and seems to amount to little more than blackmail.

Proposals to Restrict Research on Non-human Primates

17. Non-human primates have particularly high levels of neurophysiological sensitivity and cognitive development, which is akin to humans'. The public consultation carried out by the EU found that the level of pain suffered by animals was a more important consideration than the purpose of the experiment.[21] Overall, the public places more weight on ethical than scientific considerations, and therefore believes it is legitimate to place ethical restrictions on animal experiments. 81.1% of respondents stated that experiments on non-human primates was either probably (10.2%) or certainly (80.9%) not acceptable, as opposed to just 14.5% who felt positively to such experiments.

18. Bearing in mind the widespread ethical concerns regarding the use of non-human primates, the Commission's proposed restrictions are inadequate. In particular, the provision allowing for the use of non-human primates in procedures that merely aim to "advance knowledge" is difficult to justify on harm-benefit grounds as the ultimate practical benefits of such research are intrinsically uncertain. Furthermore, such fundamental research on non-human primates will also tend to perpetuate such experiments because it will generate new data and encourage the development of hypotheses specific to those animals. Thus it conflicts with the Commission's aim of replacing animal experiments, particularly on non-human primates.

19. The proposed restriction on the use of non-human primates to treat life-threatening or debilitating human diseases is a reasonable approach to structuring the operation of the harm-benefit assessment that reflects public concern. Complaints from animal research interests regarding the restrictions this will place on their activities should be interpreted in the light of the House of Lords Select Committee on Animals in Scientific Procedures finding that scientists fail to give sufficient priority to the development of non-animal methods.[22] It is the duty and right of citizens to place ethical restrictions on scientists to help institutionalise more ethically acceptable research methods.

[19] The Royal Society and the Department of Trade and Industry, who both support animal experimentation, expressed this view to the House of Lords Select Committee on Animals in Scientific Procedures (HL Paper 150-I, para 5.31) (2002).

[20] 91.6% of public respondents believed that the EU probably or certainly should play a leadership role in promoting in the international arena a greater awareness of animal welfare and protection, in particular regarding animals used in experiments? (http://ec.europa.eu/environment/chemicals/lab_animals/pdf/results_citizens.pdf)

[21] http://ec.europa.eu/environment/chemicals/lab_animals/pdf/results_citizens.pdf

[22] Paragraphs 4.9–4.15.

Authorisation

20. Uncaged believes that the administration required by the draft Directive falls moderately short of adequately satisfying the objectives of the Directive. Paragraphs 1 to 7 above discuss the major problems caused by the lack of sufficient detail in the proposed mechanism for the authorisation of projects, and this reflects the fact that this issue is the most important decision point in this policy area. We also have concerns about the following aspects of the draft Directive.

21. Reporting non-compliance solely to the establishment's permanent ethical review body (Article 24, paragraph 1, point d) trivialises animal welfare, is insufficient to maintain independence and accountability in animal research, and falls short of current UK measures. Instead, non-compliance must also be reported to the Inspectorate and the member state's competent authority.

22. The absence of a stipulation for lay, ethical or independent membership of the establishment's ethical review body (Article 25, paragraphs 2 to 4) means that the remit of such bodies as set out at Article 26, paragraph 1 could not be satisfied in an independent and accountable manner. The composition and structure of an establishment's ethical review body should reflect human research ethics committees.

23. To ensure independent and pluralistic policy-making in this controversial area, it is necessary to add a requirement for Inspectorates to have a majority of independent members (Article 33). We define independent as not being involved in animal research, not being a member of the same professional, public or political body as an applicant, and having no financial interest in entities engaged in animal research. Members of the Inspectorate should include scientists in relevant fields of research, scientists and clinicians independent of animal research, veterinarians and ethicists (especially if the Inspectorate, as it does now in the UK, also performs the role of the competent authority and undertakes ethical evaluation of projects).

