Pandemic Influenza

Report with Evidence

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ABSTRACT

There have been influenza pandemics roughly three times a century since at least the 1600s, and it appears inevitable that there will be further pandemics in the future. It is not possible to say when they will happen, or even to assign meaningful probability to the timing of the next pandemic, though it seems unlikely that it will be in the next twelve months. However, since 2003 a virulent strain of avian flu in south east Asia has passed from birds to over 100 humans. Even though there are as yet no confirmed cases of human-to-human transmission, the evidence suggests that the world is closer now to a pandemic than at any time since the 1960s.

The consequences of a pandemic would undoubtedly be serious, but how serious it is impossible to say with certainty. Previous pandemics have varied hugely in the number of deaths and in the degree of economic and social dislocation caused. It is essential, given these profound uncertainties, that the Government provide strong leadership. The Government and their agencies must issue clear and consistent information, and the media should report the dangers and risks responsibly.

In our 2003 report Fighting Infection we noted that the United Kingdom Pandemic Influenza Contingency Plan, on its first appearance in 1997, was “was widely seen as a model to follow”. We still believe, on the basis of the evidence heard in this inquiry, that the United Kingdom is amongst those countries best prepared for responding to a pandemic. Nevertheless, the impact of a pandemic would potentially be so grave and wide-ranging that there remains much to be done. We therefore make several recommendations to the Government, including:

• The first line of defence against a pandemic must be to prevent the emergence of a dangerous new virus, by means of effective surveillance and control of avian influenza. The Government should increase their support for the work of international agencies in south east Asia accordingly.

• Investment in generic healthcare facilities in south east Asia offers the best long-term prospect that outbreaks of new diseases, should they occur, can be controlled within the region, rather than becoming global pandemics. The Government should give their full backing to the recent World Bank initiative to support such development.

• The Government should as a matter of urgency clarify their policy on prophylactic and early use of antiviral drugs in the event of a pandemic reaching the UK, and ensure that adequate supplies are available to implement the policy.

• More work should be done on translating the over-arching Contingency Plan into detailed plans covering health and emergency services, local government and businesses, in particular food distributors and retailers.

• Regulatory and ethical clearance barriers to research projects should be modified, and projects planned, with assured funding, in advance of any pandemic—if a pandemic has started it will be too late.

• The Government should provide stronger cross-departmental leadership. A pandemic would affect every part of society and every branch of Government, not just health services. There should be a Cabinet-level Minister for Contingency Planning, within whose portfolio pandemic preparedness would fall.
CHAPTER 1: INTRODUCTION

1.1. In July 2003 we published our Report *Fighting Infection*,\(^1\) in which we asked which infectious diseases posed the biggest threat to the United Kingdom in the foreseeable future. We also analysed the main problems encountered in the surveillance, treatment and prevention of human infectious disease in this country. We examined the advances in surveillance, diagnostic and vaccine technologies that might benefit the United Kingdom, and made recommendations on policy interventions that would assist in preventing outbreaks of infectious disease in future.

1.2. The report drew upon influenza more than once to illustrate some of the threats to the health of the population and drew attention to both strengths and weaknesses in the United Kingdom’s preparedness for major epidemics or pandemics. We highlighted, for example, the potential strain on vaccine manufacturing capacity and also some of the difficulties of surveillance.\(^2\) We also drew attention to the United Kingdom’s Contingency Plan for responding to an outbreak of pandemic influenza, and commented as follows:

“There are some good examples of plans about how to respond to infection outbreaks, such as the UK pandemic influenza Plan. This describes the national response in the event of a new influenza virus appearing which has the potential to cause a world wide pandemic … The plan was prepared to facilitate a prompt, effective national response. It describes a phased response and defines the roles of the organisations which would be involved. At the time of the appearance of H5N1 influenza in Hong Kong in 1997 the UK was one of the few countries to have such a plan in place and it was widely seen as a model to follow.” (*Fighting Infection*, p. 21)

1.3. Since *Fighting Infection* H5N1 avian influenza has continued to spread across south east Asia and beyond—indeed, as we started our inquiry in October 2005 the first cases in birds in Europe were confirmed. Since 2003 over 60 people in south east Asia, who have caught the disease from birds, are known to have died. The threat of a human pandemic is if anything higher now than in 2003.

1.4. We therefore considered it timely to carry out a short inquiry into the threat of pandemic influenza, and the Government’s continuing preparations to meet this threat. Our witnesses generally agreed that the United Kingdom remains among the best prepared countries in the developed world, and we see no reason to dissent from this view. The Pandemic Influenza Contingency Plan has been regularly reviewed and updated;\(^3\) advice has been issued to frontline healthcare workers; the Government have ordered sufficient antiviral drugs to treat one quarter of the population; work to expedite the manufacture of a vaccine is underway.

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\(^1\) Fourth Report from the Science and Technology Committee, Session 2002-03 (HL Paper 138).
\(^2\) Ibid., pages 20, 29.
1.5. Nevertheless, while the United Kingdom may be better prepared than most other countries, it is clear that if a pandemic were to emerge this winter we, along with every other country in the world, would face a grave crisis. In this report we therefore make recommendations which we hope will assist in focusing minds on the top priorities of prevention and rapid response.

1.6. We have also considered the contingency plans that have been prepared against the possibility of a pandemic reaching the United Kingdom. We have not had time to produce a comprehensive report on this complex area, and are conscious that there may be gaps in our analysis. We have not, for instance, considered the particular problems that would affect closed communities such as boarding schools, university halls of residence or prisons. Nor have we looked in detail at preparedness in business and industry. However, our recommendations draw attention to a number of key areas in the Government’s overarching Contingency Plan where more work is urgently needed.

1.7. Contingency plans, by their nature, evolve in response to events. We trust that the Government will review their Contingency Plan in light of the recommendations in this report, and give notice that we intend to return to this subject in the near future to review the progress that has been made.

**Acknowledgements**

1.8. The membership of the Committee is set out in Appendix 1, and our call for evidence in Appendix 3. We would like to thank all those who submitted written and oral evidence, who are listed in Appendix 2. We held an informal seminar on 11 October, at which we heard presentations from Dr Jeremy Farrar, Professor Neil Ferguson and Sir John Skehel, and we wish to thank them for providing us with such a clear introduction to the issues raised in our inquiry.

1.9. Our Specialist Adviser for this inquiry was Professor Julius Weinberg, Director of the Institute for Health Sciences, City University, London, who was also the adviser on our previous Report *Fighting Infection*. We are enormously grateful to him for his assistance throughout the inquiry.
CHAPTER 2: INFLUENZA

The influenza virus: background

The disease

2.1. Influenza, or flu, is a viral infection caused by the influenza virus, affecting the respiratory tract. The virus was first identified in 1933, though the disease was familiar long before this. The symptoms include fever, runny or blocked nose, cough, sore throat, aching muscles and joints, tiredness, headache, vomiting and diarrhoea. However, similar symptoms, particularly the first few, can be caused by other respiratory viruses, and what is commonly described as “the flu” is usually caused by other viruses which cause upper respiratory illness, such as the common cold virus.

2.2. For the purposes of contingency planning, influenza can be divided into three categories:

- “Ordinary” influenza circulates constantly in the human population, typically peaking in the winter months, and affecting around 10 percent of the population over the course of a year;
- “Avian” influenza is a disease of birds, caused by strains of the virus that are endemic in wild birds, and which do not normally infect man, though they periodically cause destructive epidemics among poultry;
- “Pandemic” influenza in humans, so called because of its global spread, typically infects around a quarter of the world’s population within the space of a few months. It occurs on average around three times a century, when a strain of avian influenza acquires the ability to infect and pass efficiently between humans. As this is a new virus to humans, there is no immunity, and the disease spreads rapidly. Strains of pandemic influenza vary widely in virulence. Some past pandemic strains have in fact been less virulent than “ordinary” influenza; others (notably in 1918-19) have been significantly more virulent, with high mortality rates.

The virus: classification

2.3. The most severe infections, whether avian or human, are caused by “influenza A” type viruses, which are in turn divided into subtypes by reference to their 15 different haemagglutinin (H) and nine different neuraminidase (N) antigens. These are protein spikes on the virus surface. Haemagglutinin allows the virus to bind onto healthy cells, while neuraminidase allows the virus to break out of infected cells, so that it can move onto other cells and spread infection throughout the body. H and N antigens are important in immunity to and treatment of influenza.

2.4. Influenza A viruses are found in many different animals, including ducks, chickens, pigs, whales, horses, and seals—and of course humans. However, birds are the primary reservoir, and since it was established that bird flu was caused by the influenza A virus in 1955 more than 90 species of wild birds have been found to carry influenza A, excreting large quantities in their

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In addition each of the various H and N antigens has further subtypes, so that there is, for example, considerable variety within “N1” neuraminidase antigens.
faeces, yet remaining apparently healthy. All known H and N subtypes have been identified in wild birds.

2.5. Avian influenza A viruses are divided into two broad classes: High Pathogenicity Avian Influenza (HPAI) and Low Pathogenicity Avian Influenza (LPAI). In poultry LPAI can cause a range of illnesses, including a mild illness with ruffled feathers, reduced egg production and cough, while more virulent HPAI strains can kill an entire flock within 48 hours. Since 1959 there have been 24 outbreaks of HPAI recorded worldwide, of which 14 have occurred since 1995. Only one strain (known as H5N1) has spread internationally.

*The virus: mutation*

2.6. Influenza viruses change continually as a result of two main mechanisms: “antigenic drift” and “antigenic shift”. Antigenic drift occurs all the time as a result of the inherent instability of the virus: gradual mutations result in the virus envelope undergoing minor changes, resulting in a new strain that may not be recognized by antibodies to earlier influenza strains. As a result people or other animals that have already been exposed to influenza may be re-infected by a new, slightly different strain, although exposure to a previous strain may confer partial immunity, so that the severity of the illness is reduced. The instability of the virus means that a wide variety of different strains are present at any one time in different animal species. For example, H1N1 (the “Spanish flu” virus of 1918-19), H1N2 and H3N2 currently circulate among people; H7N7 and H3N8 circulate in horses.

2.7. Antigenic shift occurs more rarely, and as the name implies represents a more dramatic change in the virus. It can occur as a result of the “recombination” or “reassortment” of two different strains affecting different species, and this appears to be one means whereby the virus can jump from one species (e.g. poultry) to another (e.g. humans). For instance, a human and an avian virus, both simultaneously infecting the same “mixing vessel” (an animal susceptible to both viruses, such as a pig), could combine. The result would be the emergence of a virus containing a high proportion of the genetic material of existing human strains, but incorporating a new haemagglutinin, against which humans have little or no immune protection.

2.8. New research, however, shows that the effect of antigenic shift can also be achieved through mutation without recombination. An avian virus can by itself acquire the ability to infect humans and transmit from person to person without recombination in a “mixing vessel”. Such a mutation seems to have led to the emergence of the “Spanish flu” virus in 1918.

*Influenza pandemics*

2.9. We have already noted that a pandemic occurs when a new highly infectious strain of influenza appears, normally an avian virus which has undergone antigenic shift. It is thought that south east Asia is the most likely location for such a virus to develop, largely because of the number of people living in close proximity to very large populations of domestic birds and pigs.

2.10. Roughly three influenza pandemics have been documented each century since the 1600s, occurring at irregular intervals of from 10 to 50 years. They usually spread to all parts of the world within less than a year, and affect more than a quarter of the world’s population. The following graph
illustrates the predicted course of a pandemic in the United Kingdom, starting from the introduction of one single case of influenza on Day 1:

**FIGURE 1**  
Predicted course of an influenza pandemic in the UK (one import only)

![Graph showing the predicted course of an influenza pandemic in the UK](image)

*Source: Professor Neil Ferguson. “Day” starts from introduction of first UK case; the modelling assumes a reproduction rate of 1.8. The curve derives from a classic “SEIR” model, classifying individuals as Susceptible, Exposed, Infectious or Recovered from the disease.*

2.11. In reality pandemics may not follow this simplified model exactly. Further waves, for instance, sometimes with more severe disease, generally follow the first wave, but the reasons for such repeated waves, and their likely timing and effect, are not well understood or modelled. The courses of the three pandemics of the 20th century illustrate both the common elements and the variations between pandemics that make any attempt at prediction so difficult.

*“Spanish flu” (1918, H1N1)*

2.12. The 1918-19 pandemic, known as “Spanish flu”, was one of the most deadly disease events in human history. Estimates of the number killed range from 20-50 million, but there is general agreement that within one year more people died from influenza than were killed in the first World War in the years 1914-18.

2.13. The first outbreaks occurred in March 1918 in Europe and the United States. The infection then travelled via troopships and by land to Asia and Africa. The first wave was highly contagious but not particularly deadly. The second wave started at the end of August 1918 in France, Sierra Leone and the United States and saw outbreaks with a ten-fold increase in the death rate. The highest death rate was in fit young adults—unusually, as influenza commonly kills the very young and very old.

institutions, including schools, were closed. The wide imposition of quarantine and isolation probably had little effect, although strict maritime quarantine delayed the arrival of the epidemic in Australia until the start of 1919. By this time the virus had become less lethal, and Australia had a milder, though longer, period of influenza activity than elsewhere. Even in Australia 60 percent of deaths occurred in persons aged 20 to 45 years.

2.15. During the 1918-19 pandemic no part of the world was spared and 25-30 percent of the world population fell ill. The capacity to respond—for instance the supply of hospital beds for the sick, or of burial space and coffins for the dead—was overwhelmed.

“Asian flu” (1957, H2N2)

2.16. At the beginning of May 1957 reports of epidemics in Hong Kong and Singapore were received. Subsequently it became clear that epidemics had begun at the end of February in China, spread throughout that country in March, and reached Hong Kong by mid April. Since 1918 understanding of influenza had advanced considerably. The virus had been identified in 1933 and vaccines for seasonal epidemics had been developed. Antibiotics were available to treat complications. The World Health Organization (WHO) Global Influenza Surveillance Network—a virological monitoring and early warning system—had been in place for 10 years. By mid-May, laboratories had isolated the virus and identified it as a new subtype.

2.17. By autumn 1957 every part of the world had experienced cases. In Europe the epidemic coincided with the September return to school. It peaked rapidly and was over by December. Mortality showed a similar pattern to that seen in seasonal epidemics, in that excess deaths were confined to infants and the elderly. Cases were concentrated in school-aged children and those crowded together such as in military barracks. A second wave followed one to three months later with very high rates of illness and increased fatalities.

2.18. Quarantine measures were generally found to be ineffective, at best postponing the onset by weeks. Spread within some countries was associated with public gatherings, and the banning of such gatherings and the closing of schools were considered the only measures that could slow spread. Vaccines became available in the United States (August), United Kingdom (October) and Japan (November), but quantities were too small for wide-scale use. Total excess mortality globally has been estimated at more than two million deaths.

“Hong Kong flu” (1968, H3N2)

2.19. The 1968 pandemic was even milder than that of 1957. In mid-July a British newspaper published a story about widespread acute respiratory disease in China. During July the disease spread to Hong Kong, causing half a million cases within two weeks. The virus was rapidly identified as a novel subtype and on 16 August the WHO warned of possible pandemic.

2.20. The disease spread more slowly rather than in previous pandemics, apart from in the United States. Here the epidemic, introduced by troops returning from Vietnam, began in September in California, and affected the whole country by late December. A significant increase in deaths, concentrated in the elderly, occurred during January. In Europe symptoms were mild and
excess deaths negligible. In the United Kingdom the epidemic began in December, and demands on medical services were not excessive. Recorded deaths from influenza-like illness and pneumonia were actually lower than the year before.

2.21. Vaccine manufacturing began within two months of the virus being isolated, but only 20 million doses were ready by the time the epidemic peaked in the United States. Global excess mortality was probably around one million. It is thought that the mildness of the 1968 H3N2 pandemic may have been because those exposed to the 1957 H2N2 strain enjoyed partial protection against the shared N2 subtype.

*Summary: pandemic viruses*

2.22. There are crucial differences between the viruses that caused the 1918 and the 1957 and 1968 pandemics. The full sequence of the 1918 H1N1 virus gene has recently been characterised. Hitherto it has generally been assumed that pandemic strains emerge as a result of reassortment, but it now appears that the 1918 virus was a “pure” avian virus, which acquired through spontaneous mutation the features necessary to infect humans readily and transmit from person to person. It is not known if this occurred rapidly or took place over a number of years. It is thus possible that Spanish flu emerged as a result of a gradual process; it does not appear to have resulted from a one-off antigenic shift as a result of reassortment with a human virus.

2.23. In contrast, analysis of viruses from the 1957 and 1968 pandemics shows that they are both reassortants (mixtures) of human and avian viruses. The 1957 H2N2 virus comprises three genes from an avian virus and the remaining five genes from the previously circulating human H1N1 strain (which in turn derived from that which caused the 1918 pandemic). The 1968 H3N2 strain also has three genes from an avian virus and the remaining five from the circulating human H2N2 strain (derived from 1957 pandemic virus). In both cases, it is suggested that the pandemic strains emerged as a result of reassortment in pigs, probably in those parts of Asia where large numbers of people live in close proximity to ducks and pigs, providing ideal conditions for the virus to cross between the species.

2.24. The recent discoveries regarding the 1918 virus raise crucial questions. It appears that the exceptional virulence of that pandemic can be explained at least in part by the fact that it derived from a “pure” avian source, totally new to humans, with the result that people had no immunity (in marked contrast to the 1957 and 1968 viruses). The process of adaptive mutation in bird populations may also mean that it emerged in several locations more or less simultaneously, rather than in one “big bang”. Worryingly, the current virus circulating in bird populations, H5N1, resembles the H1N1 virus responsible for Spanish flu, not only in its exceptional virulence, but also in its process of mutation. As the authors of the recent characterisation of the H1N1 virus note, “a number of the same changes [as occurred in the H1N1 virus] have been found in recently circulating, highly pathogenic H5N1 viruses”.

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The H5N1 virus

2.25. Occasionally an avian influenza virus infects a person, normally as a result of close contact with infected birds—characteristically poultry workers and veterinarians are most at risk. There have been about 11 documented episodes since 1959, with from one to 133 people (in the current H5N1 outbreak) infected.

2.26. Human infections with avian influenza viruses usually produce mild disease followed by full recovery. H5N1 has been the exception. The first outbreak of H5N1 avian influenza in poultry, in Hong Kong in 1997, caused 18 cases of human infection and six deaths. It was controlled by culling of the domestic poultry population, 1.5 million birds in total. Although this brought the initial outbreak to an end, sporadic cases of H5N1 in China during 2003 suggested the virus was still circulating in wild bird populations.

2.27. The current outbreak of H5N1 avian influenza became apparent in December 2003, with reports of the deaths of large numbers of chickens in the Republic of Korea. As the disease spread laboratory tests identified the cause as the H5N1 virus. In January 2004 Vietnamese health authorities reported an unusual cluster of severe respiratory disease in 11 previously healthy children, of whom seven had died and two were in critical condition. On 8 January Vietnam confirmed that highly pathogenic H5N1 was the cause of the deaths in poultry, and on 11 January H5N1 was confirmed in samples from fatal cases of human infection in Hanoi.

2.28. The scale of the outbreak soon became apparent: on 12 January Japan reported the detection of H5N1 in poultry; by 19 January five fatal cases had been confirmed in Vietnam; on 23 January Thailand reported H5N1 in humans and poultry; by the end of 2004 nine countries in south east Asia had experienced H5N1 outbreaks in birds and two countries (Thailand and Vietnam) had reported cases in humans. By 29 November 2005 three more countries, China, Cambodia and Indonesia, had confirmed human cases, with total reported cases numbering 133 and deaths 68.6

The start of a pandemic?

2.29. For a pandemic to start three conditions need to be met:

- A novel virus subtype must emerge to which the general population will have no or little immunity.
- The new virus must be able to replicate in humans and cause serious illness.
- The new virus must be efficiently transmitted from one human to another; efficient human-to-human transmission is seen as sustained chains of transmission causing community-wide outbreaks.

2.30. The first two of these conditions have been met: we know that a novel virus (H5N1) has emerged. It has infected people and animals, and has shown that it can replicate and cause serious illness. However, there is no evidence at present of efficient or sustained human-to-human transmission of the virus.

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2.31. With a view to monitoring progress towards the fulfilment of these conditions more closely, the WHO has published a table summarising the various phases of pandemics, and this table is given below.\(^7\)

**TABLE 1**

**WHO Pandemic Phases**

<table>
<thead>
<tr>
<th>Inter-pandemic period</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection or disease is considered to be low.</td>
</tr>
</tbody>
</table>

| Phase 2 | No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease. |

<table>
<thead>
<tr>
<th>Pandemic alert period</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 3</td>
<td>Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.</td>
</tr>
</tbody>
</table>

| Phase 4 | Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans. |

| Phase 5 | Larger cluster(s) but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk). |

<table>
<thead>
<tr>
<th>Pandemic period</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 6</td>
<td>Pandemic phase: increased and sustained transmission in general population.</td>
</tr>
</tbody>
</table>

| Post pandemic period: return to inter-pandemic period |  |

2.32. The world currently stands at Phase 3: cases of human infection have been reported, but no human-to-human spread has been confirmed, and certainly no significant clusters reported. This offers some comfort, given that the H5N1 virus emerged as long ago as 1997, and yet has still not succeeded in adapting to human-to-human transmission. Nor is it known to what extent the current outbreak of H5N1 influenza in birds increases the likelihood of a human pandemic. Thus many uncertainties remain.

2.33. Even if it is assumed that H5N1 will at some point adapt to human-to-human transmission, the timing is impossible to predict: it could be in early 2006, or it might not be for many years. Nevertheless, on the basis of its summary of pandemic phases, the WHO warn that the world is closer now to an influenza pandemic than at any time since 1968. There are good reasons

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to treat the possibility of the development and spread of the H5N1 virus very seriously.

**The likely impact of a pandemic**

2.34. One of the major difficulties faced by all governments in planning for a possible influenza pandemic is the huge uncertainty over its likely impact. Scientific and economic advances since 1968 should mean that the international community is better prepared for a pandemic than ever before. However, the example of the relatively small-scale outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003 demonstrates the economic cost and social dislocation that can arise as a result of new diseases and, perhaps more significantly, of the control measures taken to prevent their spread.

2.35. Moreover, the three influenza pandemics of the twentieth century demonstrate the enormous variability of the virus. The 1918 pandemic was among the most destructive and fast-moving ever known: previously healthy young adults dropped dead in the street. The mortality rate among those infected is thought to have been about three percent. In contrast, the 1957 and 1968 viruses were, though affecting very large numbers, of similar severity to normal seasonal influenza, with mortality rates in the range 0.2-0.4 percent.

2.36. This raises a broader question: what causes mortality in influenza cases? In the case of ordinary seasonal influenza, the “at risk” groups are the elderly, the very young and those with chronic respiratory conditions or depressed immune responses. Members of these groups are susceptible both to direct attack by the virus on the respiratory system, and to secondary infections, such as pneumonia.

2.37. However, in 1918-19, the highest mortality rates were seen in young adults. It may be that they did not die as a result of the direct action of the virus, but as a consequence of their own immune response. Proteins called cytokines, a normal part of the immune response, can be harmful if over-produced, damaging the lungs and other organs. This could explain why those with the strongest immune response had the highest mortality rates.

2.38. It is impossible to say what form the H5N1 virus will take, if it acquires human-to-human transmissibility. However, it resembles the 1918 H1N1 virus in virulence, and has hitherto mutated in similar ways; if it continues to do so, remaining a “pure” avian virus, there is concern that it would both bring a significantly higher mortality rate than the 1957 or 1968 pandemics, and that it might kill a disproportionate number of young adults. Against the backdrop of these uncertainties, the Government’s assumptions that there would be an attack rate of 25 percent, and a mortality rate of 0.37 percent, producing excess mortality in the United Kingdom of around 50,000, appear to be at the lower end of possible estimates.

2.39. Similarly, the economic costs of a pandemic are shrouded in uncertainty. The Government’s written evidence to this inquiry helpfully put some figures on possible costs to the United Kingdom:

- Illness-related absenteeism from work could take £3 billion to £7 billion off GDP;
- Excess mortality could take a further £1 billion (0.37 percent mortality) to £7 billion (2.5 percent mortality) off GDP;
• Loss of future lifetime earnings could cost in the longer term anything from £21 billion to £172 billion.

2.40. Our own analysis bears out these figures. However, they are inevitably broad-brush, and subject to enormous uncertainty, for instance over the groups most at risk, who could be either the elderly or the young and economically active. Similarly, the direct consequences of excess mortality and absenteeism do not appear to take into account secondary effects, such as the impact of school closure and resulting absenteeism of working mothers; or the potential disruption to transport networks either as a direct result of illness, or of control measures.

2.41. In a pandemic such costs would be replicated around the world. The World Bank, in a paper presented to a WHO conference in Geneva on 7-9 November, put the total cost of a pandemic to the world economy speculatively at $800 billion, representing about two percent of global GDP over a whole year (compared with a two percent loss to east Asian GDP as a result of SARS in the second quarter of 2003).

Treatment and prevention

2.42. In most healthy people, influenza will resolve in seven to ten days. Simple remedies to ease symptoms are all that is needed. However, in the case of a pandemic medical intervention either to prevent or treat infection will be required. Infection can be prevented by vaccination; or the disease itself can be treated by use of antiviral drugs.

Vaccination

2.43. The vaccine contains a killed version of the influenza virus, which stimulates the body to produce antibodies. The effect is not immediate—it takes about two weeks for the body to create enough antibodies to resist infection by the live virus.

2.44. Vaccination against seasonal influenza is a well-established part of health-care in developed countries. The instability of the virus means that new strains emerge constantly, with the result that immunisation is provided every autumn, on the basis of an informed analysis of the likeliest strains that will circulate in the coming winter. Immunisation prevents most cases, although protection varies with age, health status, and how closely the virus strains contained in the vaccine actually match those that ultimately circulate. However, even if the vaccine does not prevent the disease the presence of antibodies can reduce the severity of flu symptoms and decrease the risk of complications.

2.45. From the point of view of pandemic contingency planning, the crucial point is that influenza vaccines are specific to particular strains of the virus. Vaccination against the currently circulating strains of the H3N2 virus, for instance, will offer no protection against H5N1 strains, and only limited protection against newer strains of H3N2 itself. The Government has recently ordered over two million doses of H5N1 vaccine for at-risk and key workers, based on the current avian virus. However, while this may protect against the current circulating strain of “avian flu”, there is no guarantee that

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it will offer protection against any pandemic strain of H5N1 that emerges in future.

2.46. This need to tailor vaccines to particular strains means that only when a new pandemic strain has emerged can it be isolated and rendered safe, and only then will it be possible to commence vaccine production. According to Dr John Wood, of the National Institute for Biological Sciences and Control (NIBSC), the process before a viral strain can be made safe for distribution to vaccine manufacturers would take “about ten or eleven weeks”. From that point the manufacturers would have to incubate the virus in hens’ eggs, harvest, purify and prepare the vaccine, and distribute it to health services, with the result that, in the words of Dr Kevin Bryett of Chiron Vaccines, “from the receipt of the antigen to the first product being available is about four to six months”. (QQ 33, 37)

2.47. This means that under current conditions, from the first outbreak of an influenza pandemic to the availability (initially in small quantities) of vaccine, could take anything from seven to nine months. By this time the first wave of the pandemic, and possibly even the second wave, would have passed.

Antivirals

2.48. For rapid response to a pandemic, antiviral drugs will be the most important weapon available to health services. Antivirals work by inhibiting the action of particular proteins on the virus. The four medications available to treat influenza can be divided into two classes:

- Amantadine and rimantadine, so-called “M2 inhibitors”, which probably work by preventing the virus from entering the host cell;
- Zanamivir (sold as Relenza) and oseltamivir (sold as Tamiflu), so-called “neuraminidase inhibitors”, which work by blocking the release of the virus from an infected cell.

2.49. These drugs act directly on the virus, rather than stimulating the production of antibodies. They appear to be most effective when used prophylactically—that is, to prevent infection in those who have been exposed to the virus. They are also effective in treating the disease, as long as they are taken within 48 hours of the onset of symptoms—the earlier the better. If used in this way they can reduce the severity and duration of symptoms, and reduce the spread of the disease to others. However, antivirals work only so long as they are being taken: they confer no long-term immunity, and the protection ceases as soon as the course is completed. They are not a substitute for immunisation.

2.50. In addition, many of the strains of the H5N1 avian influenza circulating in south east Asia show signs of resistance to amantadine. Therefore pandemic preparedness plans have focused on neuraminidase inhibitors, particularly oseltamivir, which, as it is available in tablet form, is easily stored and administered. The Government told us that they were “keeping a very close eye on” any indication of the emergence of resistance to oseltamivir. (Q 249)

Other precautions

2.51. Finally, there are simple precautions which everyone can take to reduce, if not avoid, the risk of infection. Influenza spreads when an infected person sneezes or coughs. Infection occurs when droplets are inhaled, or when the
virus is picked up from a contaminated surface and then passed to mouth or nose. The best way to prevent the spread of influenza is by limiting the spread of droplets (using a handkerchief, covering the mouth and nose) and by hand-washing to prevent contamination. The Contingency Plan, and other Government-issued guidance on pandemic influenza, explain these simple precautions fully.

2.52. In addition, masks may have some value. The virus particles are too small to be caught by a normal surgical or dust mask, and there is no good evidence that the routine wearing of a mask will protect a wearer from catching influenza. However, the mask may slightly reduce the risk of an infected person passing the disease on to others. The mask should be a filtering face-piece mask, have a good fit and be changed regularly.
CHAPTER 3: PREVENTION IS BETTER THAN CURE

3.1. Avian influenza is a disease of birds, not people. Many strains of the influenza virus are found in wild bird populations, particularly waterfowl, and present no significant risk to human health. Occasionally a particularly virulent strain, such as H5N1, will emerge, and become endemic in domestic as well as wild birds, with serious economic consequences, but without any necessary impact on human health.

3.2. At present H5N1 remains primarily a disease of birds, which only rarely infects people. While there have been over a hundred cases of human infection in south east Asia, those concerned have almost without exception worked closely with infected birds. Cases in other animals (such as the tigers in a zoo near Bangkok which died after eating the carcases of infected birds) have also been traced back to avian sources. While these cases are in themselves a matter of serious concern, there is no current indication that the virus is capable of sustained transmission other than within bird populations.

3.3. As a disease of birds, the economic consequences of H5N1 have already been serious—the United Nations Food and Agriculture Organization (FAO) estimates the cost to south east Asian economies at $10 billion, though Dr Slingenbergh of the FAO conceded that this was a “back of the envelope calculation”. However, such costs would be dwarfed by those of a human pandemic, which, as we have already noted, the World Bank puts speculatively at $800 billion. (Q 16)

3.4. Thus, as Dr Fresco, also of the FAO, said, “to control the animal side is absolutely key … the real work has to be done in the backyards in Indonesia, in the waterways of the Mekong Valley”. Preventing a pandemic from happening must be the top priority, though “prevention” in this context cannot be absolute. But even if it is only possible to reduce the frequency of influenza pandemics through effective control of avian viruses, this will bring huge human and economic benefits. (Q 303)

3.5. Despite the spread of H5N1 via wild birds into Europe, the size of the domestic bird populations in south east Asia (China contains, according to Dr Slingenbergh, 700 million domestic ducks, some 70 percent of the world’s total population), and the patterns of agriculture (in particular the close proximity between birds, other domestic animals, and human populations), mean that the likeliest source of the next influenza pandemic remains south east Asia. Efforts to prevent a pandemic must therefore be focused in that region. (Q 26)

3.6. The keys to preventing a pandemic are well known. They have been demonstrated both in Hong Kong in 1997, where H5N1 was effectively eradicated, and to a lesser extent in Thailand since 2003, where incidence of H5N1 in domestic poultry has been much reduced. They are:

- Effective surveillance of bird populations, and good bio-security, including measures to separate wild and domestic birds;
- Rapid culling of infected flocks;
- Targeted vaccination of flocks to disrupt transmission cycles.

3.7. However, the practical barriers to such action remain formidable, particularly in Vietnam, Indonesia and China. They include: poor veterinary
infrastructure; the lack of a co-ordinated and efficient system of information exchange; traditional patterns of agriculture, including the huge “backyard” poultry population; and the lack of compensation arrangements for farmers, creating an incentive to send sick birds to market rather than reporting them. Dr Slingenbergh, who outlined these barriers, also noted that the FAO had only $25-30 million of funding in hand, as against some $160 million required in order to deal effectively with current problems. (QQ 24-26)

3.8. Dr David Nabarro, the United Nations (UN) Senior System Co-ordinator for Avian and Human Influenza summarised the position as follows: “It is absolutely vital to … deal with the avian flu outbreak at source and we are not winning this battle in several of the severely affected countries. The only organisation we have globally which has the potential penetration to do this is the Food and Agricultural Organization of the UN. They are under-funded.” (Q 304)

3.9. This message has not been wholly lost on the international community. Dr Nabarro highlighted the offer of the Dutch government to supply not just cash, but personnel. In November the World Bank announced the establishment of a $500 million fund to support regional development, including the strengthening of medical and veterinary systems, and support for vaccine and culling programs. At the same time the Bank announced that it was discussing with the European Commission and UN agencies the establishment of a multi-donor trust fund to support longer-term investments.

3.10. The Department of Health has actively supported the WHO in improving surveillance in south east Asia, and the United Kingdom hosts one of four WHO Collaborating Centres for Influenza at the National Institute for Medical Research (NIMR). The Department’s memorandum further notes that a senior British epidemiologist is seconded to the European Centre for Disease Control, assisting the WHO’s influenza work, while the Health Protection Agency (HPA) provides further support.

3.11. Nevertheless, we are concerned at the apparent lack of co-ordination of United Kingdom efforts in south east Asia. It does not, for instance, appear that the Department of Health provides direct support for the FAO or the World Organization for Animal Health (OIE). As for other departments, the Government’s memorandum states that Department for International Development (DFID)—

“has encouraged UN agencies to use existing resources to focus on avian flu as a potential precursor for a flu pandemic. It is also urging relevant UN agencies to work with affected countries to develop affordable plans for tackling avian flu and improving wider pandemic preparedness.” (p. 83)

3.12. It was clear from our discussion with Dr Slingenbergh that the FAO is fully aware of the need to focus on avian influenza, and that the agency is held back from effective action primarily by a shortfall in funding. Encouragement and urging from DFID will do nothing to remedy the situation. On the other hand, the memorandum goes on to note that Defra has “provided technical supplies and expertise” to FAO as well as to individual countries.

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3.13. The lack of co-ordination is further shown by the fact that the HPA, while internationally it works closely with other agencies and Departments (notably DfID and Defra), has to finance international work out of its “business as usual” budget for health protection. It cannot, for instance, draw on DfID funding for long-term projects in south east Asia, though the Minister told us in a letter that DfID might consider funding the HPA through the WHO or other multilateral organisations. We are concerned that this fragmentation of international efforts along departmental lines risks undermining the United Kingdom’s contribution in south east Asia. (p. 103)

3.14. In the longer term it will be essential to gain a better understanding of transmission dynamics—the processes whereby avian viruses infect mammals or humans, and the mutations within the virus that make human-to-human transmission possible. The current spread of H5N1 offers an exceptional opportunity to conduct detailed serological surveys and analysis, which will inform future responses to the threat of pandemics.

3.15. It looks at present as if this opportunity is being missed. Dr Klaus Stohr, of the WHO, described surveillance of the virus in animals as “sub-optimal”; there had for instance been “no large-scale serological investigation” to ascertain whether the virus was circulating in pigs, generally regarded as the likeliest “mixing vessels” for recombination of avian and human influenza viruses. In some countries human cases had been reported “before there was knowledge of the presence of the disease in animals”. (Q 202)

3.16. Even where data are available they are not necessarily shared among agencies or researchers: Dr Slingenbergh noted not only that the Center for Disease Control in Atlanta held details of virus samples which “they are very often not prepared to share with the international scientific community”, but that the WHO influenza network itself was not “communicating fully” with the OIE and FAO networks. One of Dr Nabarro’s key roles, as Senior UN System Co-ordinator for Avian and Human Influenza, is to bring UN agencies and other bodies together, providing a “maypole” around which they can “dance and be more effective”. (QQ 13, 301)

Conclusions

3.17. The first line of defence against a potential human influenza pandemic is effective surveillance and control of avian influenza, in particular in south east Asia. We are encouraged that there seems to be a growing consensus on this point, and in particular that the World Bank has committed $500 million to supporting the work of UN agencies and regional programs.

3.18. Nevertheless the FAO, which is uniquely well placed to tackle avian influenza at source, remains under-funded. We recommend therefore that the Government review its support, financial and institutional, for the FAO; we further urge the Government, in partnership with the European Commission and other European Union countries, to respond positively to the World Bank’s establishment of a multi-donor trust fund to support investment in the region.

3.19. The Government should also make every effort to ensure that the efforts of United Kingdom departments and agencies in both animal and human health are fully co-ordinated. We therefore recommend
that the Government review the current rules governing funding of HPA activities overseas.

3.20. We welcome the appointment of Dr David Nabarro as UN Senior System Co-ordinator for Avian and Human Influenza. The performance of UN agencies, and the co-ordination between different agencies, has not always been optimal. We look to Dr Nabarro to ensure that the UN is well placed to co-ordinate international efforts to prevent the current epidemic of avian influenza turning into a full human pandemic.
CHAPTER 4: NIP A PANDEMIC IN THE BUD

4.1. We have already noted that the processes of disease transmission and virus mutation which might lead to an outbreak of pandemic influenza are not adequately understood. At the most basic level it is impossible to predict whether a pandemic strain will be a “pure” avian virus, or a reassortment of human and avian influenza viruses produced in a “mixing vessel” such as a pig.

4.2. This uncertainty has profound implications for pandemic planning. Reassortment could lead to a “big bang”—a sudden leap in the development of the virus, which could, almost overnight, acquire the capacity to pass efficiently between humans. On this assumption an initial cluster of cases would rapidly expand into a pandemic. Progressive mutation of an avian virus, on the other hand, could result in the virus gradually acquiring the ability to move between humans. Initial clusters, of which there might be several, would be small and slow-growing, as longer chains of human infection developed. Clusters would be harder to spot, but easier to deal with once identified.

4.3. Recent modelling by Professor Neil Ferguson and others, the results of which were published in Nature on 8 September,10 shows that once an initial outbreak is identified there is a short period during which a pandemic could be stamped out, by isolation of known cases, restrictions on movement, and intensive, targeted prophylactic use of antiviral drugs. This ground-breaking work has allowed the WHO to establish a rapid response strategy, and as a direct result of this article Roche Products Ltd, manufacturers of oseltamivir (Tamiflu) announced the donation of three million courses of the drug to the WHO to form a rapid response stockpile. In addition, China has announced that in the event of an outbreak it would quarantine the affected area, so providing some prospect that the other prerequisite for success—isolation—could be achieved.

4.4. However, the modelling appears to be based on the assumption that the outbreak will occur in a rural area; it is far from clear what would happen were it to occur in a major conurbation. Furthermore, even in rural areas the practical difficulties would be enormous. Rapid diagnosis of the initial cluster would be essential—at our seminar Dr Jeremy Farrar even suggested that once the number of cases exceeded 50 it would be too late to prevent a global pandemic. At the same time he painted a vivid picture of the logistical difficulties involved in getting suspected cases from rural villages in Vietnam to properly equipped hospitals where tests could be carried out. Even once a diagnosis is made, antiviral drugs would have to be distributed rapidly to possibly remote and inaccessible locations, which would also have to be sealed off. As Dr Stohr, of the WHO, said, the chances of success are “not huge”:

“The models say it can work; the reality would say we have areas in Asia where 80 per cent of the country can only be reached by four-wheeled drive vehicles; where the challenge is to treat in ten to 15 days 80 per cent of a population with a drug which has to be taken over a certain period of time; where you have to have a very high compliance rate; where you have to

 practically seal off the territory and make sure nobody gets in or out. It is a huge challenge.” (Q 210)

Commenting on such issues, Dr Nabarro noted that it might be necessary to draw on “military capability” to implement the rapid response measures. This seems to us to be a sensible and proportionate strategy. (Q 308)

4.5. A further limitation of the modelling is that it does not take account of the different processes by which a pandemic might emerge: in the words of the Medical Research Council, “It is less clear how effective these strategies would be in the face of a gradual evolution of strains with more efficient human-to-human transmission, and/or diffuse emergence on a widely dispersed geographic front in remote districts with poor communications”. There is clearly an urgent need for further work in this area. (p. 138)

4.6. In the longer term it is clear that the best way to develop a rapid response capability is to invest in improved surveillance and healthcare facilities in the region. The priorities for rapid response were summarised by Dr Stohr: local healthcare workers who are “aware of the clinical science and … attentive”; hospitals within reach of rural communities; regional laboratories able to propagate virus samples and diagnose infection with avian influenza. Much of this investment will thus involve upgrading generic healthcare facilities and skills; it should therefore bring enormous collateral benefits to the region, and the international community, through improving the detection of all infectious disease threats, as well as improving response times to a potential influenza pandemic. (Q 202)

Conclusions

4.7. Recent modelling by United Kingdom researchers suggests that by rapid diagnosis and targeted response it may be possible to nip a pandemic in the bud. While this research has profound implications, further refinement of the modelling is urgently required, and we look to the Medical Research Council to make this a high priority within its influenza research programme.

4.8. While it may be theoretically possible to nip a pandemic in the bud, the practical difficulties remain formidable. We welcome the donation by Roche Products Ltd of three million courses of oseltamivir to the WHO, and we also welcome the efforts of the UN and its agencies to improve surveillance and implement a co-ordinated rapid response strategy. We urge the Government to give their full backing to these efforts.

4.9. We further believe that substantial investment by the international community in improving healthcare in south east Asia represents the best long-term strategy to prevent future influenza pandemics. We recommend that the Government, in collaboration with international partners and the World Bank, make such investment a high priority.
CHAPTER 5: MITIGATION

Stopping a pandemic reaching the United Kingdom

5.1. So far we have focused on either preventing a pandemic by targeting avian influenza, or on the possibility that a potential pandemic could be averted by isolating the region of origin and targeting the population with antiviral drugs. However, there is no guarantee that these strategies will succeed. Modelling shows that if a new and highly infectious virus were to spread beyond its region of origin, and particularly if a cluster of cases were to occur in an urban centre, it would rapidly become difficult, if not impossible, to prevent a global pandemic. This chapter therefore focuses on the measures that the Government may be tempted to introduce in order to slow or mitigate the impact of such a pandemic.

5.2. In the case of the SARS outbreak in 2003 measures taken in various countries included:

- Travel restrictions;
- Quarantining of those suspected of being infected;
- Thermal screening at airports.

It is likely that there will be pressure to introduce some or all of these measures in the event of an outbreak of pandemic influenza. The question is, will they have any effect?

5.3. SARS vividly demonstrated the speed with which infection can travel around the globe along the path of major air routes. There will be an obvious temptation, in the event of an outbreak of pandemic influenza in south east Asia, to impose restrictions on air travel from the affected area. However, even in the case of the 1918-19 pandemic, Australia, through stringent maritime isolation and quarantine, succeeded only in securing a more protracted, milder outbreak. Since then international travel has expanded beyond all recognition, and there are now approaching two billion passenger journeys by air each year. In addition, travel via third countries is commonplace.

5.4. To be effective travel restrictions would have to be rigorous, and would involve huge economic cost. Expert opinion is that a reduction of international travel by 90 percent would only achieve a small delay in spread of the disease. Indeed, modelling of the development of a pandemic in the United Kingdom shows that reducing the number of imports of infection from 10 to one a day would succeed only in deferring the peak of a pandemic by around a week, while reducing the number of new cases per day at the peak from around 1.2 million to a million:
5.5. Blanket quarantining of arrivals from affected regions might be more effective in slowing down imports of the disease, and the United States government already has a number of quarantine stations that could be used in the event of a pandemic. However, the costs would again be very considerable, regardless of the implications for civil liberties. There is also a risk that were quarantine arrangements to be announced many travellers would find ways to avoid quarantine by entering the country via unaffected third countries.

5.6. Another strategy employed by some countries to restrict the spread of SARS was the thermal screening of arrivals at airports, allowing in theory for the identification and isolation of those with early symptoms of infection. However, recent research suggests that such screening would have very limited effect in detecting early infection with influenza, which has no symptoms and leaves body temperature unchanged.$^{11}$

Mitigating the effects: antiviral drugs

5.7. If the virus were to be introduced into the United Kingdom, various strategies could be used to mitigate its effects and limit or slow down its spread. The most promising of these involve the use of antiviral drugs either to treat those infected with influenza or as prophylaxis for those who are at risk of infection. The options were summarised at our seminar by Professor Ferguson:

- Treatment-only use of antiviral drugs;

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Blanket prophylaxis;
• Treatment plus limited prophylaxis (e.g. “household prophylaxis”);
• Treatment plus limited prophylaxis plus control of large gatherings, closure of schools or workplaces, and so on.

5.8. The backdrop to all these options is the Government’s order of 14.6 million courses of the antiviral drug oseltamivir (Tamiflu). This order, which will be fulfilled by autumn 2006, is based on the assumption that the disease will have a 25 percent “attack rate”—in other words, that one quarter of the population will be infected, and that for each person infected one course of the drug will be required.

5.9. A “treatment-only” approach is thus the Government’s preferred option. Assuming that the virus does not develop resistance to the drug, cases would be less severe, and hospitalisation and mortality correspondingly lower. However, for the drug to have an effect the course has to start within 48 hours of the onset of symptoms—the earlier the better. At the peak of pandemic, with around one million new cases each day, there would be huge strains on the health service in diagnosing new cases and getting drugs to patients within this timescale. We look at this issue in more detail in our next chapter. In addition, we are seriously concerned over the robustness of the assumptions made regarding the “attack rate” of a new virus, which in reality could be either significantly below or above 25 percent. If the latter were to be the case, supplies would simply run out.

5.10. At the other extreme, blanket prophylaxis does not appear feasible. Antivirals provide protection only as long as they are being taken, and each course of oseltamivir lasts five days. It would be prohibitively expensive for the whole population to be provided with antiviral drugs until such time as a vaccine was available against the pandemic strain, possibly up to nine months after the initial outbreak. Even if this approach were affordable, the limited supply of antivirals globally would prevent it.