24. The severity classifications are liable to challenge and involve a degree of subjective, discretionary judgements. They are not infallible. As the Home Office makes clear, independent scrutiny is essential to improve the reliability of severity assessments. Hence it is necessary to ensure thorough accountability for apparently milder procedures. Any lacuna in accountability will undermine public confidence in the regulatory systems and unfairly privilege the interests of researchers at the expense of animal welfare, thus we recommend that this Article 36, paragraph 2 should be deleted. We recommend the deletion of Article 38, paragraph 4 on the same grounds.

25. Similarly, Amendment 167 to Article 35, paragraph 1 of the Commission proposal, which removes the requirement for independent prior authorisation of procedures of "mild" severity altogether, significantly weakens the draft Directive on its most crucial provision. It appears to be based on an ignorance of the potential harms caused to animals by housing, husbandry, handling/restraint, identification, blood sampling and unforeseen consequences of genetic modification.[23]

26. For example, single-housing rats may have harmful effects "such as lack of the comfort and stimulation that comes from social contact with other animals, boredom and perhaps frustration, and in some cases maybe even physical effects of self-harm".[24] The Home Office acknowledges that pain, suffering, distress and/or lasting harm can result from husbandry and housing conditions, as well as cumulative procedures such as the repeated insertions of hyperdermic needles.[25]

27. Researchers would be free to underestimate the severity of procedures as "mild" in order to avoid scrutiny, and there would be no mechanism for checking that the mild "assessment" is accurate, or allowing independent evaluators to assess the scientific validity of the proposed project and the proper application of the 3Rs, for example by requiring environmental enrichment to reduce and alleviate the harm caused to animals by single-housing.[26]

28. It cannot be right that researchers can inflict pain on animals in ways that would normally be illegal under the Animal Welfare Act without any accountability. Independent authorisation of all potentially painful experiments by public bodies that are democratically accountable is essential to help minimise what is acknowledged to be a moral wrong—the infliction of unnecessary suffering on animals.[27]

[23] As Universities Federation for Animal Welfare suggests, "it is likely that too little weight is given at present to some forms of mental suffering, for example, mental states such as boredom and other suffering resulting from solitary confinement or changes in the social housing of animals". (quoted in APC (2003) p39.) See also discussion of such harms in Nuffield Council on Bioethics (2005) *The Ethics of Research Involving Animals.* Nuffield Council on Bioethics: London; p73–81.

[24] Animal Procedures Committee ['APC'] (2003) Review of Cost-Benefit Assessment in the Use of Animals in Research. London: Home Office; p39.

[25] APC (2003) p37.

[26] APC (2003) p39.

[27] House of Lords Select Committee on Animals in Scientific Procedures (HL Paper 150-I, para 2.5) (2002).

29. Regarding Article 37, paragraphs 3 and 4: An additional area of expertise that would assist the scientific and medical assessment of the project would be clinical experts independent of the institutions, bodies and companies to whom applicants is affiliated. The current wording of the Article allows competent authorities to use their discretion to restrict the expertise and independence of ethical evaluators.

30. We also believe that the proposals regarding the harmonisation of national inspections are insufficient (Article 34), and require the establishment of an EU inspectorate. This would ensure consistent severity assessments and the sharing of best-practice. We note that this would help to fulfil the as-yet-unimplemented recommendation of the House of Lords ad hoc Select Committee on Animals in Scientific Procedures "that the Inspectorate should be subject to periodic review, by a body other than the Inspectorate itself".[28]

31. Reports from those involved in animal experiments in the UK[29] indicate that retrospective assessments have major animal welfare and scientific benefits as they allow amendment of original harm-benefit assumptions, identify poor animal models and methods, and so help prevent unnecessary suffering and poor science. In any activity, retrospective assessment is essential to learn and improve processes. Given the sensitivity and costs involved in animal research, retrospective assessment is even more vital in this sphere. Therefore, Article 38 should be amended to ensure retrospective assessment of all experiments.