5.11. Targeted or “household” prophylaxis in the initial stages of a pandemic falls between the two extremes of blanket prophylaxis and treatment-only. We have already noted that antivirals are particularly effective when taken preventatively. The object of limited prophylaxis would thus be to target the first cases, identifying close contacts (such as family members and healthcare workers) and prescribing antivirals in such a way as to slow down the spread of the disease. In principle this could buy more time which could be used for the development of a vaccine.

5.12. At our seminar Professor Ferguson estimated that “household prophylaxis” could lead to a reduction of around 30 percent in the number of cases of infection over the first 180 days of a pandemic. The HPA were more tentative, but accepted that if the first importation of the virus could be identified targeted prophylaxis “might just slow [the virus] down for a few weeks which gives us time”. However, in the absence of evidence from well-conducted trials, or the experience of an actual epidemic, these projections remain somewhat speculative. (Q 116)

5.13. Despite the views of the HPA, the Government have not publicly committed themselves to using antiviral drugs as prophylaxis to target the first cases. The Minister, indeed, said in terms that “we believe that this should be used for treatment and not used prophylactically”. The Contingency Plan, while
noting that “short term prophylaxis” could be used to delay the establishment of a pandemic, states that this would be “done on a case by case basis and is … not the main use of antiviral drugs” (p. 46). Moreover, whereas the Government’s order for 14.6 million courses leaves little or no spare capacity for prophylactic use, a strategy of “household prophylaxis” would require from 30 to 100 percent more antivirals than are currently on order. Not only would there be significant cost implications, but there could be a substantial delay between an order being made and the delivery of the drugs. (Q 222)

5.14. “Household prophylaxis” could also be combined with limits on public gatherings, for instance the closure of schools or workplaces, suspension of football matches, and so on. Targeted at the initial outbreaks, such additional measures could significantly delay the spread of the disease, albeit at the expense of considerable social disruption. The Contingency Plan simply states that they are “being kept under review” (p. 48). It is worth noting that under the terms of the Civil Contingencies Act 2004 the Government have very wide powers in the event of a national emergency (which could include a pandemic) to take steps of this kind at short notice.

5.15. There is an overarching issue of cost. The Government have committed £200 million to the existing order for oseltamivir. The drug has a limited shelf-life (five years), so if there is no pandemic within this time-frame the stockpile will have to be discarded and (assuming the world remains on pandemic alert) replaced. Yet so far as we were able to ascertain from the Minister this commitment has been made without any cost benefit analysis (see QQ 222-223). It is difficult to predict what such analysis would reveal—it might show that household prophylaxis, although more expensive in absolute terms, represented a more cost-effective strategy than treatment-only. In the absence of comprehensive modelling of the best and most cost-effective way to use antiviral drugs, the Government’s open-ended commitment of considerable sums to their purchase is a matter of serious concern.

5.16. Finally, there remains the possibility that the virus could develop resistance to oseltamivir. We have already alluded to the fact that some H5N1 strains in south east Asia have developed resistance to M2 inhibitors such as amantadine, and that research is being undertaken into the optimum combinations of antiviral drugs in order to minimise further development of resistance. Although there is no confirmed case of resistance to oseltamivir, it would be prudent for the Government to consider a back-up plan, possibly involving zanamivir (Relenza) or combination use of oseltamivir with M2 inhibitors.

Conclusions

5.17. Once an influenza pandemic is established, in south east Asia or elsewhere, there is no realistic prospect of preventing its spread to the United Kingdom. Travel restrictions, quarantine or screening at airports, while they would be highly visible, would only delay the spread of the virus.

5.18. The early and targeted use of antiviral drugs, not only to treat the first cases in this country, but to provide prophylactic protection to close contacts such as family members or health workers, could both delay and lower the peak of a United Kingdom pandemic. This would
reduce the strain on health services, and give more time for the production of a vaccine.

5.19. **We are therefore extremely concerned at the lack of clarity in the Government’s policy on prophylactic use of antiviral drugs, and at the possibility that the Government’s order of only 14.6 million courses of oseltamivir may have tied them into a treatment-only policy on using the stockpile.**

5.20. **We recommend that the Government work together with the HPA and the research community to establish the optimal strategy for the use of antiviral drugs, and that further orders, if required, should as a matter of urgency be placed to allow this strategy to be implemented. We further recommend that this strategy should incorporate a rigorous cost-benefit analysis.**

5.21. **We recommend that the Government develop back-up plans in case resistance to oseltamivir emerges. These should encompass possible combination therapies or the acquisition of reserve stocks of zanamivir.**
6.1. If a pandemic reached the United Kingdom, the major challenge for the Government would be to limit the damage and ensure a rapid recovery. The Contingency Plan describes the Government’s strategy for meeting this challenge.

6.2. We said in *Fighting Infection* that the United Kingdom Contingency Plan had for several years been among the best in the world, and we see no reason to change this assessment now. But at the same time we have considerable sympathy with the caveat expressed by Mr Kevin Hawkins, Director General of the British Retail Consortium:

“[One should] remind oneself of Field Marshal von Moltke’s famous rumination that no battle plan ever survives contact with the enemy and all contingency planning is based to a great extent on known scenarios, on hard-won experience in the past. The problem with a pandemic is that none of us have had experience of it and we do not know until it starts exactly what the depth of the crisis will be and how many people will be laid low by it.” (Q 366)

6.3. With this caveat, we have looked at a number of issues around contingency planning, particularly insofar as it affects health services, local and emergency services, and businesses. Finally, drawing these various strands together, we have asked whether the Government are providing strong enough leadership to ensure that all those who will be affected by a pandemic participate fully in contingency planning; and whether the Government’s communication strategy is adequate to keep the public well-informed.

**Health services**

6.4. The health service response will be crucial in a pandemic. The strain on frontline services will be enormous. While projections are inevitably uncertain, and depend on the virulence of the virus that eventually emerges, it is possible that at the peak of a pandemic there could be over one million new cases of influenza each day, with general practice consultations rising from a baseline of 30 per 100,000 population per week to 5,000-10,000 per 100,000 population per week; pandemic-related occupancy of intensive care beds alone could be over 200 percent of total current capacity. At the same time, health services, like all other organisations, could see illness-related absenteeism of 25 percent or more.

6.5. Responsibility for co-ordinating the health service response in England and Wales rests with the HPA, and the HPA *Influenza Pandemic Contingency Plan* is in effect a sub-plan of the overarching Government Contingency Plan. It assigns responsibilities to the various NHS authorities, from the Department of Health itself, which will establish a national “Operations Room”, through Regional Public Health Groups, Strategic Health Authorities, hospital and ambulance trusts and Primary Care Trusts (PCTs).

6.6. The HPA’s top-level plan begs a number of questions. For instance, is the HPA’s funding, which has been cut in recent years, adequate for it to fulfil its own commitments? How deep does the planning go? Have the implications of a pandemic for frontline health services been fully assessed? While we have not had time in the course of this short inquiry to explore all the
ramifications of health service contingency planning, we have identified some particular areas of concern.

**HPA funding**

6.7. In the course of the Department of Health’s review of arm’s length bodies the HPA’s funding has come under close scrutiny. It is clear that this has presented problems in the context of planning for an influenza pandemic. As Professor Troop said,

“We came under extreme scrutiny and had our budgets squeezed. That … does make planning for an influenza pandemic quite challenging. We do get small amounts of money for specific activities but most of this has been found by internal efficiencies, and while influenza is a priority of course all the other infectious diseases do not go away whilst we do this.” (Q 98)

6.8. The Minister, in contrast, responded to a question on HPA funding by saying, “If you wanted to send us any information that you were particularly told that they would not be able to do, please do so. That is certainly not what we are feeling at all.” She accepted that “there may well be room for certainly efficiency savings in terms of things like backroom staff or whatever”, but argued that “the idea of that is to put more resources at the frontline, not to cut funding to organisations”. This is a wholly unconvincing response in light of Professor Troop’s comments, and particularly given that the HPA is not formally considered a “frontline” service under the arm’s length body review process. (QQ 257-259)

**Information gathering and reporting**

6.9. Given the inherent uncertainties of contingency planning, and in the case of a pandemic the particular uncertainties over the effects of the virus, the best treatments, outcomes for individual patients and so on, flexibility in applying and if necessary adapting contingency plans will be essential. This will require constant surveillance and the rapid interchange of information between frontline health services and the centre.

6.10. The Minister sought to provide reassurance on this point, drawing attention to the “very good information reporting systems” that have been tested in the context of severe winters and ordinary seasonal flu. More detail was provided by Dr Salisbury, who noted that information from a range of frontline services would be brought through a single “gateway” controlled by the HPA, who would in turn “be doing the epidemiological surveillance, and the modellers can be taking data and making projections on the pattern of the pandemic which will then allow informed policy decision-making”. (Q 263)

6.11. A key contribution to this exchange of information should be made by the Royal College of General Practitioners (RCGP) influenza surveillance unit. However, Professor Mathers of the RCGP claimed that they had been unable to secure formal agreement from the Department that the unit would continue to receive support beyond April 2006. In the words of Professor Mathers, “As it currently stands, our contract runs out in April 2006, which gives us problems with the continued employment of the staff. It is almost as though there is a planning blight.” In contrast, Dr Salisbury, of the Department of Health, said, “we have already been having discussions with the RCGP about their central surveillance scheme, including expanding the scheme to take in parts of the country which were not previously covered.”
We are unable to reconcile these apparently contradictory statements. (QQ 164, 265)

**Managing resources and manpower**

6.12. We have already noted that hospitals, GP surgeries, and other frontline health services, can expect significant absenteeism in the event of a pandemic, either as a direct result of illness or as a result of failures in public transport. Professor Menon, of the Intensive Care Society, estimated that Intensive Care Units could lose “20 to 50 percent of ... nursing staff”. Professor Mathers suggested that if those working in small general practices followed guidelines recommending voluntary quarantine for those with influenza-like symptoms, “very rapidly you are going to close down the practice”. Dr Peter Bailey, of the Monkfield Medical Practice, noted that under pessimistic scenarios his practice, with a staff of around 20, might see “a greater than 1:4 probability ... [of] the death of a team member.” Ms Lynne Young, of the Royal College of Nurses, suggested that the Government should consider putting out a call to “recently retired nurses” or “nurses who have actually chosen to leave the profession”—though these would need training if called upon. (QQ 157, 176, p. 132, Q 165).

6.13. In response, the Government has ordered some 2.5 million doses of H5N1 vaccine, for distribution among key workers, including frontline healthcare workers. The vaccine may provide some protection against infection, though how much is far from certain. In addition, the Contingency Plan indicates that planners at local levels are expected to decide on issues such as the provision of protective equipment to staff, and the rostering of staff so as to minimise the spread of infection within health service premises (p. 51). However, we are unclear as to the measures in place either to reallocate staff among PCTs, or to call on extra staff, for instance the recently retired, to provide support in an emergency.

6.14. In addition, many of our witnesses argued that if frontline services were tocope with a pandemic certain core day-to-day services would have to be set aside. Ms Helen Young, Director of Nursing at NHS Direct, noted that if contingency plans came into effect, “we would be unable to continue with what we call the core business, the business that we currently do.” Professor Menon was equally pragmatic with regard to hospital beds and operating facilities: “your hip operation is going to be delayed, elective surgery is going to be delayed and lots of things are going to have to wait. People have to realise that that is a fact of life.” The RCGP argued that “GPs will need to have their quality targets in other areas protected if the workload due to a pandemic affects their performance in these areas.” (QQ 168, 177, p. 55)

6.15. Ms Winterton, however, offered no guarantees:

“What is important is that at the moment we establish the relationships between GPs and those they would be working most closely with in the event of a pandemic, so that it is quite clear what would happen and who is doing what. I can understand that some people would say, ‘We want to know everything now’, but quite honestly we have to give out the information depending on the circumstances of the moment.” (Q 260)
Structural reform

6.16. Health Services, particularly Primary Care Trusts, continue to undergo radical reform. The effects of this upon preparedness clearly varies widely between regions and individual PCTs. Professor Mathers described the effect of reorganisation as a “planning blight … it is very difficult for PCTs actually to focus down on one particular topic, such as the flu pandemic.” Mrs Jan Hutchinson, of NHS Alliance, while noting that “we may see new primary care trusts coming into existence round about this time next year”, and that this might “not be a good time to have new organisations coming into existence,” was reassured by the stability provided by the HPA. Ms Lynne Young was much less sanguine: “We are hearing from our nurse members every day about what utter chaos and confusion there is in primary care trusts at the present time.” (QQ 162, 98, 185)

6.17. Ms Winterton rejected any suggestion that health service reform should be scaled down in view of the threat of a pandemic: “As we have said already, one has very little idea as to, if a pandemic did strike, when exactly it would be, in how many years’ time it might be. It would be a slightly curious proposition to say that we could never do anything to the NHS in case this upset planning and took people’s minds off the job.” Ms Winterton did not give any indication as to whether the Government’s position on health service reform might be reviewed if the state of pandemic alert was raised further. (Q 254)

Rapid diagnosis and treatment

6.18. In the event of a pandemic, the first line of defence for those infected will be antiviral drugs. The Government’s stockpile of 14.6 million courses of oseltamivir will be complete by September 2006, and will (subject to the issues we have already raised concerning prophylaxis) be sufficient to treat 25 percent of the population. If a pandemic were to occur before September 2006, of course, the stockpile would be incomplete, and there would be a serious risk that health services would simply run out of antivirals. In such circumstances, or if the 14.6 million courses themselves turned out to be inadequate, decisions on rationing would have to be taken. Drawing attention to this possibility, Dr Jarvis of the British Medical Association argued that “under no circumstances can we let individual GPs and nurses on the frontline have to make decisions of that magnitude; it needs to come from the centre.” We agree. (Q 197)

6.19. However, even once the stockpile is complete, and assuming it is adequate, the diagnosis of up to a million new cases of influenza a day and the rapid distribution of drugs (which, to be effective, have to be taken within 24-48 hours of the onset of symptoms) will be a huge challenge. We have already drawn attention to the potential burden on general practices—alternatives to attendance at GPs’ surgeries will be needed.

6.20. We draw some comfort from the evidence of Ms Helen Young, of NHS Direct, whose telephone operators already triage callers by reference to standard algorithms, starting with the “worst case scenario” and working backwards. Ms Young assured us that the service already had “algorithms available for a potential flu pandemic”. These would distinguish between those capable of “self-care” and those in need of personal consultations. (QQ 173-174)
6.21. However, there is still much to be done in this area. Ms Winterton emphasised that part of the Government’s communications strategy would be to encourage people “to look out for symptoms in themselves and their families” (Q 262). But self-diagnosis is inevitably problematic, however good public information may be. Dr Salisbury appeared to imply that in the event of a pandemic “false positives” would have to be tolerated:

“the public will be receiving information that not only tells them what sort of things to look out for in terms of flu-like symptoms but tells them what to do about it and also tells them where they can get more advice. Much harder is telling them about everything else which is not influenza. During the times when you do not have a pandemic, clearly you are going to have to take great note of people who think they have got pandemic flu to see what they have got. At the time of the pandemic, most people with flu-like symptoms will have influenza.” (Q 269)

6.22. If rapid diagnosis is to be feasible, the availability of a simple, “dipstick” test for influenza would be invaluable. No such test for H5N1 exists at present; Professor Zambon, of the HPA, confirmed that research into such a test was a priority, but it was unlikely to be available in the next six to twelve months. We note in this context that among the projects being supported by the HPA is that of Professor Helen Lee, of Cambridge University, who in October was awarded the Lord Lloyd of Kilgerran award for her contribution to the application of technology to diagnostic development, with particular reference to the third world. Rapid and affordable diagnostic tests will be especially important to such countries in the event of a pandemic. (QQ 117-118)

6.23. There is still the question of how antiviral drugs would be supplied to those patients, particularly those quarantining themselves at home. The Government appear to be examining possible mechanisms for this. Dr Harper noted that in the event of self-diagnosis “we would look at Primary Care Trust level to have in place arrangements to get the antiviral to the people who needed them. That is the sort of consideration we are looking at right now.” Similar considerations would also apply to the availability of oxygen and antibiotics to treat secondary infections. (Q 262)

Emergency and local services

6.24. We have also explored the extent to which emergency and local services are prepared for a pandemic. Under the Civil Contingencies Act 2004, “Category 1 responders” (e.g. emergency services, health services, local authorities) are required to put in place emergency plans, to co-operate with other responders, to provide information to the public and businesses, and so on. At regional level the response to a pandemic or any other emergency is led by Regional Resilience Forums, based on police areas, which bring together Category 1 responders and other organisations such as utilities or transport companies. Such Forums are required to be in place from November 2005.

6.25. Both Deputy Chief Constable Alan Goodwin, of the Association of Chief Police Officers and Mr Philip Selwood, of the Ambulance Services Association, offered reassurance that these arrangements are indeed falling into place, and that there is what Mr Goodwin called “very close liaison at all levels”. Mr Goodwin also told us that he was “confident that within every regional and local resilience forum there have been very detailed discussions
around the national pandemic flu plan and also some very large scale exercises at the local level to test the plan”. (QQ 327-328)

6.26. The role of the forum is preparation. Mr Zyg Kowalczyk, of the London Resilience Team, described what would happen once a pandemic or another emergency actually occurred. The Civil Contingencies Committee at the Cabinet Office (COBRA) would at this point activate Regional Civil Contingencies Committees, which would in turn co-ordinate regional responses to a crisis. These would in effect be the same as the Forums—there would be “a change of name and a change of function but most of the personnel around the table will be the same.” It is not, however, clear to us what would happen if a quarter or a third of these personnel fell ill. (Q 334)

6.27. The major challenge that the emergency services, like health services, will face in the event of a pandemic, will be to maintain core services while losing, in Mr Goodwin’s words, “25 to 40 percent of the workforce”. Demands on the emergency services would also inevitably increase, with ambulances answering increased numbers of 999 calls, police having to protect stocks of antiviral drugs, and so on. Mr Goodwin confirmed that arrangements for reallocating police resources between regions were “well tried and tested”, and that there was “the potential for military assistance”. Mr Selwood said that the ambulance service had had “dialogue with private ambulance services”. (QQ 315-316, 337)

6.28. As for local authorities, which are obliged by statute to contribute to Regional Resilience Forums, and which, in the event of a pandemic, would have a major role, and whose key public services, from waste disposal to social services to mortuaries, would be under considerable strain, we had considerable difficulty in securing any evidence. The Local Government Association declined to give evidence, and although we did ultimately talk to the London Regional Resilience Forum, they were of course unable to speak for local government across the country. We find the lack of evidence from this sector a matter of great concern.

The private sector

6.29. Like local government, representatives of the business community were reluctant to come forward to give evidence. In the event, we were grateful to Professor Jim Norton, of the Institute of Directors (IOD), Mr Kevin Hawkins, of the British Retail Consortium (BRC) and Mr Alan Lacey, of J Sainsbury plc, for their willingness to talk to us. Their evidence was probably the most alarming that we heard in the course of our inquiry.

6.30. Professor Norton, for instance, highlighted a survey conducted by the IOD which showed that only 50 percent of member companies had contingency plans in place—the lack of planning was particularly marked among smaller companies. This was compounded by the lack of resilience in a whole range of services that are critical to business, partly as a result of the fact that “for very good economic reasons and very good business reasons, we have taken much of the slack out of our systems in many sectors”. He warned of the vulnerability of the electricity network, mobile phone networks, and so on, whose collapse could rapidly lead to “cascades of failure”. (QQ 347, 352)

6.31. Similar vulnerability affects the food distribution and retail sector. Mr Hawkins noted that “the level of stock … generally is much lower than it used to be.” As a result, during the fuel protests of 2002 “the food supply
chain came within a few days of collapse”. In particular he drew attention to three crucial areas:

- The “shortage of qualified heavy goods vehicle drivers”, on whom the entire food distribution network, from farmers to distribution centres to shops, depends; in the event of a pandemic the possibility of recruiting qualified drivers to replace those falling ill would be “very remote”;

- The impact on the large numbers of mostly part-time staff who actually put food on supermarket shelves;

- The possibility of panic buying. (QQ 352-354)

6.32. Attempts to plan for such contingencies have not had much encouragement from the Government. In answer to a series of questions, our witnesses made it clear that they had received no guidance from the Department of Health, the HPA or local government, and that there had been no discussion between Regional Resilience Forums and the major retailers about maintaining food supplies in the event of pandemic. The only meeting with Government of which Mr Hawkins was aware had been arranged at the request of the BRC, and had been attended by Defra officials working on disease control, rather than business continuity. He pleaded for more proactiveness from Government: “We seem to have to take the initiative every time in order to get answers to questions … one would have thought it would have been in their own interests to initiate an early dialogue with the key parties within that supply chain.” (QQ 367-373)

Communications and leadership

6.33. There has been considerable media coverage of avian and pandemic influenza in recent months, much of it ill-informed and alarmist. An effective and proactive communications strategy will be essential in the event of a pandemic in order to provide reassurance and advice to the public. The Government have already made a good start in this area, with the circulation of guidance, including useful background material on pandemic influenza, to general practices.

6.34. However, other examples of Government efforts to communicate with the public on health issues are less reassuring. Mr Hawkins cited two. When the Sudan 1 scare broke out, the Food Standards Agency (FSA) on the one hand said there was only a “small risk to human health”, and on the other said that the public should not eat products containing Sudan 1, but should return them all to retailers. And then in the autumn when concerns over avian influenza were heightened, the FSA “simply put out a statement saying that chicken was perfectly safe to eat on its website”, when they needed “something which is a lot more proactive, especially in the context of tabloid headlines”. (QQ 351, 349)

6.35. The need to give clear, unambiguous messages is tied up with a broader issue of Government leadership. Although contingency planning is co-ordinated by the Cabinet Office through COBRA, the Cabinet Office role is largely administrative. On policy individual departments lead as appropriate—in the case of pandemic influenza, the Department of Health leads, and in fact the Cabinet Office declined to give evidence to our inquiry.

6.36. But in the case of a possible influenza pandemic, an emergency that would affect every branch of social life—hospitals and schools, the transport system,
food supplies and prisons—there must be some doubt over whether the Health Department is capable of communicating effectively with all those involved in contingency planning. The food retailers have regular channels of communication to Defra, the police to the Home Office, and so on. It does not appear that all these channels of communication are yet being used effectively or consistently.

6.37. Mr Hawkins emphasised that “What we learned during foot and mouth … is that there needs to be one simple message communicated by all the relevant government departments and it needs to be repeated and repeated and repeated”. A related point was made by Dr David Nabarro, the Senior UN System Co-ordinator for Avian and Human Influenza, who argued that within governments there was “a necessity to take the responsibility for preparedness planning above the level of the Minister of Health versus the Minister of Agriculture versus the Minister of Interior versus the Defence Minister and to have an over-arching ministerial responsibility … it is very hard to get different government departments and ministers to work together in a joined-up way on contingencies unless they are encouraged to do so by the highest authority in the country.” (QQ 349, 311)

6.38. It was striking that at the same time on 1 November as we discussed United Kingdom preparedness with Ms Winterton, Minister of State at the Department of Health, in Washington President Bush was announcing a $7.1 billion programme of action and research on influenza. This vividly demonstrated what Dr Nabarro called “the political dimension, the kind of thing we saw today which is quite courageous from the US President, where a senior figure steps out and gives additional political cover to the ministers of health or the ministers of finance.” (Q 302)

Conclusions

6.39. The Government’s Contingency Plan is an excellent top-level account of the United Kingdom health service response to a pandemic, but an enormous amount of work remains to be done at lower levels. We therefore recommend:

- That cuts in HPA funding be reviewed and if necessary reversed, to ensure that the HPA’s ability to provide leadership to the health service response is not compromised;
- That the Government review the resilience of systems for supplying information from frontline health services to the centre, and in particular that they ensure that funding for the Royal College of General Practitioners’ surveillance service is extended;
- That the Government provide advice to PCTs and general practices on the mechanisms for reviewing and if necessary suspending performance targets in the event of a pandemic—such advice is needed now if frontline health services are to develop robust and well-informed contingency plans;
- That mechanisms for storing, prescribing and distributing antiviral drugs be urgently reviewed; and that the availability of antibiotics, oxygen and other supplies be examined and if necessary reinforced.
6.40. We commend the work of the emergency services in developing contingency plans. However, despite the duties imposed on local authorities by the Civil Contingencies Act 2004 to develop contingency plans and participate in Regional Resilience Forums, we are not convinced that local government is yet fully aware of the implications of an influenza pandemic. We urge the Government to provide clear and unambiguous direction and guidance in this area.

6.41. We are alarmed at the risk of serious disruption to food supplies, and at the lack of contact between the Government and the major food retailers. The Government urgently needs to address the resilience of food distribution networks.

6.42. All departments of Government need to work together in preparing for a possible pandemic, but we do not believe the Department of Health can provide strong enough leadership to achieve this. We therefore support the view of Dr David Nabarro that the importance of pandemic influenza contingency planning should be underlined at the highest level within Government. The development and implementation of contingency plans should be the responsibility of a Cabinet-level Minister for contingency and disaster planning, located within the Cabinet Office.

6.43. In the event of a pandemic a clear message and direction from all branches of Government will be critical, and we recommend that the Government develop and publicise a strategy for proactive dissemination of key information and advice, using all forms of national and local media.
CHAPTER 7: A LONG-TERM STRATEGY

7.1. Up to this point we have concentrated on the steps that can be taken to prevent a pandemic happening and on the measures that will be required to minimise the disruption that a pandemic would cause. We now turn to longer term planning and research.

Vaccines

Manufacturing technology

7.2. We have already noted, in our overview of the treatment and prevention of influenza, that it would probably take seven to nine months from the initial outbreak of a pandemic to prepare a vaccine. In other words, by time a vaccine was ready there would be a chance that the pandemic would have passed its peak—as happened in 1957 and 1968. On the other hand, if vaccine production can be accelerated, the time cut from, say, nine to six months, there would be huge benefits not only in the event of an influenza pandemic (in protecting the population from second and subsequent waves), but more generally in improving our ability to respond to new diseases.

7.3. At present the killed virus from which vaccines are manufactured is incubated in hens' eggs, a technology dating back to the 1950s, which would appear to be particularly vulnerable in the event of a pandemic of avian-derived influenza. New methods of production are long overdue, and their importance was underlined on 1 November by President Bush’s announcement of a $2.8 billion programme to promote the development of cell-culture technology, which he argued would “produce enough vaccine for every American within six months of the start of a pandemic”.12 Work on cell-culture of vaccines is also underway in Europe, and Dr Bryett, of Chiron, told us that his company would “be looking to have the product available” in “about a couple of years”. (Q 55)

7.4. However, it is not entirely clear how much difference the introduction of cell-culture would make to the time taken to produce a vaccine. Dr Bryett downplayed expectations of a radical improvement, telling us that cell-culture would remove “the delay of getting the hens’ eggs into the system” (one egg for each dose of vaccine), but that the actual time taken to cultivate the virus would remain broadly similar. He did not put a figure on the time that would be saved by moving to cell-culture. (Q 56)

Inter-pandemic demand

7.5. Even when a vaccine is ready, limited manufacturing capacity within the industry means that there will be a significant delay before orders can be fulfilled and the vaccine made generally available. Both Chiron and the UK Vaccine Industry Group (UVIG), which represents all six UK-based vaccine manufacturers, argued, in Chiron’s words, that “Current production capacity reflects ongoing inter-pandemic demand, and is far from sufficient to meet a global pandemic requirement … the Government needs to take steps to increase inter-pandemic demand for vaccines, and drive investment in new production facilities”. (p 24)

7.6. In other words, the manufacturers argue that the Government should both increase take-up of the normal annual flu-jab by those at risk, and broaden their definition of “at-risk” groups, so as to build up manufacturing capacity and help manufacturers to increase output in the event of a pandemic.

7.7. Chiron went on to state that “despite relatively high coverage in the age group 65 years and over, only an estimated 42 percent of at-risk patients in the UK are currently vaccinated”. The Minister, on the other hand, defended the Government’s record, although she was vague about the exact figures: “We have a very good track record in terms of achieving the targets we have set, which was something like 70 per cent of people over 65, or 60; I cannot remember which.” In effect, she blamed other countries: “There are some countries that are not up to the level that we are in terms of seasonal flu vaccination and manufacturing thereof.” (p 24, Q 229)

7.8. We are sceptical about both sides of this argument. On the one hand, increasing the take-up of the annual flu-jab will not in itself be sufficient to raise manufacturing capacity to the point where the companies can respond rapidly to the requirements of a pandemic, in which governments around the world will be urgently seeking to vaccinate their entire populations. On the other hand, we are disturbed by the complacency of the Minister’s response, and the implication that other countries are to blame for the shortfall in manufacturing capacity. Increasing the take-up of the annual flu-jab among at-risk groups will bring its own health benefits, and should be a high priority for the Government regardless of the danger of a pandemic. Furthermore, the distribution problems that resulted in the announcement on 22 November that stocks of seasonal influenza vaccine were all but exhausted suggest that the Government need urgently to review guidance for general practitioners as well as the public.13

7.9. There is a related issue to do with advance purchase agreements for any new vaccine. We were told that the Government would, by this means, secure delivery in the event of a pandemic of 120 million doses of vaccine (enough to provide the necessary two doses to each person in the United Kingdom). However, the precise commercial arrangements are as yet unclear, and even Dr Bryett, of Chiron, noted that “so far we do not have any details”. (Q 58)

7.10. While the existence of an advance purchase agreement offers some comfort to the people of the United Kingdom, it also opens up the possibility that those developed countries able to negotiate such agreements will, in the event of a pandemic, take up all the manufacturing capacity, leaving none for developing and other countries. This could potentially have a dramatic effect on international relations.

7.11. We note the comment of Mr Richard Stubbins of UVIG, that the industry has discussed ways “to distribute vaccines as equitably as possible” between countries, possibly providing vaccines “on a proportional basis, based on a government’s purchase of the vaccines in the inter-pandemic period”. Though this arrangement would provide an incentive to all governments to increase their take-up of annual influenza vaccine, it is debatable whether it would be any more equitable than a first-come-first-served distribution. It would also mean that the United Kingdom, which normally purchases

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around 12 million doses of trivalent influenza vaccine, would have access to just 36 million doses of monovalent pandemic vaccine, well short of the 120 million doses required to cover the whole population. (Q 60)

Reducing the dose

7.12. Other measures, both to improve the efficacy of vaccines and to speed up the regulatory and bureaucratic processes necessary before a new vaccine can be approved, hold out more promise. On efficacy, various vaccine manufacturers, including Chiron and GlaxoSmithKline, are currently studying the potential for incorporating an “adjuvant” in the influenza vaccine, which will allow the vaccine to be delivered in much lower doses without diminishing its effectiveness. In effect this would mean that any given volume of virus cultivated, whether in eggs or cell-culture, would yield many more doses than at present.

7.13. Trials by Chiron of an adjuvant known as MF59 have shown that the amount of antigen required to produce an immunological response can be reduced from the normal monovalent dose of 15 micrograms to 7.5 micrograms without loss of efficacy. This would have a significant effect upon the industry’s ability to manufacture large quantities of vaccine in a limited time. However, MF59 is a proprietary product, which can only be used by other manufacturers subject to licensing arrangements. Asked whether this could be a barrier to large-scale production, Dr Bryett, Managing Director of Chiron UK, said merely that the company was “reviewing the capacity for the adjuvant very actively.” (QQ 48-49)

Regulation and “mock-up” dossiers

7.14. Rapid regulatory clearance for a new vaccine will also be critical. The European Medicines Evaluation Agency (EMEA) has already established a “mock-up dossier” for a pandemic vaccine. This will allow the manufacturers to go through many of the stages of regulatory approval (quality tests, trials and so on) on the basis of one of the strains of the virus already circulating. Once the actual pandemic strain is identified it would then simply replace the mock-up strain without having to go through the whole regulatory process from scratch. As Dr Salisbury said, the objective is that “the various regulatory processes that are necessary in that period of time can be brought together and made to run concurrently rather than sequentially so that the interval between having a pandemic virus and having the seed material for production is brought down to the absolute minimum”. (Q 243)

7.15. However, mock-up dossiers are expensive—of the order of €11-13 million per candidate vaccine—and Dr Bryett noted that “it would be a mock-up file for each vaccine; it is not a question of a single generic mock-up file. Each manufacturer will have a different way of producing the vaccine and probably different testings.” Approval in principle by the EMEA is therefore not in itself sufficient to ensure that this investment will be made. The evidence we received from the Minister and her colleagues was somewhat vague, but there does not seem to be any guarantee that the Government will finance mock-up dossiers. (QQ 37, 223-228, 243)

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14 Take-up in 2005 was higher, with the result that the Government announced on 22 November that the 14.5 million doses ordered by GPs had been exhausted.
7.16. In light of the proposed fast-tracking of the regulatory checks on a new vaccine, the manufacturers also expressed concerns over their potential liability should any vaccine have adverse effects. The Minister emphasised that “it goes without saying that we would do everything to make sure that safety was not compromised.” Nevertheless, Dr Salisbury conceded that the manufacturers felt “very vulnerable”, and that “indemnity will have to be resolved one way or another between the industry and those that are buying vaccines.” The same day as we heard this evidence, proposals to indemnify manufacturers were backed by President Bush, who, in announcing his $7.1 billion pandemic influenza programme, called on Congress to “pass liability protection for the makers of life-saving vaccines”. (QQ 243-244)

Other treatments

7.17. Although the focus of our inquiry, as of the Contingency Plan, was on vaccines and antivirals, there remains the possibility of other treatments. For example the Academy of Medical Sciences mentioned the “fractionation” of blood plasma from convalescent patients, which could ultimately produce a “bank of immune immunoglobulin for future prophylaxis”. That is to say, the antibodies derived from the plasma could either prevent or attenuate infection in others. Dr Wood, of the NIBSC, believed that the preparation of immune immunoglobulin “would be quicker than making vaccine”. However, this approach is precluded by current precautions to prevent the spread of vCJD. Dr Wood suggested that in the event of an emergent pandemic there would have to be “a risk analysis” to identify whether the benefits of fractionation outweighed the risks—though it is doubtful whether such an analysis could be completed in time in such circumstances. However, some preparatory risk analysis could be undertaken using reasonable assumptions for the risk of transmission of vCJD and the benefit or reducing influenza morbidity and mortality. (p 132, QQ 79-80)

Research opportunities

7.18. While an influenza pandemic would be a destructive and costly event, it would also be a unique opportunity for research. As Professor Menon, of the Intensive Care Society, noted, one of the reasons the world is so poorly prepared for a potential pandemic is that “previous pandemics have not been subjected to the rigorous research that modern research techniques allow”. (Q 178)

7.19. Some of this research—for instance, into the impact of different combinations of antiviral drugs on patient outcomes and into the incidence and type of secondary infections such as pneumonia—would feed directly back into the health service response to the pandemic. In Professor Menon’s words, “If we are going to use antivirals, we need to know: does it make a difference … whether the antiviral was given on day one or day four? If, on day four, it was making no difference to the severity of the illness, then that makes a difference to how we treat people at the end of the pandemic.” (Q 178)

7.20. Other research would have longer term significance. For instance, we have already drawn attention to the high mortality among young adults in 1918-19, and to the theory that they were killed by their own immune response. In the event of a new pandemic it would be possible to show definitively “whether what is killing [patients] is the disease or whether it is the host
response.” Professor Menon noted that such extreme immune responses may be “genetically-driven … There is a case to be made for trying to understand the genetics underlying how badly people do or how well they do”. This would in turn “inform our understanding of a lot of major illnesses both infectious and non-infectious”; undertaking such research would be “not only a duty but also an opportunity”. (Q 178)

7.21. Once a pandemic starts, however, there will be formidable practical, ethical review and regulatory barriers to getting research underway. Professor Troop of the HPA noted that there needed to be “rapid access to research funds”, which had proved “very difficult to achieve in SARS” (Q 125). Nor will there be time to go through the normal system of regulatory approval for such research. Professor Menon pointed out some of the potentially time-consuming regulatory requirements:

- Assessments of drug efficacy would probably be construed as clinical trials, falling with the ambit of the Clinical Trials Directive.
- With regard to children or those too sick to give informed consent, such consent would have to sought in accordance with the terms of the Mental Capacity Act 2005.
- The storage of blood and DNA samples would have to be conducted in compliance with the Human Tissue Act 2004. (Q 181)

7.22. Professor Menon supported the suggestion that in the event of a pandemic normal legal requirements should be suspended in order to facilitate research. Professor Zambon, of the HPA, recommended “planning ahead” in order “to engage the research councils and ensure that there are rapidly responsive mechanisms for funding research proposals and ethics approvals”. (Q 125)

7.23. The Minister refused to be drawn on these points in her oral evidence, repeatedly assuring us that “these are all issues which are being looked at very closely at the moment”, but offering no clear guarantees. In a follow-up letter she drew a distinction between “collection and analysis of data for public health and health protection surveillance purposes” and “research projects”. The former (which we assume could include collection of data on patient responses to antiviral treatment) would not require “the formal approval of a Research Ethics Committee”. However, by implication the latter, which would include many of the projects described by Professor Menon, would require approval. In practice research projects would probably never get off the ground in time. (Q 291, p. 104)

Conclusions

7.24. In the event of a pandemic the speed with which a vaccine can be prepared, manufactured and distributed will be crucial. We therefore make the following recommendations:

- The Government should follow the example of the United States in making a major investment in developing new vaccine production techniques. The industry has been too conservative in relying on tried and tested methods; it is time for the Government to show leadership;
• The Government should explore mechanisms to encourage the free exchange of proprietary technology between vaccine manufacturers;

• With a view to promoting public health, the Government should continue to encourage take-up of the annual “flu jab” by at-risk groups. However, we do not believe that the corresponding increase in manufacturing capacity will be sufficient to meet the challenges of a pandemic. The Government should explore other incentives to the industry to develop surge capacity;

• In the event of a global pandemic, inequitable distribution of limited vaccine stocks could have serious implications for international relations. We therefore urge the Government, in conjunction with United Nations agencies, to examine ways to develop vaccine manufacturing capacity globally;

• We welcome the initiative of the European Medicines Evaluation Agency in developing a “mock-up” dossier for a pandemic vaccine. We recommend that the Government invest in one or more “mock-up” dossiers with a view to removing the regulatory barriers to a new vaccine.

7.25. We recommend that the Government fund further research on alternative treatments for pandemic influenza. This should include a full assessment of the risks and benefits of fractionation. If such risk analysis is left until a pandemic outbreak it will be too late.

7.26. We agree with Professor Menon that a pandemic would present a unique opportunity for detailed research into the effectiveness of treatments, immune responses, the causes of mortality, and related issues, which could offer enormous long-term health benefits. The Government have a duty to facilitate such research, which will not be possible without advance ethical clearance, rapid access to funding, and the suspension of various legal and regulatory requirements.

7.27. We therefore recommend that the Government initiate a public dialogue on the regulatory barriers to research in the event of a pandemic. We believe the public would support this research if its benefits were properly explained.
CHAPTER 8: CONCLUSIONS AND RECOMMENDATIONS

Prevention is better than cure

8.1. The first line of defence against a potential human influenza pandemic is effective surveillance and control of avian influenza, in particular in south east Asia. We are encouraged that there seems to be a growing consensus on this point, and in particular that the World Bank has committed $500 million to supporting the work of UN agencies and regional programs.

8.2. Nevertheless the FAO, which is uniquely well placed to tackle avian influenza at source, remains under-funded. We recommend therefore that the Government review its support, financial and institutional, for the FAO; we further urge the Government, in partnership with the European Commission and other European Union countries, to respond positively to the World Bank’s establishment of a multi-donor trust fund to support investment in the region.

8.3. The Government should also make every effort to ensure that the efforts of United Kingdom departments and agencies in both animal and human health are fully co-ordinated. We therefore recommend that the Government review the current rules governing funding of HPA activities overseas.

8.4. We welcome the appointment of Dr David Nabarro as UN Senior System Co-ordinator for Avian and Human Influenza. The performance of UN agencies, and the co-ordination between different agencies, has not always been optimal. We look to Dr Nabarro to ensure that the UN is well placed to co-ordinate international efforts to prevent the current epidemic of avian influenza turning into a full human pandemic.

Nip a pandemic in the bud

8.5. Recent modelling by United Kingdom researchers suggests that by rapid diagnosis and targeted response it may be possible to nip a pandemic in the bud. While this research has profound implications, further refinement of the modelling is urgently required, and we look to the Medical Research Council to make this a high priority within its influenza research programme.

8.6. While it may be theoretically possible to nip a pandemic in the bud, the practical difficulties remain formidable. We welcome the donation by Roche Products Ltd of three million courses of oseltamivir to the WHO, and we also welcome the efforts of the UN and its agencies to improve surveillance and implement a co-ordinated rapid response strategy. We urge the Government to give their full backing to these efforts.

8.7. We further believe that substantial investment by the international community in improving healthcare in south east Asia represents the best long-term strategy to prevent future influenza pandemics. We recommend that the Government, in collaboration with international partners and the World Bank, make such investment a high priority.

Mitigation

8.8. Once an influenza pandemic is established, in south east Asia or elsewhere, there is no realistic prospect of preventing its spread to the United Kingdom.
Travel restrictions, quarantine or screening at airports, while they would be highly visible, would only delay the spread of the virus.

8.9. The early and targeted use of antiviral drugs, not only to treat the first cases in this country, but to provide prophylactic protection to close contacts such as family members or health workers, could both delay and lower the peak of a United Kingdom pandemic. This would reduce the strain on health services, and give more time for the production of a vaccine.

8.10. We are therefore extremely concerned at the lack of clarity in the Government’s policy on prophylactic use of antiviral drugs, and at the possibility that the Government’s order of only 14.6 million courses of oseltamivir may have tied them into a treatment-only policy on using the stockpile.

8.11. We recommend that the Government work together with the HPA and the research community to establish the optimal strategy for the use of antiviral drugs, and that further orders, if required, should as a matter of urgency be placed to allow this strategy to be implemented. We further recommend that this strategy should incorporate a rigorous cost-benefit analysis.

8.12. We recommend that the Government develop back-up plans in case resistance to oseltamivir emerges. These should encompass possible combination therapies or the acquisition of reserve stocks of zanamivir.

**Damage Limitation**

8.13. The Government’s Contingency Plan is an excellent top-level account of the United Kingdom health service response to a pandemic, but an enormous amount of work remains to be done at lower levels. We therefore recommend:

- That cuts in HPA funding be reviewed and if necessary reversed, to ensure that the HPA’s ability to provide leadership to the health service response is not compromised;

- That the Government review the resilience of systems for supplying information from frontline health services to the centre, and in particular that they ensure that funding for the Royal College of General Practitioners’ surveillance service is extended;

- That the Government provide advice to PCTs and general practices on the mechanisms for reviewing and if necessary suspending performance targets in the event of a pandemic—such advice is needed now if frontline health services are to develop robust and well-informed contingency plans;

- That mechanisms for storing, prescribing and distributing antiviral drugs be urgently reviewed; and that the availability of antibiotics, oxygen and other supplies be examined and if necessary reinforced.

8.14. We commend the work of the emergency services in developing contingency plans. However, despite the duties imposed on local authorities by the Civil Contingencies Act 2004 to develop contingency plans and participate in Regional Resilience Forums, we are not convinced that local government is yet fully aware of the implications of an influenza pandemic. We urge the Government to provide clear and unambiguous direction and guidance in this area.
8.15. We are alarmed at the risk of serious disruption to food supplies, and at the lack of contact between the Government and the major food retailers. The Government urgently needs to address the resilience of food distribution networks.

8.16. All departments of Government need to work together in preparing for a possible pandemic, but we do not believe the Department of Health can provide strong enough leadership to achieve this. We therefore support the view of Dr David Nabarro that the importance of pandemic influenza contingency planning should be underlined at the highest level within Government. The development and implementation of contingency plans should be the responsibility of a Cabinet-level Minister for contingency and disaster planning, located within the Cabinet Office.

8.17. In the event of a pandemic a clear message and direction from all branches of Government will be critical, and we recommend that the Government develop and publicise a strategy for proactive dissemination of key information and advice, using all forms of national and local media.

A long-term strategy

8.18. In the event of a pandemic the speed with which a vaccine can be prepared, manufactured and distributed will be crucial. We therefore make the following recommendations:

- The Government should follow the example of the United States in making a major investment in developing new vaccine production techniques. The industry has been too conservative in relying on tried and tested methods; it is time for the Government to show leadership;
- The Government should explore mechanisms to encourage the free exchange of proprietary technology between vaccine manufacturers;
- With a view to promoting public health, the Government should continue to encourage take-up of the annual “flu jab” by at-risk groups. However, we do not believe that the corresponding increase in manufacturing capacity will be sufficient to meet the challenges of a pandemic. The Government should explore other incentives to the industry to develop surge capacity;
- In the event of a global pandemic, inequitable distribution of limited vaccine stocks could have serious implications for international relations. We therefore urge the Government, in conjunction with United Nations agencies, to examine ways to develop vaccine manufacturing capacity globally;
- We welcome the initiative of the European Medicines Evaluation Agency in developing a “mock-up” dossier for a pandemic vaccine. We recommend that the Government invest in one or more “mock-up” dossiers with a view to removing the regulatory barriers to a new vaccine.

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immune responses, the causes of mortality, and related issues, which could offer enormous long-term health benefits. The Government have a duty to facilitate such research, which will not be possible without advance ethical clearance, rapid access to funding, and the suspension of various legal and regulatory requirements.