Subsidiarity and Legal Base

32. Animal research is an international activity and variable regulation in member states causes significant problems in the areas of animal welfare, scientific validity, public accountability and economic harmonisation. It is therefore appropriate to set standards across the EU that ensure minimum standards in these areas while allowing individual member states to introduce more stringent regulations if demanded by their populations.

May 2009

Memorandum by the United Federation for Animal Welfare (UFAW)

1. Question 5. *Are the Administrative demands that the draft Directive would impose overall proportionate to its objectives?*

Article 22: It is not clear whether this article would result in all animals at an establishment having to be killed if the establishment were found not to comply with the requirements set out in the Directive. This could result in unnecessary killing of animals for a minor infringement and would discourage self-reporting of infringements. It is better that the regulatory body should have discretion regarding an appropriate response for minor cases of non-compliance. This is our understanding as to how the situation currently works in the UK, and it allows a proportionate and flexible response to breaches of the codes of practice or licenses.

2. Question 7. *Are the care and accommodation standards set out in Annex IV to the Directive appropriate and will they produce an adequate level of harmonisation across the EU?.*

We see this issue of being of great importance for the welfare of animals used in research. In June 2007 the European Commission adopted guidelines for the accommodation and care of animals used for experimental and other scientific purposes. These guidelines (Annex II to the Directive 86/609) were closely based on the recently revised Appendix A to the European Convention ETS 123. The source text for the Commission's Annex II was arrived at after discussion over many years and was both a compromise and a consensus between groups representing users, animal care staff, and animal welfare organisations.

3. Much of the advice provided in the June 2007 Annex II to the Directive was aimed at preventing husbandry errors. The currently proposed Article 32 and Annex IV to the Directive has converted an advisory document to a mandatory document, in the process loosing much of the useful advisory and explanatory text. Because species-specific qualifying text and general advice has been omitted, the proposed Annex IV has lost vital information that qualifies the tables, could be misleading and is likely to result in incidences of poor animal welfare. To support this position we attach an appendix listing some important examples.

4. In our view, a better solution would be to incorporate both text and tables from Annex II (Commission Recommendations June 2007) into Annex IV of the proposed Directive. To avoid enforcement difficulties, the tables could be mandatory and the text (or at least some of it) advisory and interpretative. This would provide

[28] Paragraph 5.13.

[29] See, for example, Animals (Scientific Procedures) Inspectorate (2001). Review of the "Ethical Review Process" in Establishments Designated under the Animals (Scientific Procedures) Act 1986. Para 121.

a degree of flexibility so that scientific advances in animal welfare could be taken into account as and when they occur. If this proposal were adopted, then the advice arrived at by a broad consensus of users, and animal welfare scientists would be on the shelves of all staff charged with the care of laboratory animals. There would be much clearer advice on housing provisions, and this should lead to better welfare throughout the EU, and probably, more even implementation of standards.

APPENDIX 1

EXAMPLES OF IMPORTANT OMISSIONS IN ANNEX IV

5. Minimum Weaning Ages

Minimum weaning ages have been omitted for non-human primates and farm animals. Early weaning can impact on welfare and could bias experimental results. Part B of Non-human primates for the revision of Appendix A to the Convention, drew attention to the importance of the issue:

> "Early separation results in extreme distress to the infant at the time, but it is now well established that it damages normal development and results in animals which are physiologically and immunologically abnormal, as adults. Nursery rearing, in the absence of adults, also commonly results in behavioural abnormalities, such as locomotor stereotypies and auto-aggression (Capitanio 1986, Marriner and Drickamer 1994).