8.21. We therefore recommend that the Government initiate a public dialogue on the regulatory barriers to research in the event of a pandemic. We believe the public would support this research if its benefits were properly explained.
APPENDIX 1: MEMBERS AND DECLARATIONS OF INTEREST

Members:

Lord Broers (Chairman)
Baroness Finlay of Llandaff
Lord Howie of Troon
† Lord May of Oxford
Lord Mitchell
Lord Patel
Lord Paul
Baroness Platt of Writtle
Baroness Perry of Southwark
Earl Selborne
Baroness Sharp of Guildford
† Lord Soulsby of Swaffham Prior
Lord Sutherland of Houndwood
Lord Taverne
Lord Winston
Lord Young of Graffham

† Co-opted Members

Declared Interests:

Lord Broers
None

Baroness Finlay of Llandaff
Employee of Velindre NHS Trust, Wales

Lord Howie of Troon
None

Lord May of Oxford
Emeritus Professor of Zoology, Oxford University, with a range of relevant research interests
President of the Royal Society (until 30 November 2005)

Lord Mitchell
None

Lord Patel
Fellow of Academy of Medical Sciences
Professor of Obstetrics
Chairman of NHS Quality Improvement, Scotland
Chairman of National Patient Safety Agency of England and Wales

Lord Paul
None
Baroness Platt of Writtle
   None

Baroness Perry of Southwark
   Chair of Nuffield Council on Bioethics Inquiry into the use of animals in scientific experiments

Earl of Selborne
   Chairman, Blackmoor Estate Ltd

Baroness Sharp of Guildford
   None

Lord Soulsby of Swaffham Prior
   President of the Royal Institute of Public Health

Lord Sutherland of Houndwood
   None

Lord Taverne
   None

Lord Winston
   Emeritus Professor of Fertility Studies, Imperial College
   Director of Atazoa Ltd, a company involved in exploiting viral technology supported by venture capital

Lord Young of Graffham
   None
APPENDIX 2: WITNESSES

The following witnesses gave evidence. Those marked with a * gave oral evidence:

- Academy of Medical Sciences
- Ambulance Services Association
  * Mr Philip Selwood
- Association of Chief Police Officers
  * Deputy Chief Constable Alan Goodwin
  * Professor Sue Atkinson (Regional Director for Public Health for London)
- Dr Peter Bailey, Monkfield Medical Practice
- British Medical Association
  * Dr Richard Jarvis
- British Retail Consortium
  * Mr Kevin Hawkins
- British Veterinary Association
  * Dr Robert McCracken
- Chiron Vaccines
  * Dr Kevin Bryett
- Department of Health
  * Dr David Harper
  * Dr David Salisbury
  * Ms Rosie Winterton, MP
- Food and Agriculture Organization of the United Nations
  * Dr Louise Fresco
  * Dr Jan Slingenbergh
- Mr Alan Hay (World Influenza Centre)
- Health Protection Agency
  * Dr Nigel Lightfoot
  * Professor Pat Troop
  * Professor Maria Zambon
- Institute for Animal Health and the Roslin Institute
- Institute of Directors
  * Professor Jim Norton
- Intensive Care Society
  * Professor David Menon
- London Resilience Team
  * Mr Zyg Kowalczyk
National Institute for Biological Standards and Control

* Dr John Wood

NHS Alliance

* Mrs Jan Hutchinson

NHS Direct

* Ms Helen Young

Royal College of General Practitioners

* Dr Nigel Mathers

Royal College of Nursing

* Ms Lynne Young

Research Councils UK

Roche Products Ltd

* Mr John Harrison

Royal Society

J Sainsbury plc

* Mr Alan Lacey

Dr R Salmon (Communicable Disease Surveillance Centre, Wales)

UK Vaccine Industry Group

* Mr Richard Stubbins

Wellcome Trust

World Health Organization

* Dr Klaus Stohr
APPENDIX 3: CALL FOR EVIDENCE

The risk
How is the risk of pandemic influenza emerging in south east Asia, and reaching the UK, being assessed; and how can this assessment be improved?
How great are the risks, and what confidence can be placed in these figures?
How is the UK working with international bodies to:
  • Monitor the development of the virus;
  • Reduce the risk of pandemic influenza emerging and spreading?

Contingency planning in the UK
What is the current assessment of the likely impact of pandemic influenza on the UK (both in terms of health and on wider society, including the economy)?
Are the measures described in the revised UK Influenza Pandemic Contingency Plan adequate to minimise the effects of a pandemic? What more could be done?
How well prepared and co-ordinated are health, emergency and other essential services for responding to a pandemic?
What is being done to ensure that the general public are aware of the risks and likely effects of a pandemic, and of how they should react?
Is the UK’s stockpile of antiviral treatments adequate, and how will it be distributed? What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?
What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?
What is the long-term strategy for reducing the threat of pandemic influenza?
APPENDIX 4: SEMINAR

11 October 2005

The seminar was organised at the House of Lords to give the Committee an opportunity to discuss issues connected to the inquiry with a number of experts in the field.

Members of the Committee present were Lord Broers (Chairman), Baroness Finlay of Llandaff, Lord Howie of Troon, Lord Mitchell, Lord Patel, Baroness Perry of Southwark, Earl of Selborne, Baroness Sharp of Guildford, Lord Soulsby of Swaffham Prior, Lord Taverne and Lord Winston. Also present were the Committee’s Specialist Adviser (Professor Julius Weinberg), the Clerk (Christopher Johnson), and the Committee Specialist (Jonathan Radcliffe).

The seminar began with the following presentations:

- Introduction (Professor Weinberg);
- The view from Vietnam (Professor Jeremy Farrar, University of Oxford Centre for Tropical Medicine, based at the Hospital for Tropical Diseases, Ho Chi Minh City);
- The influenza virus (Sir John Skehel, Director, and Head of Infections and Immunity Group, National Institute for Medical Research);
- Influenza epidemiology (Professor Neil Ferguson, Professor of Mathematical Biology, Imperial College).

Following the presentations the Committee discussed issues arising in the inquiry. Also present for the discussion were:

- Gerald Hetherington (Department of Health);
- Laurie Smith (Academy of Medical Sciences);
- Jonathan van Tam (Health Protection Agency);
- Maria Zambon (Health Protection Agency).


APPENDIX 5: GLOSSARY AND ACRONYMS

Glossary

*Adjuvant*
Substance added to a drug (such as a vaccine containing specific antigens) in order to stimulate a better immune response by the body, thereby reducing the required dose of antigen.

*Algorithm*
Step-by-step instructions to be followed in order to solve a problem (e.g. to make a diagnosis).

*Amantadine*
M2 inhibiting antiviral drug.

*Antibody*
Protein produced by the immune system, which binds to a specific antigen, and when produced in sufficient numbers will eliminate antigens of this type from the body.

*Antigen*
Substance, often a protein, foreign to the body, that stimulates the production of antibodies by the immune system.

*Antiviral*
Drug that is effective against a virus; may work by inhibiting proteins on the virus surface which are important to the virus getting in and out of the host cell.

*Attack rate*
The proportion of the at-risk population who become infected or develop clinical illness during a defined period of time such as an epidemic or pandemic.

*Avian influenza*
Infection in birds caused by the influenza virus.

*Epidemic*
Outbreak of disease affecting a much greater number of people than is usual for the locality, or that spreads to regions where it is ordinarily not present.

*H1N1 etc.*
Subtypes of the influenza virus, so called by reference to their haemagglutinin (H) and neuraminidase (N) antigens. A total of 15 different H and 9 different N antigens have been identified, though within each of these subtypes there are many further variations.
**Haemagglutinin**
Antigen (protein) on the surface of the influenza virus that allows it to bind onto and attack healthy cells.

**High Pathogenicity Avian Influenza (HPAI)**
The more deadly forms of avian influenza (such as H5N1), leading in many cases to the rapid death of entire flocks of poultry.

**Low Pathogenicity Avian Influenza (LPAI)**
The less deadly forms of avian influenza, often producing a relatively mild infection.

**M2 inhibitor**
Antiviral drug that probably works by preventing the virus from entering host cells.

**Neuraminidase**
Antigen (protein) on the surface of the influenza virus that allows it to break out of infected cells.

**Neuraminidase inhibitor**
Antiviral drug that limits the action of the neuraminidase proteins in the influenza virus.

**Oseltamivir**
Neuraminidase inhibiting antiviral drug marketed under the name “Tamiflu”.

**Outbreak**
Significant increase in occurrence of infection.

**Pandemic**
Epidemic widely distributed in space, usually involving several countries or the whole world.

**Prophylactic**
Preventative (of treatment).

**Prophylaxis**
Treatment to prevent the onset of disease.

**Reassortment or recombination**
The mixing of human and avian influenza viruses, though simultaneous infection of an animal susceptible to both strains—such as a pig—leading to the production of a new virus sub-type incorporating both human and avian influenza virus genetic material.
Recombination
See reassortment.

Reproduction rate
The average number of secondary cases of infection to which one primary case gives rise throughout its infectious period.

Rimantadine
M2 inhibiting antiviral drug.

Zanamivir
Neuraminidase inhibiting antiviral drug marketed under the name “Relenza”.

Acronyms and abbreviations
BRC  British Retail Consortium
COBRA  Cabinet Office Briefing Room A, location of the Civil Contingencies Committee
Defra  Department for Environment, Food and Rural Affairs
DfID  Department for International Development
EMEA  European Medicines Evaluation Agency
FAO  Food and Agriculture Organization of the United Nations
FSA  Food Standards Agency
H  Haemagglutinin
H1N1 etc.  See Glossary
HPA  Health Protection Agency
HPAI  High Pathogenicity Avian Influenza
IOD  Institute of Directors
LPAI  Low Pathogenicity Avian Influenza
N  Neuraminidase
NIBSC  National Institute for Biological Sciences and Control
NIMR  National Institute for Medical Research
OIE  World Organization for Animal Health
PCT  Primary Care Trust
RCGP  Royal College of General Practitioners
Ro  Reproduction rate (see Glossary)
SARS  Severe Acute Respiratory Syndrome
UN  United Nations
UVIG  United Kingdom Vaccine Industry Group
vCJD  Variant Creutzfeldt-Jakob disease (human form of BSE)
WHO  World Health Organization
Session 2001–02
2nd Report Science in Schools: Government Responses
3rd Report What on Earth? The threat to the science underpinning conservation (follow-up to 1st Report 1991-92)

Session 2002–03
2nd Report Chips for Everything: Britain’s opportunities in a key global market
3rd Report What on Earth? The threat to the science underpinning conservation: The Government’s response and the Committee’s commentary
4th Report Fighting Infection
5th Report Science and the RDAs: SETting the Regional Agenda

Session 2003–04
1st Report Chips for Everything: follow-up
2nd Report Science and the RDAs: follow-up
3rd Report Science and Treaties
4th Report Renewable Energy: Practicalities

Session 2004–05
1st Report Science and Treaties: follow-up
2nd Report Radioactive Waste Management: Government Response

Session 2005–06
1st Report Ageing: Scientific Aspects
2nd Report Energy Efficiency
Minutes of Evidence
TAKEN BEFORE THE SCIENCE AND TECHNOLOGY COMMITTEE
THURSDAY 13 OCTOBER 2005

Memorandum by the British Veterinary Association

INTRODUCTION

1. The British Veterinary Association (BVA) is the national representative body for the veterinary profession in the United Kingdom and represents circa 10,000 members. Our chief interest is to protect and promote the interests of the veterinary profession in this country and we therefore take a keen interest in all issues affecting the veterinary profession, be they animal health, animal welfare, public health or employment concerns.

2. The BVA welcomes the opportunity to submit evidence to the House of Lords Science and Technology Select Committee’s enquiry investigating the UK’s preparations for a potential outbreak of pandemic influenza. BVA have consulted with the relevant representative BVA divisions and the newly formed BVA Avian Influenza Advisory Group in order to formulate the response below.

SUMMARY

3. BVA would like to provide comment on the potential risk of avian influenza mutating into a strain of influenza that would be highly infectious to man (in either the UK or abroad) which could lead to a pandemic. It is not appropriate for the Association to comment on the possibility of human to human transmission or any aspects of preparations for a potential outbreak of pandemic influenza in the UK in humans. We would however like to highlight the need to annually vaccinate with the human flu vaccine those working closely with avian species, their close family and those who would be called upon to assist in the event of an outbreak of avian influenza.

4. This has the potential to reduce the risk of an outbreak of pandemic influenza, by limiting the ability of the virus to mix with a human flu virus and mutate into a form dangerous to man. The Joint Committee on Vaccination and Immunisation (JCVI) currently advise that routine vaccination of poultry workers and veterinarians with seasonal human flu vaccine cannot be recommended, but should be used in a confirmed outbreak of avian flu as a protection against the possibility of re-assortment with human flu virus. Vaccine will be given as soon as possible, either before or at time of exposure, and at least within 48 hours of initial exposure. BVA strongly recommend that this measure should be re-considered immediately, given the potential speed of the spread of infection, and the need to take rapid action in the event of an outbreak to stamp out disease. Should an outbreak of High Pathogenic Avian Influenza (HPAI) or Low Pathogenic Avian Influenza (LPAI) in domestic poultry be identified in the UK it is most probably that poultry workers will refuse to work unless they have adequate protection including being vaccinated and have access to antiviral therapies. This could seriously hamper the ability of Government (Defra) to rapidly deal with the outbreak quickly and efficiently.

5. Detailed responses to the questions outlined in the call for evidence are provided in paragraphs 12 to 43. A brief description of avian influenza is also provided in paragraph 9, along with updates on past outbreaks, and the current outbreak, in paragraphs 10 and 11.

6. The risk of an avian influenza outbreak in the UK is currently considered to be low as is the risk of an outbreak resulting in an influenza pandemic. The risk of contacting the disease is highest amongst those working or living in close proximity to poultry, either in this country or abroad. If a person in close proximity to poultry were to become infected with avian influenza, and a human form of influenza at the same time, this could lead to mixing of the two strains, which could result in the virus mutating into a highly infectious strain in man, and could potentially result in a pandemic. The larger the population of the susceptible animal species
exposed, the greater the potential for multiple cycling of the virus throughout the population and hence the
greater the potential for mutation (eg mutation is more likely to occur in a flock of 100,000 birds than a flock
of 100 birds). In general the larger the pool of circulating influenza virus—avian or human—the greater the
risk of genetic recombination into a dangerous form. Therefore the risk of an influenza pandemic arising is
greater in Asia than in Europe at the present time.

7. The BVA have provided comment on two of the possible routes of infection which could lead to a pandemic
in the UK.

— The possibility that infection of humans could occur via close contact and exposure to the secretions
of infected poultry in the UK (this is currently a very low risk). The poultry could be infected from
close contact with infected waterfowl for example (which is also currently a very low risk, however
this will change if wild birds become infected with high pathogenic forms of the virus).

— The possibility that infection of humans could occur via the mutation of avian influenza to an
infectious form in another country, which would spread to the UK if infected humans travelled to
the UK and passed the infection to other humans (This is currently a low risk. It is our opinion that
the risk of the introduction of pandemic influenza into the UK, is far more likely to come from this
route than the first route).

Infection could also occur from avian influenza infection in illegally imported domestic poultry, wild birds and
game birds, or illegally imported poultry products.

8. BVA have commented on the current surveillance and control strategies in place for avian influenza
globally as well as the need for increased surveillance of wild birds and domestic pigs. BVA would like to stress
that the current risk is low, however this situation could change if wild birds in the UK become infected with
high pathogenic forms of the disease. To ensure a pandemic doesn’t happen, it is essential that the situation
with avian influenza is kept under careful review. Surveillance levels may need to be further increased if the
present H5N1 virus circulating in Asia is identified in countries closer to the UK. It is also essential that any
outbreaks in poultry are identified and stamped out immediately to prevent the possibility of the virus
mutating.

9. Description of Avian Influenza

— Avian Influenza is caused by type A strains of the influenza virus, and there are many strains in
circulation globally.

— The virus can be HPAI or LPAI—High Pathogenic Avian influenza is a serious, highly infectious
viral disease of bird species caused by different strains of the virus.

— All highly pathogenic isolates have been type A of subtypes H5 and H7—which are notifiable
diseases. The strains currently causing the most concern are those classified as H5N1.

— The main natural reservoirs for avian influenza strains are migratory waterfowl. Infection may cause
no signs of disease, which makes it difficult to spot.

— Infection of domestic poultry often results in a very high mortality rate (up to 100 per cent).

— Spread of the disease usually occurs through contact with secretions from infective birds,
particularly faeces.

— Indirect contact with contaminated clothing, footwear and vehicles can all result in transmission of
the disease. People can be biological carriers for the disease.

— All cases of human infection have resulted from high pathogenic forms and close contact with
avian species.

— HPAI has not been reported anywhere in the EU at present.

10. Previous Outbreaks

Hong Kong 1997: H5N1 18 humans affected 6 died. Virus jumped directly to humans.
Hong Kong 1999 and 2003: H9N2: 2 and 1 mild cases in children.
Hong Kong 2003: H5N1: 2 cases, 1 death.
Netherlands 2003: H7N7: 83 mildly affected, 1 death (vet).
Indonesia 2005: H5N1: 2 deaths.
11. Current outbreak: H5N1—The total number of human deaths in the current Asian outbreak is in double figures (57 human deaths as of 1 September 2005). In 2003–04 an outbreak was reported in Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand and Vietnam, which was reported under control by March 2004. In June 2004 the next deadly outbreak occurred in Cambodia, China, Indonesia, Malaysia, Thailand and Vietnam (still ongoing). In August 2005: outbreaks were reported in Russia and Kazakhstan, although no human case has been reported so far in these areas. This outbreak involves several strains of the H5N1 virus and has affected not only poultry but also a wide range of wild bird species and mammals including people and cats, both domestic and wild. Human infections have been reported from Thailand, Vietnam and Cambodia. The outbreak differs from other outbreaks of HPAI elsewhere in the world, as highly pathogenic H5N1 viruses have been circulating in Asia since 1996, whereas previous outbreaks have involved the mutation of LPAI from wild birds into HPAI.

BVA Response to Questions

Please note: BVA can only comment on the risk of avian influenza getting to the UK and mutating to a strain that would be highly infectious to humans, or the same happening in another country.

The Risk

How is the risk of pandemic influenza emerging in south-east Asia, and reaching the UK, being assessed?

12. At the EU level the risk is currently being assessed through:


— Surveillance of the disease in the poultry and wildfowl populations also under the above legislation—the EU started intensive surveillance of domestic and wild birds in 2003 (which will continue under the new proposed EC Directive on the Control of Avian Influenza). Member States have also increased surveillance in line with the Directive on a voluntary basis. An expert commission group have also released guidelines for better surveillance of wild birds to help Member States.

— Computer Modelling to try and establish if the current biosecurity measures in use are sufficient to identify and control the disease. Defra have collated the data available from government databases such as the Agricultural Consensus and the Egg Marketing Inspectorate Database. However the resulting database is not felt to be sufficiently accurate in a number of aspects for modelling avian influenza.

13. Defra and the Commission Standing Committee on the Food Chain and Animal Health Working Group on Avian Influenza concluded that the occurrence of several outbreaks of disease in Russia and Kazakhstan was a cause for concern, however they noted that the epidemiological situation was not fully clear. Member States and the Commission are continuing to keep the situation under review. The World Animal Health body (OIE) are currently tracking the disease and carrying out a study on birds in Siberia to assess the risk of avian influenza spreading to countries in Africa and then to the EU, which is due to be completed in October.

How can this assessment be improved?

14. In the UK:

— It is agreed amongst the veterinary profession that better surveillance of wildlife populations is needed within the UK (particularly for LPAI) to ensure that the current situation in the UK is constantly monitored. Defra are currently reviewing the situation and are increasing surveillance along high-risk routes for migratory birds.

— It is also advised that a more extensive database of poultry holdings is necessary to include game birds and backyard flocks, which are a largely unknown population of birds.

— There is a general consensus that more needs to be known about the epidemiology of LPAI and HPAI in wild bird population(s)—to help assess the risk of infection via this route.
15. All Member States have been asked to urgently review and intensify the surveillance programmes already planned for 2005–06, by increasing sampling on migratory waterfowl along the flyways that could pose a risk for disease introduction, and have asked for improved cooperation under coordination of the Commission. All Member States should also review bio-security measures implemented at farm level and reinforce wherever necessary.

16. Emerging in SE Asia:

The EC have commented that the current situation does not allow us to understand if and if so to what extent the further spread of disease to Russia and Kazakhstan has been caused by wild birds, and have commented that further co-operation between EU, third country experts and international organisations is necessary to ascertain this.

How great are the risks, and what confidence can be placed in these figures?

17. The risk of an avian influenza outbreak in the UK:

The Commission Standing Committee on the Food Chain and Animal Health Working Group on Avian Influenza concluded that the immediate risk of the introduction of avian influenza via migratory wild birds is probably remote or low, however they recommended that a number of actions are taken (see sections on control below). There is always a risk of avian influenza in the UK, due to the natural level of infection within the global wildfowl population, however the risk of an outbreak of LPAI in the UK is currently considered to be low. It is considered inevitable that influenza viruses will continue to circulate in the world’s wild bird population, and that infected wild birds will arrive in Europe and the UK at some point in the future. However it is not inevitable that it will appear in domesticated birds, although extensively reared, domesticated birds are more likely to become infected due to the inherent lack of biosecurity of these husbandry systems.

18. In August 2005, Defra updated its provisional assessment of the risk from avian influenza in Central Asia. At present, the risk of H5N1 reaching the EU is not considered to be great enough to call for all poultry keepers to keep their birds in-doors. It concluded that recent reports of the H5N1 virus in Russia do not significantly alter previous conclusions regarding the increased (but still low) likelihood of the introduction of the H5N1 virus to the UK. Outdoor flocks present the greatest risk of avian influenza becoming established in the UK because there is a greater opportunity with these husbandry systems for infected wild birds carrying virus to mix with domestic poultry. In the recent Dutch avian influenza outbreak the initial infection with LPAI was passed to free range poultry. This LPAI then mutated into a HPAI through circulation of the virus within large domestic poultry populations. Back-yard poultry are also considered to be a significant risk, due to the unknown quantity and location of these birds and their close proximity to humans, however, generally the larger the flock, the greater the chance of mutation to a dangerous form.

19. The risk of pandemic influenza:

No proven human case of infection has been associated with the eating of poultry meat or eggs, although there is much evidence that the wet slaughter of poultry involving de-feathering in houses and restaurants can result in the transfer of virus from carcass to human. Transmission via this route has occurred however with other mammal species. All human cases of infection with avian influenza to date have involved people working or living in close contact with sick birds.

20. The risk of the avian influenza virus mutating to a highly infectious, highly pathogenic human strain is present, but it is low. With the widespread distribution of the more infectious strain H5N1 HPAI in Asia, there have been millions of opportunities for viral change and the virus has not taken advantage of any of these. The present H5N1 circulating in Asia and previous subtypes of HPAI have not been found to spread rapidly from person to person. The risk of a flu human pandemic is therefore likely to involve mutation and is likely to start in areas where disease is common (Asia). All reported human cases have resulted from a transmission from infected animals to human beings, all occurring after direct and close contacts. However the World Health Organisation (WHO) have warned that a wide spread of the animal disease may promote the emergence of a mutated influenza virus fully adapted to humans, which could spread rapidly from human-to-human.

21. The key point is that for mutation of avian influenza to a highly infectious form of human influenza to occur, ie re-arrangement of the virus’s genetic make-up with that of another strain, a single species needs to be infected simultaneously with the avian influenza and a human influenza virus. This is when antigenic shift occurs as two different influenza viruses infect the same cell and genetic re-arrangement takes place (this is what
occurred in the 1957 and 1968 pandemics, with both avian and human gene segments present in the influenza virus). This can result in highly lethal pandemics because humans have no immunity to the new strain. This differs from antigenic drift, the accumulation of point mutations by natural variation, which contributes to the ability of the influenza virus to cause recurring epidemics and necessitates annual re-formulation of human influenza vaccines.

22. The H5N1 virus is currently a cause for concern as it may mutate and acquire genes from flu viruses that can affect other species; it has caused severe disease in humans; and birds that survive infection excrete virus for at least 10 days orally and in faeces. It is believed that the virus was probably spread through several routes, including trade in poultry within and between countries and possibly by the movement of wild birds. Although it is believed that wild birds are responsible for the spread of the disease, the movement of infected poultry or contaminated equipment and people associated with the poultry industry are likely to have been more important, especially given the presence of these viruses in live bird markets and clinically normal domestic waterfowl. In some countries, the dissemination of virus from these sites is facilitated by marketing and husbandry practices that result in the mixing of different species of poultry on farms and in live bird markets, and by the recirculation of contaminated equipment between markets and farms1.

23. The involvement of other species:
Circumstantial evidence exists to show that avian influenza viruses may circulate in domestic pigs and act as a reservoir and as a mutation factory. However, whilst we must be alert to such a possibility, there is no evidence to confirm such a role for pigs in the present H5N1 virus circulating in Asia. Avian influenza has also been found in other mammal species. BVA recommend that surveillance for avian influenza is extended to domestic pigs to assess the real risk.

*How is the UK working with international bodies to:*

— _Monitor the development of the virus;_
— _Reduce the risk of pandemic influenza emerging and spreading?_

24. At the EU level:
The UK is helping to monitor avian influenza by monitoring the overseas distribution of disease and keeping in close contact at EU level to monitor the situation through the OIE. The UK is carrying out constant scanning surveillance for HPAI, raising awareness of the need for biosecurity measures amongst poultry owners, an annual survey to determine the prevalence of LPAI infection in commercial poultry, game birds and wild birds (part of an EU-wide initiative), and monitoring wild bird die-offs for avian influenza by the Veterinary Laboratories Agency at Defra4.

25. In April 2005, the Commission adopted a proposal for a new Directive on the control of avian influenza, updating the existing legislation (Directive 92/40/EEC). This proposal has a comprehensive approach and thus takes into account the potential risk for a flu pandemic originating from avian influenza8. Member States have already introduced voluntary measures in the proposal, such as surveillance programmes in domestic and wild birds. The Commission also convened a meeting on experts in August 2005 who concluded that a generalised ban from keeping poultry outside was not justified by the recent events due to the low risk of spread of disease by migratory birds.

26. The Commission Standing Committee on the Food Chain and Animal Health Working Group on Avian Influenza have recommended that all Member States review their surveillance and bio-security at farm level (with high standards of personal hygiene); increase awareness amongst farmers; review and if necessary update existing contingency plans for avian influenza in accordance with Community legislation (including the need to provide adequate protection for poultry workers); and ensure thorough application of the existing measures and controls at the external borders of the EU. In the UK the Health Protection Agency are currently responsible for the provision of advice to poultry workers and those likely to be exposed to infected poultry. Defra’s contingency plan for the control of avian influenza was laid before Parliament on 21 July 20055 and requires, under EU legislation, disease control by slaughter of infected birds and dangerous contacts, and the imposition of movement controls around infected premises.

27. The Commission adopted in January 2004 several decisions to ensure that no poultry meat, untreated meat products and birds other than poultry (such as ornamental and pet birds) are imported from countries where avian influenza has occurred, these measures were amended in August 2005 to include Russia and Kazakhstan.
28. At an international level:

There is general agreement that more needs to be done to clarify the situation in the far east and Russia and from this a strategic drive is needed, at an international level, to control and contain the infection in domesticated birds—by the WHO and OIE. For countries in which the infection has become widespread and entrenched, it is unlikely that the official veterinary services will be able to eradicate it from major areas/ populations in the short to medium term. In the short term it is important to manage the risks to human health and prevent the disease spreading. Improving biosecurity, stamping-out of known infection, vaccination and the implementation of basic public health measures can be used to achieve these objectives (see section below for long-term strategies). In practice the combined application of all these measures as appropriate to the local conditions will give the greatest likelihood of success. It is felt imperative that active surveillance systems are established, based on the Food and Agriculture Organization of the UN’s (FAO) guiding principles for diagnosis and surveillance of HPAI to detect the infection early and to manage the disease effectively.

CONTINGENCY PLANNING IN THE UK

What is the current assessment of the likely impact of pandemic influenza on the UK (both in terms of health and on wider society, including the economy)?

29. It is inappropriate for BVA to comment.

Are the measures described in the revised UK Influenza Pandemic Contingency Plan adequate to minimise the effects of a pandemic? What more could be done?

30. The Joint Committee on Vaccination and Immunisation (JCVI) currently advise that routine vaccination of poultry workers and veterinarians with seasonal human flu vaccine cannot be recommended, but should be used in a confirmed outbreak of avian flu as a protection against the possibility of re-assortment with human flu virus. Vaccine will be given as soon as possible, either before or at time of exposure, and at least within 48 hours of initial exposure. BVA strongly recommend that this measure should be re-considered immediately, given the potential speed of the spread of infection, and the need to take rapid action in the event of an outbreak to stamp out disease. Should an outbreak of HPAI or LPAI in domestic poultry be identified in the UK it is most probable that poultry workers will refuse to work unless they have adequate protection including being vaccinated and access to antiviral therapies. This could seriously hamper the ability of Government (Defra) to deal with the outbreak quickly and efficiently.

How well prepared and co-ordinated are health, emergency and other essential services for responding to a pandemic?

31. It is inappropriate for BVA to comment on the measures for human health.

32. BVA can only comment on the veterinary response to an outbreak of avian influenza, which could potential lead to a pandemic. There are very few poultry vets in the UK, and general practitioners would have to be called in to assist in the event of an outbreak. They would not be ready to deal with such an occurrence at present due to a lack of knowledge about how to diagnose and deal with the disease in different avian species.

33. BVA would also like to stress the importance of communicating the real and perceived risks of the disease to those working in close proximity with poultry. It has been noted that the veterinary profession and other workers may not wish to have direct contact with infected animals when controlling the disease, due to the real or perceived risk of contracting the disease. It is felt that more needs to be done to educate and alert the veterinary profession and others to the risk involved when dealing with an outbreak of notifiable avian influenza or a human pandemic, and the necessary steps that would need to be taken to reduce these risks.

What is being done to ensure that the general public are aware of the risks and likely effects of a pandemic, and of how they should react?

34. It is inappropriate for BVA to comment.
Is the UK’s stockpile of antiviral treatments adequate, and how will it be distributed? What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?

35. The Association cannot comment for the general population, however BVA believe that all those involved with poultry work should be offered the annual human influenza vaccine. This reduces the risk that a person who might contract H5N1 would be infected with a human influenza virus at the same time, thus reducing the risk of re-assortment occurring. This recommendation must also be considered for those who may be drafted in at short notice to participate in a large-scale slaughter programme.

What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?

36. There is currently no vaccine for the prevention of the H5N1 avian flu in people, though one is being developed. The UK Government have purchased a limited supply of the H5N1 vaccine for avian species which will be used for further research.

37. With regards to vaccine development for use on avian species: Vaccination is considered to be impractical to use at a large scale at present by Defra. However in accordance with the local conditions, the FAO has recommended the controlled use of appropriate vaccines formulated in accordance with OIE guidelines. Countries using vaccines should implement monitoring systems to assess the effectiveness of their vaccination campaigns and to detect the emergence of any antigenic variants. It is suggested that the composition of the vaccine should be assessed regularly against the currently circulating strains of virus to ensure a reasonable antigenic match. There has been no internationally validated study to determine whether vaccines are effective in domestic waterfowl, a question that needs to be investigated urgently.

What is the long-term strategy for reducing the threat of pandemic influenza?

38. Continue current surveillance and controls:

We can’t stop avian influenza getting into the UK but we can reduce the possibility of it gaining access to domesticated birds. Furthermore we can spot it early by regular surveillance of wildlife, and can enhance testing of those domesticated flocks most at risk of infection and subsequent mutation. It is important therefore to spot disease early and cull quickly at the outset of an outbreak. The proposed EC Directive on Control for Avian Influenza should help to ensure that this is the case. In terms of international control, it is also essential that existing control measures and surveillance are maintained, if they are relaxed there is a risk of a resurgence of disease. The ability of LPAI to mutate into a more virulent form also means it is essential for surveillance to continue and to make sure that any outbreaks are dealt with ruthlessly to ensure eradication of the disease. It is strongly suggested therefore that all infected animals should be killed on-site and not transported to an abattoir to be slaughtered as the transportation of diseased animals by trucks (which are hard to clean) will encourage the spread of disease.

39. Vaccination:

Vaccination is not currently an option for birds as it is not highly effective, and many strains of the virus exist. However vaccines are in development. As part of control measures, tactical, targeted vaccination campaigns can play a useful role in reducing the impact of avian influenza. In sectors where the risk if disease is high and biosecurity cannot be relied upon to prevent re-infection, vaccination may be required to limit the spread of infection, allowing other strategic control measures (including rapid identification of infected flocks and their immediate killing and disposal) to work effectively.

40. Additional Measures:

In the longer term, it is recommended that infected countries should try to contain the virus within specific geographical zones or production sectors by developing, maintaining and gradually enlarging disease-free regions. The elimination of H5N1 viruses for domestic poultry in these countries will require the smallholder/village sectors to be restructured which will significantly affect the countries’ economic and social fabric. The trading of poultry and other avian species in live bird markets will need to be strictly controlled, and contacts between chicken and waterbirds, farmed and wild, will need to be restricted.

41. Surveillance, reporting and disease management systems have greatly improved in recent years, however some countries still lack the infrastructure required to implement them effectively. These countries need a sustained commitment of resources to help them achieve these objectives. The FAO’s emergency support has
helped countries to improve their surveillance and diagnostic systems with regional networking and is expected to help with early warning for the future. However it is essential that they receive further funding and assistance in the future.

42. The OIE have joined forces with the FAO and the WHO to set up a multi-point plan of action for avian influenza which will be made available to the international community, they have also set up a US$100 million strategy to boost veterinary defences against bird flu, and sees this as the best way to limit the threat of a pandemic. It warned that governments were spending hundreds of millions of dollars on stocks of antiviral drugs, and said that some funds should be spent on animal surveillance and disease control at the source.

43. Whilst most European countries have veterinary systems in place to deal effectively with an outbreak of avian influenza, many places such as Africa need funds to build defences. They stressed that priority should be given to the situation in small-scale and backyard farms, the scene of the majority of human cases in the current outbreak including: educating farmers on the risks and how to change their practices, to ensure the segregation of different species and eliminate intermingling between animals and humans, to encourage farmers to report suspected cases and apply control measures, to pursue vaccination of poultry flocks as part of the response in high-risk areas.

REFERENCES:

8. For BVA response to Defra’s consultation on the proposed EC Directive on controls for avian influenza please see their website http://www.bva.co.uk/policy/

Examination of Witnesses

WITNESSES: Dr JAN SLINGENBERGH, Senior Officer, Animal Health Service, FAO, and Dr BOB MCCracken, past President, the British Veterinary Association, examined.

Q1 Chairman: May I welcome you to this first public hearing of the Select Committee short inquiry into pandemic influenza. I would like to remind you before we get going that the meeting is being webcast live and is being filmed by the broadcasting companies. I would also like to draw the public’s attention to the information note and list of the Committee members, etcetera on the bench at the back of the room. May I ask you to introduce yourselves first?

Dr McCracken: Bob McCracken. I am the immediate past President of the British Veterinary Association. Dr Slingenbergh: Jan Slingenbergh. I am a Senior Officer of the FAO Animal Health Service in Rome, Italy.

Q2 Chairman: Thank you. I would just like to draw everyone’s attention to the huge potential impact of pandemic influenza and the fact that a pandemic could emerge at any time, hence the urgency of this current inquiry. It is therefore crucial to us that the UK and the international community should do everything in their power both to prevent a pandemic and to develop contingency plans for reacting to it should it occur. The purpose of this first public meeting is to gather some of the essential background focusing on avian flu, its spread among birds and poultry in Asia and into Europe and its economic and health impacts. Dr Slingenbergh, I would like to ask you the first question. There have been many news stories in recent days concerning the spread of the avian flu virus westwards, with reports from Turkey and Romania. I am not sure about the status of the Romanian situation. What is the latest information that you have?

Dr Slingenbergh: My Lord Chairman, I hope that no harm will be done to the messenger because I am afraid the latest news is not good. Two hours ago—I do not know if anybody else has later information still—I believe there was a session of a team of EU
experts, including veterinary experts from Weybridge. Also present was Dr Guus Koch, a Netherlands specialist with whom we have had personal contact. The consensus in the meeting with the Ministry of Agriculture this morning at nine o’clock was that the disease that was looked into by the EU specialist team was avian influenza H5. With regard to the N, there was almost certainty that we were dealing with N1. There are further follow-up investigations to be done that will give a definitive end result. When we take this latest news together with the fact that the positive samples concerned swans, there were 40 dead swans found and we all know that swans and ducks make up part of the anseriform group, and the information that we heard about the Danube river system and the latest progress of Asian avian influenza poultry virus H5N1 in Russia progressing westwards, the suspicion is that the Asian poultry avian influenza H5N1 virus has now entered Europe and that will cause a bit of a stir. May I just mention that yesterday in the newspapers in Italy it was reported that there had been a 30 per cent drop in the consumption of poultry meat. I am saying this not because it is based on rational risk assessment, but the public at large is likely to become very excited and nervous about these novel events.

Q3 Chairman: Has positive identification of the virus got to Romania and not beyond that?
Dr Slingenbergh: For the moment we are talking about Romania. There is already a report of H5 in Turkey. We will have definite results at the end of this afternoon. It does not really matter too much because, whatever the outcome of the Turkey investigation, the fact is that migrating birds apparently are capable of bringing the Asian poultry virus from Asia into Europe and there could be more in Romania that have been missed out or are still yet to come.

Q4 Baroness Finlay of Llandaff: May I just ask you how widespread you think avian flu is beyond those new index cases, covering really the border of Europe into Asia and across then into Asia and beyond.
Dr Slingenbergh: For the moment there is the evidence of China, Vietnam and Indonesia where the virus is actively circulating in domestic poultry. There is evidence that the virus might also be present in a number of other countries in south-eastern Asia. We think that several countries in southern Asia currently not affected are at risk, particularly Bangladesh and India. There has been H9 and N7 virus circulation in Pakistan, but this has been going on for years and it is not directly related to the current problem of the pandemic threat. I am mentioning India and Pakistan because it would fit with the flyways of the anseriform birds, it would fit with the fact that eastern India and Bangladesh do have a very significant number of domestic ducks and particularly in Bangladesh this is associated with wetlands hydrology and river systems, which is an important factor that we believe also brings the contact between wild and domestic ducks.

Q5 Lord Soulsby of Swaffham Prior: I would just like to clarify what you said about Romania. Is the virus in Romania now or is there some doubt about that?
Dr Slingenbergh: There is 100 per cent certainty that avian influenza H5 is present in Romania. There is almost certainty that there is H5N1 in Romania. Taking this together with the fact that there have been recent westward advances of the Asian H5N1 in Russian wild birds and poultry, we have reason to suspect that indeed the Asian H5N1 poultry virus has now encroached into Europe.

Q6 Lord Soulsby of Swaffham Prior: How is the virus spread in bird populations, and what is the role of migrating birds? Are there different species that are more important in migrating birds than others? What special precautions should western European states take to prevent the introduction of the virus via migrating birds?
Dr Slingenbergh: Let me just bring to your attention a report that has just come out by the European Food Safety Authority with a scientific panel on the risk of avian influenza. I believe it is easy to find on the internet. It is very worthwhile reading because it has a lot of pertinent information on the possible role of migratory birds. It contains an extensive inventory of records on the presence of different H5, H7, H6 and H9 viruses that have been encountered in different geographical areas of the world in the past decades. In conclusion, and coming directly to the question you raised, there is as yet, with one single exception concerning South Africa in 1961, no evidence of wild migratory birds being a very important vector of a highly pathogenic influenza virus. What we are seeing here is a bit of a novelty and what one wouldn’t expect is that migratory birds may carry the virus; but based on a recent joint investigation by the OIE and FAO in Kazakhstan, we have strong indications that indeed migratory water fowl arriving from Asia did bring the virus into Kazakhstan. So migratory water birds are a vector, but there is a big question mark over the claim that the virus can sustain and persist in migratory birds and it is somewhat illogical because the virus is very aggressive and perhaps a bit too nasty in its current form to sustain itself in water birds. Finally, with regard to the different species, there is overwhelming evidence that we should not bring all the migratory birds under the same umbrella here. We are talking about anseriform birds, which include ducks, geese and swans, and apparently we are talking about swans in Romania as well.
Amongst the wild ducks we have the mallard which is by far the most important wild duck implicated in H5 and N7 avian influenza viruses. There is a further small bird group, the shore birds, which includes also the gulls, that does carry a broad variety of avian influenza viruses and they make up part of the common wild bird avian influenza reservoir or pool, but I think we should single out the anseriform birds, the ducks and mallards in particular.

Q7 Lord Soulsby of Swaffham Prior: Once the virus gets into a country, are there any other species where it can infect? I am thinking about pigs. In Western Europe there are a lot of outdoor pigs. Could this species be a reservoir of avian flu? Of course, pigs are susceptible to avian flu and human flu. I wonder if Dr McCracken could comment on that.

Dr McCracken: Perhaps before answering that specific question I could go back to the last point. I agree with my colleague, there are times when some people believe that a bird is a bird is a bird in relation to H5N1. There are many different species of birds, hundreds of them out there and the virus behaves differently in each of those species just as one virus behaves differently in a sheep as it does in a cow and we tend to forget that at times. Certainly my reading of the literature is that the duck, particularly the mallard duck, under experimental conditions can be infected with the H5N1 strain, show no clinical signs whatsoever and yet it excretes and it has an ability to transmit the virus for 16 or 17 days. To my mind that is quite significant when we think of migrating birds. The traditional story is that waterfowl carry the low pathogenic strain. This is a new situation as far as history is concerned in that the virus appears to have escaped from the domestic fowl, presumably from where it did mutate into the more highly pathogenic strain back out into wild birds. If it kills that particular species of wild bird it is of no significance in inter-continental spread, but if the birds are susceptible to infection and do not show clinical signs then there is every likelihood of it spreading. Just as we meet people at crossroads going in a different direction, migrating birds will also meet other migrating birds at crossroads and there is the potential for the exchange of the virus at those crossroads. The crossroads in the case of birds obviously are lakes and waterways. So I think we have to be cognisant of the fact that wild birds can certainly become infected with the highly pathogenic strain and can carry it. In answer to the other question, speaking as a veterinarian, I believe the veterinary profession has two major roles. The first one is to protect the health of birds. The second one is to assist the medical profession in trying to reduce the likelihood of that further mutation, the further reassortment where we end up with a virus that is capable of spreading readily from man to man. That has not happened yet. We hope it will not happen. There is no doubt, literature tells us that swine are probably a significant animal in the re-arrangement of flu viruses; in other words, literature suggests that a pig may be infected with the human strain and with an avian strain and that the genetic material of those two can be exchanged to combine into a new more potent virus. That has not yet occurred and hopefully it will not occur, but we have to be aware of the fact that there are many pigs outdoors in Europe and therefore their ability to have contact with wild migrating birds that may be infected is a potential danger.

Q8 Baroness Sharp of Guildford: How well prepared do you think the UK is to implement control measures to prevent the introduction of avian influenza by migrating birds or its subsequent spread if we were to find them here? How far have we got the infrastructure that is necessary to implement such measures?

Dr McCracken: My Lord Chairman, it is a very valid question. I believe we have to accept that there is the potential for H5N1 to arrive in the UK through something like migrating birds, but the fact that it is in a migrating bird standing at the side of a lake does not necessarily mean it has gained access to domestic poultry. Nevertheless, there is very little we can do, quite honestly, at this stage of the game to try and ensure that affected migrating birds do not arrive on our shores. We must be able to identify when such a group of birds is likely to be arriving. If the birds in Romania turn out to be H5N1 then I think that is a clear indication to us that the virus has spread considerably in a westward direction and our defences need to be reviewed in light of that. The first thing we must be aiming to do is to prevent the transfer of the virus from infected migrating birds to our domestic poultry. The word bio-security has been banded around quite a lot, but I believe it is very appropriate for those domestic birds that are indoors. I am firmly of the view that we are dealing with a virus that has a limited ability to spread through the air, unlike Foot and Mouth Disease, and therefore the poultry keeper has poultry that are in houses that are “bird proofed” then, by practising good bio-security, there is no reason why any of those birds within the houses should ever become infected with the avian influenza virus. The only means of it getting in will be through the personnel or equipment moving into that house and therefore bio-security would prevent that happening. Our aim must be, and I believe that Defra agrees with this, to identify avian influenza in domestic poultry as soon as it happens and take immediate action and that action at this moment in time really does mean the slaughter of the infected birds and the removal of the infected birds and the removal of the virus with them. This is not an
infection that will spread from farm to farm by airborne means and therefore there is every chance we should be able to deal with it effectively provided we have adequate surveillance and provided we move quickly.

Q9 Chairman: Do we have adequate surveillance? Dr McCracken: My Lord Chairman, indeed we have. Throughout Europe there has been a requirement for a number of years now for us to carry out surveillance. That surveillance is in two forms. Where wild birds have been caught in a net or where they are shot or where dead ones are found, Defra have a programme where such birds will be sampled with a view to checking whether or not they are infected. Secondly, and very importantly in my view, domestic poultry that are kept outdoors are also being sampled and such birds are normally those that are on the known flight pathways of migrating birds, particularly those that have access to water where migrating birds may come down to drink. Those are the sort of areas that Defra is targeting and have been targeting and are sampling. I take comfort from the fact that Defra have always claimed that their programme will be under continual review. I have no doubt that if the Turkey and Romanian viruses turn out to be H5N1 then Defra and indeed the whole of the European Union will be taking much more stringent steps than is currently done.

Q10 Earl of Selborne: Are you suggesting that if H5N1 is indeed identified in Europe we should have contingency plans to move domestic fowls, which at the moment are free range, into a contained area? Dr McCracken: That should be done wherever possible. I believe that the first preference should be to those free range outdoor birds that are anywhere near waterways and migratory pathways. All of this is a risk assessment. I am perhaps speaking from a BVA point of view here rather than a government one. If there were outdoor birds that were some distance from waterways then I think one would have to question whether the risk justifies trying to place them in a house. The reason I say that, my Lord Chairman, is that we have to accept that in many instances houses that contain free range birds are fine in relation to an overnight “bed and breakfast”, but the accommodation in many instances would be inadequate for those birds to remain indoors day and night for weeks on end. Therefore, we have to recognise that there has to be some other solution. Bringing the birds indoors or netting them in some manner is one possibility, but there has to be recognition of the fact that that will not be possible in all instances.

Q11 Lord Sutherland of Houndwood: Dr McCracken, you have stressed properly the importance of speed of response in a situation such as this and one element of that clearly has to be the co-operation of those who work in the industry, ie poultry workers. I want to relate that to a question about the evidence which the BVA submitted, which we appreciate very much. You did point out fairly sharply that the co-operation of the poultry workers presumed that they would believe that they were having adequate support in terms of vaccines and so on and in so doing questioned the current policy of the Joint Committee on Vaccination and Immunisation and I wondered if you would like to elaborate on that for a moment or two.

Dr McCracken: From what angle?

Q12 Lord Sutherland of Houndwood: Can I just read out the section? “The Joint Committee on Vaccination and Immunisation currently advise that routine vaccination of poultry workers and veterinarians with seasonal human flu vaccine cannot be recommended but should be used in a confirmed outbreak of avian flu as a protection against the possibility ... The vaccine should be given as soon as possible and at least within 48 hours. The BVA strongly recommend that this measure should be reconsidered immediately.” I just wondered what the reasons were behind that.