6. Fish

The provisions for fish have been completely omitted. This is a grave omission given the potential for poor welfare if environmental conditions are wrong, and the numbers of fish used in research (The most recent 2005 European statistics indicate that 1.7 million were used, 15% of the total no of animals).[30]

7. Dogs

The proposed tables permit dogs to be housed, under procedure, singly in half the space normally required to house a pair. However, the text of the revised Appendix A to the Convention and of the June 2007 Commission recommendations make clear that pair housing is expected to be the norm and that separation should not be for more than four hours per day.

8. Gerbils

There is good published peer-reviewed evidence that gerbils require either a burrow with a long connecting entrance or a very deep quantity of substrate if the development of abnormal behaviour is to be avoided (Wiedenmayer 1995, 1996, 1997a and 1997b reviewed in Waiblinger in prep).[31]

9. Guinea-pigs

The advice that mesh floors have the potential to cause serious injuries for this species has been omitted.

10. Temperature

Temperature ranges have been removed for all the mammalian species but kept for reptiles and amphibians. If temperature guidelines are abandoned there is the risk that more animals will need to be used in research as a result of increased variation and decreased replicability. It is generally accepted that temperature might be a confounding variable viz: The US NRC Guide (NRC 1996):[32]

> "Animals can adapt to extremes by behavioural physiologic and morphologic mechanisms, but such adaptation takes time and might alter protocol outcomes or otherwise affect performance (Garrard and others 1974; Gordon 1993; Pennycuik 1967)".

Temperatures outside animals' thermoneutral zone can impact on welfare, particularly when housing conditions do not permit the animals to adjust their micro environment. It is known, for example, that when mice are cold stressed, immunocompetance is impaired below 20°C, and pup growth below 18°C. In fact, it is

[30] COMMISSION STAFF WORKING DOCUMENT Annex to the: REPORT FROM THE COMMISSION TO THE COUNCIL AND THE EUROPEAN PARLIAMENT. Fifth Report on the Statistics on the Number of Animals used for Experimental and other Scientific Purposes in the Member States of the European Union {COM (2007) 675 final}. http://ec.europa.eu/environment/chemicals/lab_animals/pdf/staff_work_doc_sec1455.pdf

[31] Waiblinger (in prep) The Laboratory Gerbil. The UFAW Handbook on the Care and Management of Laboratory Animals, Eighth Edition).

[32] National Research Council (1996) Guide for the Care and Use of Laboratory Animals. National Academies Press, Washington D.C. Available from URL: http://www.nap.edu/readingroom/books/labrats/

possible that guidelines provided in Annex II already need updating as the thermo neutral zone of mice is 26–34°C, cf the current recommendations of 20–24°C see (Gaskill *et al* 2008).[33] Similarly for pigs, important detail was provided in Annex II on appropriate temperatures that was based on scientific evidence.

The temperature ranges for amphibians and reptiles have been wrongly transcribed, which could lead to poor welfare—see attached document.

11. Social Housing

In paragraph 3.3(a) Housing, the proposed Directive states "Animals, except those which are naturally solitary, shall be socially housed in stable groups of compatible individuals". This could lead to attempts to socially house male rabbits, some male strains of mice and male hamsters. In contrast the June 2007 Commission recommendations provide fuller and helpful species-specific advice by pointing out that social housing:

> is difficult, when housing male mice, adult hamsters or gerbils, as this can result in severe conspecific aggression.

And for rabbits

Adult entire males may perform territorial behaviour and should not be housed with other entire males.

12. Other Examples of Species-specific Good Advice Now Omitted

Include: The importance of taking into account communication by odours when cleaning out animals (Annex II, 4.9.4); The importance of social contact during critical periods for dogs and cats Tables 3.1, 4.1, for example).

2 June 2009

[33] Gaskill, B N, S A Rohr, E A Pajor, J R Lucas, J P Garner. (2009) Some like it hot: mouse temperature preferences in laboratory housing. Applied Animal Behaviour Science 116: 279–285.

ISBN 978-0-10-844498-2

9 780108 444982

Printed in the United Kingdom by The Stationery Office Limited
11/2009 435145 19585