Dr McCracken: My understanding is that if an individual is vaccinated with the human flu strain, such as H1, and was subsequently to meet the H5 strain then, since the individual is immune to H1, there is less likelihood of a re-assortment or sharing. The comments there largely relate to the role we believe we have within the veterinary profession in assisting the medical profession in stopping the re-assortment occurring as opposed to doing anything that would improve the health of that individual because obviously the human vaccine does not impart any resistance to H5N1. Given the circumstances, we believe that migrating birds are the most likely source. The other one we have always been concerned about is the illegal importation of pet birds. If we recognise that migratory birds are important and indeed at the moment in the cases coming from Turkey and Romania they are very important, then we have to recognise that poultry workers potentially could be exposed. Let us remember at the same time that there have been many thousands of birds affected with H5N1 in 11 countries. Of those known to doctors, 119 people have become affected and 60 of them have died. It is not as though everyone who gets close access to an infected bird develops bird flu. It is a relatively uncommon event even when there is contact with infected birds.
Q13 Lord Taverne: I want to ask three questions related to monitoring. First of all, how effective is the monitoring in south-east Asia of developments in the influenza virus in livestock? Secondly, what is the reliability of the data? Is it sufficiently timely and reliable so that one can get to a good up-to-date assessment? Thirdly, how satisfied are you with the level of international and national co-operation?

Dr Slingenbergh: My Lord Chairman, I consider these questions to be extremely pertinent for reasons which I hope I can explain. We have created what we call sub-regional networks. A sub-region is a cluster of Asian countries such as southern Asia, south-eastern Asia or eastern Asia. We have created these clusters with the aim of establishing effective epidemiological surveillance in these geographical areas, including the exchange of pertinent laboratory data. As you will be aware, it is very difficult to have a systematic collection of data and a transparent exchange of these findings. I have listed a few practical points from our working experience which I wish to share with you and the power of these enhance the headaches we are facing. It took about one year to make Pakistan and India agree which one would become the reference laboratory for the sub-region and which one would take the lead in the coordination of epidemiological surveillance and these are very costly delays. Another example is that China and Vietnam are countries where the political environment is such that it does not always work to insist on rapid and transparent communication of the data that come from national laboratories. There is also the fact that because of political and economic changes the role of chief veterinary officers in countries has changed quite dramatically. There is no more line management. A chief veterinary officer can jump high or low but the district authorities may or may not listen to him or her. This is quite different from what it used to be. I am not against market liberalisation and decentralisation and everything that goes with it. It is evident that the diminishing role of the chief veterinary officer in dealing with his public veterinary services portfolio has complicated the effective and timely implementation of field measures, which were considered essential in the control and prevention of avian influenza. Countries like Laos and Cambodia, who have a level of socio-economic development that is far behind most other countries in Asia, have been totally overwhelmed. They did not have the national infrastructure to deal with problems of this nature and magnitude. Perhaps I should also mention that at the international level there have been a lot of complaints about CDC Atlanta in the US holding a lot of the genetic details of virus samples which they are very often not prepared to share with the international scientific community. There have also been problems with the WHO influenza network which is not communicating fully all the information with the OIE and FAO networks. The surveillance should be purpose driven but we know that this is very complex as purpose driven surveillance ideally should focus on the evolution of the problem. We all know the situation is dynamic. We have seen the virus originating from the wild birds reservoir making its way into domestic ducks. We saw the genotype Z emerging in coastal south-eastern China. We saw the epidemic that followed in ten or 12 countries in Asia later on. We have seen the spill over into other mammal species, cat eating birds, tigers and also into humans eating poultry products. We know that the epidemic form of the disease and the effect of spill over go together. We also know that these events make the likelihood of accelerated genetic drift or even horizontal gene transfer more probable. We know there is a link between the amount of virus circulating in poultry, the amount of exposure of susceptible humans and the likelihood of further evolution of the virus into human-to-human transmittable pathogens. A targeted surveillance that tells us how far the virus has evolved and to what extent we can stop it, under which circumstances and in which poultry systems and areas, that type of surveillance is not in place for all the reasons I have tried to illustrate.

Q14 Lord Taverne: The picture you paint is a somewhat distressing and deeply disturbing one. What can be done to remedy this by countries locally and by international authorities? It must be very tempting for farmers in local communities to avoid slaughtering their flock and get them to market instead. What role do regimes of compensation play in this? Is there a compensation scheme that can encourage better reporting and avoid the spread?

Dr Slingenbergh: These are very pertinent points. There are a few aspects that look good and there are a few very serious problems. On the positive side, we have seen that countries like Malaysia, Hong Kong, China, South Korea and Japan have all successfully dealt with it in the sense that the virus was swiftly eliminated and did not re-enter. That gives us hope that progress can be made. Thailand is also a very important example because it takes a bit of an intermediate position when it comes to the rich-poor gradient. Thailand has undertaken three x-ray surveys involving several hundreds of thousands of veterinary or medical staff, barefoot doctors or veterinary assistants who are not very highly educated in technical terms. They were given basic instructions, just four or five days of training, before undertaking a door-to-door survey countrywide. This has contributed to the earlier detection of places where the virus was circulating. It has contributed to dealing with the infected foci in terms of taking out the affected poultry, in terms of putting in place a ban
on transport and the trade of the poultry in adjacent premises, a series of measures that were taken to break the transmission cycles. It has been done three times. There has been a marked reduction of avian influenza disease in poultry and since October 2004 there have been no more human cases seen in Thailand. The FAO in collaboration with the WHO and also the World Food Programme are involved in a programme where hundreds of Tsunami-related logistics officers in Indonesia are now packing up and preparing to assist in undertaking broader programmes in Indonesia with the specific task of reaching the community and getting to backyard poultry because that is where most of the virus is circulating and where the public veterinary services cannot reach. It is not so difficult to vaccinate poultry in a commercial stock of 30,000 laying hens because there is a common interest there to protect the poultry and also serve the public good, but to reach out to the backyard has been incredibly difficult. It must go beyond what the veterinary public services can do, it should involve the NGOs and the private community and we believe that, with assistance at the inter-agency UN level, there are things that can and must be achieved in Indonesia and Vietnam. In Vietnam we have the co-operation of the FAO, WHO and UNDP. I am travelling this weekend to Bangkok to launch a campaign with USAID funds. There is a myriad of activities going on, some of it is promising but, on the other hand, there are indications that we should remain worried.

Q16 Earl of Selborne: My question is to Dr Slingenbergh and it relates to cost. You have already answered Lord Taverne and demonstrated just how diverse the poultry sector is in Asia from sophisticated units to what you described as the backyard. Have we any idea of the cost to the Asian poultry sector? The FAO has estimated a figure of some $10 billion. Does this relate to the different social impacts from the remote communities to the more industrial communities? Have we any reliance on this figure which sounds a suspiciously round figure?

Dr Slingenbergh: I beg you not to take this figure too seriously because it might affect the credibility of the FAO’s economic analysis capability. It concerns a study done by UK sources. It does not matter, it is a back of the envelope calculation. If I can just illustrate how these types of figures emerge. There has been concise information arriving from Thailand that the Thais lost $1 billion worth of exports in terms of poultry meat in the first year. In the second year they swiftly tried to convert a lot of poultry meat into packaged processed food and meals which were then exported and the losses declined by half a billion dollars. Added to all the other losses that occurred just in Thailand we were running to a figure of approximately $2 billion. There was another study carried out in Vietnam where in the first epidemic wave the direct impact of economic losses was estimated at around $200 million. We should add some guestimates as to what is going on in China. China somehow realises 12 million tonnes of poultry meat per annum which makes China a giant that dwarfs all the other poultry industries of eastern and south-eastern Asia. If we take it that there are a lot of rural smallholders, relatively poor poultry keepers in China, perhaps we should not concentrate too much on the financial loss estimates but rather on the wider social impact of the disease across eastern and south-eastern Asia.

Q15 Baroness Finlay of Llandaff: Can I just follow up and ask about the different types of birds, going back to an earlier question. Are there inherently resistant birds, particularly in the domestic range of birds, that could be selectively promoted so that you could decrease the amount of carrier status, so in these communities where they are terribly dependent on breeding their own poultry they might be encouraged to breed different strains?

Dr McCracken: My Lord Chairman, perhaps if I could make a comment first of all. We must be careful that when we say resistant we know what we mean. My understanding is that knowledge at this moment in time would indicate that all birds are probably susceptible to infection but not all birds are necessarily showing clinical signs and dying. We talked about ducks. There is something here which is important that my colleague was referring to. We are in a situation where avian flu has been around for many decades. It has appeared in countries within Europe and those countries have dealt with it, and dealt with it effectively. My colleague has indicated that some of those ten or 12 countries have also done so in the last few years in the Far East. The downside is that some countries did not manage the outbreak as effectively and as a consequence the virus is now out in wild birds. Nevertheless, if all wild birds meet the virus and become infected, they either die or become immune and the virus is no longer of relevance. I believe that we are in a critical phase at this moment in time in the sense that if birds are migrating and carrying infection with them, they meet many other populations of birds and the opportunity for the virus to continue to cycle is there. Once the migration season disappears then there is a greater likelihood that all birds will become infected and either live with immunity or die and the virus will disappear. That is a fond hope and I may be putting it rather simplistically but I think that is the way we need to be thinking certainly within these shores.
Q17 Baroness Perry of Southwark: My question is for Dr McCracken following on from that. I am wondering what is going to be the impact on the UK’s livestock industry, not only the potential of spread of avian flu but also what measures we might have to take to prevent it.

Dr McCracken: My Lord Chairman, I would have to say they are back of the envelope figures again. We have an industry that is worth well in excess of £1,000 million per annum to the UK, so it is a significant industry. I have no doubt that if we were to have an outbreak, and I am looking at the national level as opposed to farmer level in these comments, there would be a significant cost to control the outbreak and there would be a significant cost potentially in the loss of birds. I would stress, provided we ensure our surveillance is kept up and we find avian influenza on the first premises then I believe that the loss through the slaughter of birds et cetera can be kept relatively small. The big concern, of course, is the impact on trade and the consumers’ reaction or otherwise to it. We know that the meat, if cooked, even if it were to contain the virus, is of no significance but I would like to think that no bird that contains the virus will ever be presented in any manner to the consumer. The downside is that a lot of our products are exported and we are dependent on the consumer still believing this is a safe and wholesome product. That is the sort of battle, if I can call it that, that has to be won in this whole arena. There is potential for significant losses in that over £1,000 million business and I think we should all be endeavouring to ensure that the public et cetera are properly informed so that informed and objective decisions can be taken by them.

Q18 Lord Sutherland of Houndwood: A question to Dr Slingenbergh. I think it would help the Committee if you were able to outline the main responsibilities of the FAO in this area and the main tasks that you believe the FAO properly undertake and if, doing that, you could reflect a little on whether there are overlaps with the World Health Organisation or with the World Organisation for Animal Health. Is the job being done twice in some areas? Are there gaps between the responsibilities of these bodies?

Dr Slingenbergh: My Lord Chairman, I believe to best illustrate the role and responsibilities of the Food and Agricultural Organisation of the UN in this crisis we should consider three different levels: international, regional—for us regional is a cluster of countries—and country level. We work in very close collaboration with the World Organisation for Animal Health, the OIE, and I believe that almost on a daily basis we are fine tuning and harmonising our mutual activities. With regard to the collaboration with WHO, we might have done somewhat better in the past. We had Dr David Nabarro visiting us in Rome two days ago and very clearly the appointment of the UN senior co-ordinator for avian influenza in New York will help us to make sure that the different agencies within the UN work together, speak with one voice and harmonise their activities. When it comes more specifically to the areas in which FAO engages, at the international level I believe our main functions relate to harmonisation, seeking to bring about cohesion and consultation at the international level. We bring the international expertise together and we have our international conferences and workshops. We have a lot of training activities as well that are related to it. We put it under the heading co-ordination at the international level. Every major conference or meeting is invariably done jointly with OIE and in collaboration with WHO ever since our first major international conference organised in early February 2004, just weeks after the start of the crisis. A few words on the regional and country levels. At the regional level we are looking mainly into the networks of countries. What we seek is that clusters of countries collaborate and—you could almost call it social control—make sure that they pass on the relevant information, make sure that they act as a group and communicate with the international community at large which viruses they are dealing with, which activities they are doing to enhance epidemiological understanding and where the focus is with regard to response, control and prevention. We believe that country cluster co-ordination is the right thing to do but, as I indicated earlier, it is a cumbersome and difficult process. If we look at the magnitude of the problem we are not achieving as much as we would like to. If I could say a few more words at the country level. Here the mission is simple: we come with technical and other means available to assist countries in fire fighting. This means trying to get to the poultry which is particularly pertinent at the community level, at the village level, because, as my colleague indicated, the virus circulation is more prominent in open systems, in situations where the investment in hygiene and biosecurity is just not compensated for in terms of income generation. There is trade and traffic with live birds, there is contamination left, right and centre. This situation cannot be resolved by introducing policing or even military activity, you have to reach out to the people through awareness creation, through a whole package of measures that have to go along with it. I believe strongly that more efforts are justified in this regard. There are successes that are within reach but it is cumbersome and it takes more perhaps than the current capacities as they exist in FAO country and regional offices. Thank you.

Q19 Lord Sutherland of Houndwood: My Lord Chairman, clearly the complexity grows as you go further down the system and I wonder if I might just
ask Dr McCracken whether, from the point of view of a key group in the UK, the British vets, there are any reflections on how well these systems operate to help the vets carry out their responsibilities?

Dr McCracken: In relation to the UK situation?

Q20 Lord Sutherland of Houndwood: Yes.

Dr McCracken: I referred earlier to the fact that I firmly believe that the veterinary profession, with the industry, has two main roles. One is to protect the health of the birds and the other is to do our bit to ensure that further mutation does not occur. Through the BVA and its specialist division, the British Veterinary Poultry Association, we are reaching out to our clients, to those who have birds that we are familiar with and working hard with them. In the latter of those two roles, ie further mutation, my simple mind says if we have two sets of birds and in one field there are ten birds and in another field there are 100,000 birds, remembering that mutation is a chance event if one infected bird is present among ten there are nine opportunities for the virus to mutate; if, however, in the other field one infected bird is present there are 99,999 opportunities for the virus to mutate. That is theoretical but I think you can see where I am coming from. Therefore, we have a very definite responsibility to ensure that we recognise the virus when it appears in a large density of poultry and we then act effectively with government. I am firmly of the view that government is aware of these possibilities and is geared up to deal with them. I can assure you that the veterinary profession, albeit a small number, are very much in touch with poultry keepers, at least those who are involved in a commercial way. I am confident that we will continue to pass information to them. We have a poultry industry within the UK who I have no doubt would be knocking on veterinarians' doors if the Turkey and Romanian is confirmed as H5N1. The industry is very conscious of what has been happening in the Far East and Russia and hoping and praying that it will not be arriving here. Events over the last few days will make them acutely aware of increased risks and they will be seeking to try to say what they can do as well as what government can do to reduce that risk to their birds.

Q21 Lord Soulsby of Swaffham Prior: Can I come back to the BVA. This more or less follows on from what you have just said, Dr McCracken. What is the co-ordination of the BVA with organisations such as the European Union, FAO of course, World Veterinary Association and OIE? Are you active with manpower in Brussels and elsewhere co-ordinating this effort?

Dr McCracken: My Lord Chairman, if I could answer that. There are two main ways and one I would have to say is we do believe that Defra and the European Union Commission have a role to play there to help us and we accept they should be leading in many instances. Nevertheless, there are other means and ways in which we try to ensure we are kept up to date and one of those I give as the Federation of Veterinarians in Europe, and the BVA has two permanent representatives in that and that is a very useful source of information. We also have a body called the International Veterinary Officers' Council which includes a number of developed countries and we are in regular contact with them and meet annually with them and exchange concerns. Thirdly, a very useful one is one of our own groups called the Commonwealth Veterinary Association which includes many Commonwealth countries throughout the world and throughout literally almost all of Asia, Africa, Europe and America. We have regular contact there. That is the only avenue where we actively take the lead ourselves through these organisations but in other instances we rely upon the Commission or upon our national government to make contact with the FAO, WHO or other bodies.

Q22 Lord Soulsby of Swaffham Prior: Are there any snags in this collaboration that you can identify or is everything going reasonably effectively?

Dr McCracken: I will quickly respond, my Lord Chairman. The snags are that we are dealing with a problem at the moment that did not originate in any of those countries that I have mentioned. I have already mentioned that in developed countries where there is adequate infrastructure, the likelihood of avian influenza being eradicated rapidly and effectively is very high, and that is good. The downside, and the lesson we must learn from events of the last few years, is if the same were to occur again we must have some mechanism whereby we can be more effective in nipping it in the bud, more effective at giving whatever support is necessary to that country where the problem is present so that it can be eliminated there and then rather than become widespread as this one did. I am not saying for one moment that will be easy but I am saying that must be the target of developed countries, to be in a position to be effective in assisting the developing countries, be it through FAO or whatever.

Q23 Baroness Perry of Southwark: Dr McCracken, you were very reassuring about the British industry and the awareness and level of concern and careful monitoring that is going on. I was wondering about the cases you have mentioned, the mallard and the duck, where there are no clinical signs for people to monitor, particularly if some are semi-wild, and there are many public parks, for example, where children go to look at the ducks and so on, and there are large populations of ducks and mallards there. Who is
monitors that? How do you monitor it if there are no clinical signs?

Dr McCracken: Defra is monitoring wild birds. They have three main ways of doing it. I understand one is netting birds on sites such as river ways and lakes. The second is where birds have been legally shot, to ensure the opportunity is taken to sample them. The third is where any wild birds are found dead or they too can be sampled. Let us remember, just as with a child who has measles when there is only a finite period during which that child is infective, the same applies to a mallard duck. I think I mentioned a figure where the experimental work would indicate 16/17 days. By 18 days, certainly 28 days, those birds did experience infection but they were no longer infective, so they were not at risk. I would contend that in any native population of wild birds, if infection does appear it will be a very short time before we are in a situation where those birds have either died or they are still alive and fully immune and certainly not carrying the virus. The critical period for that active excretion of the virus is 16/17 days. My concern would remain the migrating birds continually coming in during the migratory season. I am not so worried about the native birds in the sense that they will become infected and will become immune and no longer shed the virus.

Q24 Earl of Selborne: My question is on the funding. In May the FAO called for further funding from donor countries and I think you indicated recently that has not been forthcoming to the extent that you would wish. Could you give us some indication as to what the shortfall is and what programmes to reduce the risk of a pandemic are failing to be funded?

Dr Slingenbergh: With regard to the funding level required to more effectively deal with the problem, we have upgraded these figures several times with the geographical deterioration of the situation and the latest figure that was mentioned in a press briefing two days ago was 160 million.

Q25 Earl of Selborne: $160 million?

Dr Slingenbergh: $160 million. We only have $30 million at hand. Not even that, say $25 million at hand. Do you want me to say a few words about what could be done should more money become available?

Q26 Earl of Selborne: What is at risk if you have that shortfall?

Dr Slingenbergh: If we take the countries in Asia where the problem today is relatively widespread, the top three countries are undoubtedly China, Indonesia and Vietnam. I am not too sure how to rank these but let me elaborate in a bit further detail what types of problems we are facing in those countries. I have already indicated that the public veterinary services in Indonesia are rather ineffective in the sense that there is a haphazard effort to vaccinate some of the commercial poultry holdings with at least four different types of vaccines, all of which have not yet been quality controlled. There is hardly any effective biosecurity imposed on the areas, particularly in Western Java where humans have been infected and five fatalities have now occurred. There is no restriction of movement upon confirmation of poultry disease tentatively diagnosed as avian influenza. In brief, we have a problem in Western Java, in Eastern Java, in southern Sulawesi, southern Bali and a number of other hotspots. If we look at the efforts now gradually brought into place, such as I described earlier to detect where the hotspots are and to make sure that at the village, community, backyard level the measures are taken to disrupt the transmission cycle and prevent the exposure to human infection, some of these measures are gradually falling into place in Western Java. Looking at the magnitude of the problem in Indonesia we would have to step up these types of efforts by at least one order of magnitude in order to stop the further evolution of the problem as we are facing it. Perhaps you are familiar with Vietnam and the fact that northern and southern Vietnam in many regards are two different worlds. The northern part also connects very closely with the adjacent provinces in south-eastern China and in terms of poultry and live bird exchanges. The measures taken in the Red River Basin near Hanoi are by no means up to the efforts that would be required to stop virus circulation in the backyard, particularly in domestic duck, free ranging duck systems. The free ranging duck systems in Vietnam tie in with the rice cropping. Most of the free ranging ducks get their main feed resource from leftovers in the post-harvest rice paddies. These are grains and snails and eggs of snails and little crabs and fishes. This constitutes the main feed resource for the free ranging ducks. The availability of domestic duck feed through the season, which ties in with the rice cropping pattern and the rice husbandry, dictates how many free ranging ducks are effectively kept and how much virus is circulating. The complexity of disease outbreaks, free ranging ducks, duck husbandry, rice cropping patterns and related wetland and river system aspects has not yet been clarified for the Red River system. It is worse even for the Mekong Delta in southern Vietnam extending into Cambodia. How

1 Many thousands of birds have died from avian influenza, many thousands of people have had direct and intimate contact with infected birds (at markets, and in slaughtering to control the disease) and yet only 119 people are known to have become infected. The conclusion is that many people had intimate contact with infected birds did not become infected. It is believed that, for a person to become infected, intimate and prolonged contact with infected birds is probably required.

2 Note: This figure was later denounced and revised to 3.
the disease and the ducks and the rice and the wetlands come together and from there how the virus is passed on to the more commercial terrestrial poultry circuits is poorly understood, even with Vietnam today announcing plans to immediately vaccinate 80 to 100 million birds in the short-term, because the next seasonal poultry disease explosion is in December, which is very soon, I am pretty sure even with the money now available—I am talking of a handful of millions of dollars—there will be no effective coverage, let alone that there will be selected targeted vaccination efforts in place that would achieve disruption of transmission cycles. What I know about Vietnam is that despite all the efforts there will be a new wave of outbreaks starting at the end of December, if not the beginning of January and there might be further human cases occurring as the disease builds up in poultry. Finally, China was the third country I listed as having an acute and immense problem. When the Z genotype virus started to take over from all the other H5N1 viruses circulating in domestic ducks in China, China saw that terrestrial poultry became increasingly affected, epidemics started to spread and at that moment in 2004 China initiated significant scale vaccination programmes and continues to do so today. The problem China faces is that it holds 700 million domestic ducks, which is the equivalent of approximately 70 per cent of the world’s domestic duck population. A very significant proportion of these ducks in China go with the traditional farming systems, the village level, integrated rice crop, barley, whatever system has been going on for centuries, if not millennia. It is this system where the rigid vaccination programmes currently implemented in the commercial duck provinces of China do not reach the village level ducks. The problem with the vaccination programmes in China could be that the vaccination coverage—incidentally with an H5N1 vaccine so you can no longer differentiate between wild and vaccine antigens—means the smallholder duck farm virus continues to evolve unnoticed. That is what is going on in China probably. It is very difficult to get into China, yet if we do not get into China, and I am talking as an international community, we are not dealing with the giant, we are just dealing with the dwarf countries around it.

Q27 Baroness Finlay of Llandaff: Could I ask you about risk assessment overall in terms of what you feel the assessment of risk is of a new viral strain which could lead to pandemic influenza either directly from the avian or other pandemic influenzas? What is its likely time and location?

Dr Slingenbergh: Perhaps we can both answer this question to give you better information. I am an FAO employee and as such I am trying to convey to you the consensus that is building up within our technical unit, harmonised with other UN agencies, as you will understand. We believe that the risk of a pandemic of human to human transmissible virus is to be taken very seriously. We believe that it may not happen in the very short-term. To explain why we come to this stance, we believe that the problem, if it does emerge, is more likely to emerge in Asia. Asia is where the house is on fire. Asia is where fire fighting must be done today. If the problem does emerge it would emerge possibly in China, Vietnam or Indonesia. These are likely countries where the virus continues to circulate in a way that creates the explosive setting required for the virus to further evolve. There is no evidence of sustained human to human transmission yet. There is also no evidence that the number of human cases infected is on the increase; on the contrary, there is evidence that there has been a progressive decrease, even in Vietnam. I have already referred to the fact that Thailand has not seen human infection since October 2004. There is also evidence that whilst the problem does persist in poultry in China, Vietnam and Indonesia, and perhaps even in the Central Plains of Thailand, there is not more poultry disease than there was one or two years ago. If we take that, together with the fact that for the human to human transmissible virus to emerge the risk there is proportional to the number of humans who are exposed to poultry virus, we understand better why the human infections so far seen are not human to human variants. There have been two instances where probably there was this first human to human transmission, particularly this mother caring for her daughter in Thailand. Her daughter was excreting massive amounts of virus and the mother was taking care of her daughter, being so close, and one can imagine that, yes, there was human to human transmission but even that staggered to extinction. It requires a longer chain and it requires more and increased lengths of chain for us to become worried about short-term evolution of human to human transmissible virus. Finally, and I will allow my colleague to give his views, there has been a very pertinent publication that appeared in Nature and also Science a week ago by Taubenberger. A group of scientists resurrected the 1918 pandemic virus and one conclusion from this study—there were several conclusions—was that the virus that caused the problems in humans was an avian or poultry virus, the same as the 1957 and 1968 pandemic viruses that transmitted human to human. The 1918 one evolved, unlike the other two, in total. In its entirety this virus adapted to human to human transmission. This is an extremely important finding suggesting that we need the build up of human chains for this type of genetic drift to occur. The genetic shift, the recombination or the re-assortment, is much more haphazard but also has a quantitative dimension. We now have to seriously consider that a 100 per cent poultry virus
can make its way into infecting humans and thus adapts to becoming a human transmissible virus kick-starting a pandemic. This reality is slowly sinking in. Veterinarians have all been brought up with the role of pigs as mixing vessel and all that, but this novel reality—that all three pandemics that have occurred in the 20th century were avian/poultry viruses and that the most important of these, the 1918 one, evolved in total—is perhaps a reality that still needs to sink in.

**Dr Slingenbergh:** Of course I entirely agree with what has been said already. May I add that given this very pertinent publication I was referring to, we now have come to realise that it takes relatively minor changes, and I am talking about 20 amino acids, for what is a 100% avian/poultry virus to become adapted and change into a human to human transmissible dynamic agent. Not only does it take relatively few amino acids to change the position, in addition to that there is a molecular pathway that would tell us from human infections how far we are on the way towards the crisis we might be running into. That is good news, as it were, as long as we keep a very close eye and make sure that we swiftly undertake molecular genetic analysis of each and every case of human infection wherever it might be encountered. That is on a positive note. I believe, my Lord Chairman, you were also thinking about this. If it comes to the poultry and the birds and what could be done to point our finger and say “There is a situation that wants to be zoomed in on”, I believe, and I hope my colleague will agree on this, that when we have epidemic poultry disease and evidence of spill over, these are environments where active virus evolution is likely to be more pronounced. In geographical terms, in terms of poultry systems, in terms of commercial and village level poultry and poultry species, we may be able to take this on when we design our surveillance systems. In fact, we are planning a technical workshop next week to do exactly that. This is all rather novel.

**Q28 Chairman:** What ability do we have to monitor the virus as it modifies itself? Do we have any ability or do we have to wait until we witness human to human transmission?

**Dr McCracken:** My understanding would be one would have to rely on those who have the ability to do the very detailed fingerprinting of the virus to see if any true shift has occurred. Sadly, the first indication we may have will be that there is human to human transmission.

**Dr Slingenbergh:** Of course I entirely agree with what has been said already. May I add that given this very pertinent publication I was referring to, we have come to realise that it takes relatively minor changes, and I am talking about 20 amino acids, for what is a 100% avian/poultry virus to become adapted and change into a human to human transmissible dynamic agent. Not only does it take relatively few amino acids to change the position, in addition to that there is a molecular pathway that would tell us from human infections how far we are on the way towards the crisis we might be running into. That is good news, as it were, as long as we keep a very close eye and make sure that we swiftly undertake molecular genetic analysis of each and every case of human infection wherever it might be encountered. That is on a positive note. I believe, my Lord Chairman, you were also thinking about this. If it comes to the poultry and the birds and what could be done to point our finger and say “There is a situation that wants to be zoomed in on”, I believe, and I hope my colleague will agree on this, that when we have epidemic poultry disease and evidence of spill over, these are environments where active virus evolution is likely to be more pronounced. In geographical terms, in terms of poultry systems, in terms of commercial and village level poultry and poultry species, we may be able to take this on when we design our surveillance systems. In fact, we are planning a technical workshop next week to do exactly that. This is all rather novel.

**Q29 Chairman:** May I just ask a wrap-up looking forward question now, bearing in mind we are quite short of time at this stage. My question is, in the longer term what systems should the international community be putting in place to monitor and reduce the risk of the emergence of new zoonotic disease with pandemic potential?

**Dr McCracken:** My Lord Chairman, without necessarily trying to defend my own profession I believe that if you are talking about zoonotic organisms, organisms that have the ability to move from animals, whatever that is, to man, then we should ensure that we have an effective veterinary profession in every country so that they can play their part, and I believe they are the core, in ensuring that any emerging disease is readily recognised, quickly recognised and action can then be taken. I go back to a point I made earlier and, however difficult it is, it is one that we must strive towards. That is where developing countries must recognise their responsibility and somehow ensure that they can play an effective role, not only in combating disease when it appears in a developed country but also play its part in ensuring that developing country has an
effective infrastructure that will allow meaningful surveillance work to be carried out because today we are talking about avian influenza, tomorrow it may be some other organism. What needs to be in place is work that will address all possibilities to ensure that we can act quickly. Like so many problems in life, if we can identify the problem readily and act quickly the problem disappears. I have mentioned on previous occasions in relation to foot and mouth disease—I will draw this analogy—if we find foot and mouth disease on the first farm of introduction we have a crisis to deal with, but if we find foot and mouth disease on the 51st farm we have a catastrophe to deal with. I believe in international terms we should be aiming at doing something on the first farm, the first premises. That is what we must be aiming at. It is not taking the focus away from our own concerns and interests within the UK, within Europe, but we must have that wider perspective to the level of ensuring that there is effectiveness out there in developing countries. Thank you.

Q30 Chairman: Dr Slingenbergh, would you like to add anything?

Dr Slingenbergh: I wholeheartedly agree with the contribution of my colleague. May I just add a few words that put the FAO and UN in perspective on this particular question. We have witnessed the introduction of HIV, and I know you are not associating HIV with livestock, but bush meat in Africa is an issue of growing concern and we are talking about millions of tonnes of bush meat, and there is a direct association of primates and bush meat and the early evolution of different HIV viruses in Africa. Being in British company I will not elaborate on BSE, but the prions have also been encountered beyond Britain and also in other animal species. We have recently learned that horseshoe bats, which are a delicacy found in food markets in south-eastern China today, were found infected with a number of genetically slightly different SARS-type corona viruses. It is not too difficult to figure out, with these horseshoe bats being for sale on the food market, together with civet cats, how the SARS epidemic emerged. There was a link with food animals on all three occasions. The same applies for avian influenza. This brings us to consider what are the factors or the drivers, if you wish to call them that, in the agriculture production environment that creates these risky situations. Perhaps we should go beyond all the efforts that concern the veterinary profession and look into how different food animal systems and forms of agriculture, particularly in the Asian setting, bring about the shift of viruses from animals to humans. It is not exclusively Asian. We have seen ostriches playing an important role in the switch from low to highly pathogenic avian influenza in South Africa and also in Europe. We have seen the open turkey systems and the wet markets in the eastern United States being implicated in this shift of low to highly pathogenic avian influenza in the Americas. Different parts of the world have their own problems. I will conclude here, my Lord Chairman. Certainly the shift of food animals related pathogens from animal to humans is an issue on the increase and it wants us to reflect on issues that extend beyond the direct veterinary profession. Thank you very much.

Q31 Chairman: Let me thank you both very much for your evidence and for your answers to the questions. I think it has been extremely useful to our inquiry. Is there anything you would like to add before we finish?

Dr Slingenbergh: It has been an honour and a pleasure to be here. Thank you very much.

Chairman: Thank you very much. If anything should occur to you subsequently to do with what we have discussed or anything else that you think would help our inquiry, may I ask you to write to us so we can consider those. Thank you very much indeed.
TUESDAY 25 OCTOBER 2005

Memorandum by the UK Vaccine Industry Group

INTRODUCTION

1. The UK Vaccine Industry Group (UVIG) welcomes the opportunity to submit evidence to the Science and Technology Sub-Committee in advance of its report on pandemic influenza. We believe that the industry has a crucial role to play in ensuring that protection against the serious effects of pandemic flu is available.

2. UVIG, working within the Association of the British Pharmaceutical Industry (ABPI), represents six pharmaceutical companies that research, manufacture and/or supply vaccines to the UK—Baxter Healthcare, Chiron Vaccines, GlaxoSmithKline, Solvay Healthcare, Sanofi Pasteur MSD and Wyeth Vaccines. UVIG’s aims are to promote the positive benefits of vaccination as a key element in public health, and to represent the UK vaccine industry to all interested parties.

3. The following response relates directly to the role of vaccines and vaccination policy in preparation for, and in the event of, an influenza pandemic and seeks to answer the specific questions posed by the Committee. It builds on comments submitted to the Department of Health in response to the UK Health Departments’ UK Influenza Pandemic Contingency Plan (The Plan). UVIG has called upon the Government to:

   — support research and development of candidate vaccines;
   — negotiate advance purchase agreements with vaccine manufacturers;
   — provide the environment for industry to build capacity by increasing access to flu vaccination during inter-pandemic years;
   — engage openly with industry.

4. There have been some welcome developments since publication of the Plan—notably the issuing of the tender for the strategic stockpile of H5N1 vaccine and a meeting between UVIG and its members and the NHS Purchasing and Supply Agency to progress development of an Advance Purchase Agreement process. However, there remains much more to be done and the Government needs to consider a more structured and timely approach to the vaccine element of the Plan.

Are the measures described in the revised UK Influenza Pandemic Contingency Plan adequate to minimise the effects of a pandemic? What more could be done?

5. The benefit of an effective pandemic vaccine cannot be underestimated and the next pandemic will be the first where there will be an opportunity to protect the UK population against the pandemic virus. The stated aim of the Government is to vaccinate all of the UK population in the event of a pandemic.¹ UVIG and its member companies’ ambition is to be able to supply the UK with sufficient doses of licensed pandemic vaccine, in as short a timeframe as possible.

6. The Plan acknowledges two important factors. First, that vaccines offer the best line of defence and secondly, that due to the nature of a pandemic, vaccines cannot be manufactured in substantial quantities until the actual pandemic strain is known. Furthermore, a pandemic would be a global phenomenon and vaccine production would be part of a global response.

¹ Pandemic Flu: UK Health Departments’ UK Influenza Pandemic Contingency Plan, March 2005.
7. To achieve the Government’s goals and minimise the effects of a pandemic, preparation needs to have begun in earnest and in advance. However, optimum preparation can be achieved neither by the public nor private sector alone. Both sectors must work together in a structured and open manner to facilitate the future availability of pandemic vaccines. The Plan posed many questions about pandemic vaccines with few answers, and despite some important progress there remains much to be done. With a realistic yet modest level of investment from Government and ongoing dialogue with manufacturers the questions can be answered and solutions put in place.

8. Government needs to:
   — provide financial assistance to vaccine manufacturers in their development of candidate pandemic flu vaccines;
   — create the necessary environment for vaccine manufacturers to participate fully in pandemic preparedness;
   — maximise the benefits of developing the flu policy in inter-pandemic years to increase capacity and to improve efficiencies in process.

Is the UK stockpile of antiviral treatments adequate, and how will it be distributed? What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?

9. The Government has made a significant financial commitment (reportedly £200 million) to pandemic preparedness by creating a stockpile of oseltamivir. Whilst these will be invaluable for treating infections in the early stages of a pandemic, it is only vaccines that are able to prevent infection.

10. With regard to vaccines, even when the pandemic virus has been identified, without investment to build capacity and preparations in the regulatory process manufacturers will not be in a position to supply sufficient volumes of vaccine to vaccinate the whole of the UK population.

11. The critical issue facing the UK, Europe and indeed the world is to ensure that there is sufficient manufacturing capacity such that the maximum quantity of vaccine can be produced as soon as possible after the declaration of the start of a pandemic. Current flu vaccine manufacturing capacity is linked to demand—90 million doses per annum are currently produced for Europe, of which around 12 million doses are for UK use.

12. While stockpiling of a candidate vaccine for the entire population is currently not practical as the exact strain will not be known until a pandemic is declared, strategic stockpiling of H5N1 for certain at-risk groups is a realistic option. This latter point appears to have been addressed by the Government with the recent tender.

13. Any increase in capacity to ensure the necessary response to a pandemic and efficiency in process would need to be driven by an increase in demand during inter-pandemic years. The decision to do this needs to be taken now. UVIIG therefore urges the UK Government to implement changes in vaccination policy in inter-pandemic years, in particular gradual extension of the age-related policy to those aged 50 years and over, a policy for children and a push to achieve 75 per cent coverage in the at-risk groups. These changes, needing to be evidence based and cost effective, would be in line with the Government’s broader public health goals.2 The Joint Committee for Vaccination and Immunisation is reviewing the evidence for a lowering of the age to 50 years.3 Furthermore there are strong economic data to support this change, in particular a recent cost effectiveness study of reducing the recommended age for vaccination from 65 to 50 years, which concludes that “Extension of the current immunisation policy has the potential to generate a significant health benefit at a comparatively low cost.”4

14. Investing in this way would be the single most effective means of ensuring adequate capacity providing 20 million trivalent doses in inter-pandemic years and therefore up to 60 million monovalent doses for a pandemic. It is not possible to have an effective and robust preparedness plan without making changes to existing policy. Moreover it is not cost-effective or practical to retain unused industrial capacity for activation in the event of a pandemic. Supply of a pandemic vaccine is therefore inextricably linked to the manufacturing capacity that exists during inter-pandemic years.

15. With regard to ensuring efficient and timely regulatory process, UVIIG recommends that companies should be incentivised to develop a mock-up dossier. This would address a key challenge for the UK Government which is to shorten the time between identification of the pandemic flu virus and delivery of an effective licensed vaccine. A mock-up dossier would take a candidate vaccine through the entire regulatory

3 JCVI Influenza Sub Group Minutes, 13th April 2005 http://www.advisorybodies.doh.gov.uk/jcvi/mins-flu-130405.htm
process such that the actual pandemic vaccine would only require a licence variation for the actual pandemic strain and quality assurance before release onto the market. This is not a means to short-cut the safety, efficacy and quality processes for a vaccine, but rather a process whereby vaccine candidates can be optimised in advance of a pandemic. This should allow provision of appropriate vaccines in a shorter period of time, estimated to save some 2–4 months. This time saving may equate to the production period required for many millions of vaccine doses in the event of a pandemic outbreak.

16. In accordance with the European Medicines Evaluation Agency (EMEA) regulations, it is possible to licence a candidate vaccine through submission of a core pandemic dossier. UVIG recommends that this approach is adopted.

17. Additional investment by Government will be necessary to achieve the above. However, this additional investment is relatively moderate. Putting it into context, for example, the estimated cost to develop a mock-up vaccine is €11–13 million ( £7.5–8.8 million) per candidate vaccine.

What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?

18. As previously noted the vaccine response to a pandemic is critical to preventing the forecast morbidity and mortality of flu. Furthermore, ensuring the development of the right vaccines and the manufacture and distribution of sufficient supplies will be a joint effort between vaccine companies, Government, public health bodies, the NHS and others.

19. The exact strain of the pandemic influenza virus will remain unknown until identified by the World Health Organisation (WHO). Until this time, however, much work can be done with existing candidate antigens to establish the ideal formulation and dosage of such a vaccine, and to optimise the manufacturing and regulatory process. Indeed, several companies are already working on the development of H5N1 strains of vaccine in response to the recent avian flu scares in the Far East.

20. European guidance on the licensing of pandemic influenza vaccines came into operation in April 2004 and provides guidance on the quality, safety and efficacy requirements for licensure of a mock-up vaccine including those formulated using a novel adjuvant.

21. It is critical that this work is undertaken by as many manufacturers as possible, in advance of a pandemic. This will generate important information, increase our knowledge about pandemic vaccines and develop expertise that will greatly enhance our ability to respond to the threat. It is vital that Government supports these endeavours.

22. To support the research and development, the development of a mock-up dossier and steps to build capacity, UVIG has recommended to Government two important processes. First, the negotiation of advance purchase agreements and second the establishment of a vehicle and process of communication between all key stakeholders, including industry.

23. An initial meeting between UVIG and the NHS Purchasing and Supply Agency has taken place during which the possible details of an advance purchase agreement were discussed. To date no conclusions have been reached but UVIG urges the UK Government to recognise the global nature of a pandemic event, the competition between countries for vaccine supply and the need to demonstrate its commitment to the issue of vaccines.

24. The details of these agreements should cover a wide range of issues that impact on supply and include, inter alia, vaccine presentation, start-up time dependent on availability of seed virus, intellectual property, public liability (third party claims), and incentive payments to assist in the development of candidate vaccines.

25. The manufacture and supply of a pandemic flu vaccine cannot be undertaken by the private or public sector in isolation. Dialogue between government and industry is essential as no single organisation can manage the whole solution. The Government has acknowledged the role of UVIG members in the development, manufacture and supply of flu vaccines, and this is to be welcomed. However, to date, this dialogue has been intermittent and has mostly been at the request of the industry. Dialogue with industry, and other agencies, in this planning phase must be undertaken in a structured, transparent, timely and inclusive manner.

5 Guideline on Submission of Marketing Authorisation Applications for Pandemic Influenza Vaccines through the Centralised Procedure (CPMP Adopted March 2004) EMEA/VEG/4986/03.
6 Influenza Preparedness: EVM Proposal for an action plan between European Vaccine Manufacturers and Member States with the support of the European Commission, February 2004.
7 CPMP/VEG/4717/03.
The Plan proposes the establishment of the UK National Pandemic Influenza Committee (UKNPIC) which will draw representation from key organisations and have the responsibility to oversee the UK’s response to a pandemic. However, the Plan suggests that this committee will be convened at the discretion of the Department of Health and only once a pandemic has been confirmed.

Preparation for pandemic vaccines must start now, and as such UVIG calls for the establishment of a Pandemic Influenza Vaccine Committee with specific responsibility for vaccine-related issues. This group would report into the Department of Health and draw its membership from the Department of Health, NIBSC, Health Protection Agency, NHS Purchasing and Supply Agency, the regulatory authorities and UVIG.

CONCLUSION

UVIG welcomes the publication of the Plan by the UK Health Departments and the recent developments, but is concerned that in order for the UK to be fully prepared to meet the Government’s stated aim of vaccinating the entire population, a number of important issues relating to vaccines need to be fully resolved.

UVIG calls on the UK Government to:

— Support the research and development of candidate vaccines;
— Negotiate advance purchase agreements with vaccine manufacturers;
— Provide the environment for industry to build capacity by increasing access to flu vaccination during inter-pandemic years;

Engage openly with industry.

The UK Vaccine Industry Group is prepared and willing to working with the Government and other stakeholders to deliver this challenging yet vital programme of work.

Memorandum by Chiron Vaccines

INTRODUCTION

1. Chiron Vaccines is the fifth largest producer of human vaccines in the world, and the second largest influenza vaccine manufacturer. Chiron Vaccines is headquartered in Oxford and has a number of facilities across Europe, the USA and Asia, including a vaccine manufacturing facility in Speke, Liverpool. This is currently the only large-scale manufacturing site for influenza vaccines in the UK.

2. Chiron Vaccines welcomes the current inquiry by the House of Lords Science and Technology Committee into the UK’s preparations for a potential outbreak of pandemic influenza. In this written evidence, we have attempted to provide answers to some of the specific questions identified by the Committee in its Call for Evidence.

Are the measures described in the revised UK Influenza Pandemic Contingency Plan adequate to minimise the effects of a pandemic? What more could be done?

3. Chiron Vaccines welcomed the publication of the UK Health Departments’ Influenza Pandemic Contingency Plan in March 2005, and particularly the recognition within the Plan of the critical role that vaccination will play in the event of an influenza pandemic. Since the publication of the Plan, the Government has announced a number of welcome initiatives to minimise the effects of a pandemic, including the stockpiling of antiviral drugs and issuing a tender for a stockpile of H5N1 vaccine for key emergency and healthcare workers.

4. However, there are a number of outstanding issues relating to the research, development and supply of a pandemic vaccine that need to be resolved during the inter-pandemic period to ensure that the UK is well placed to protect its citizens in the event of an influenza pandemic. In the interests of public health, we urge the Government to work closely and effectively with industry and other stakeholders to ensure that these issues are addressed in a timely fashion.

5. Chiron Vaccines is committed to supporting pandemic preparedness efforts and has identified a number of priority areas that need urgent attention:

— Investment in the necessary research and development to identify a safe and immunogenic pandemic vaccine;
— Development of an influenza policy which directly addresses the correlation between adequate inter-pandemic and associated pandemic vaccination coverage;
— Agreement on advance purchase contracts to allow capacity planning and avoid protracted negotiations in the event of a pandemic;
— Indemnification of manufacturers against the use of a pandemic vaccine;
— Provision of clear guidance on the policy of free movement of goods, both within the EU and outside, during a pandemic to allow for the development of an appropriate supply policy for overseas customers.

6. Failure to address these issues in the inter-pandemic period could delay production of a pandemic vaccine by a number of months, while suitable pandemic vaccine candidates are developed and evaluated.

What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?

7. Current production capacity reflects ongoing inter pandemic demand, and is far from sufficient to meet a global pandemic requirement. The Government has stated its desire to vaccinate the entire UK population in the event of a pandemic. If this is to be achievable, the Government needs to take steps to increase inter-pandemic demand for vaccines, and drive investment in new production facilities.

8. The WHO has called for national governments to aim for coverage of 75 per cent in all target groups. Currently, despite relatively high coverage in the age group 65 years and over, only an estimated 42 per cent of at-risk patients in the UK are currently vaccinated. Government and industry should work together to consider ways to increase uptake in inter-pandemic years.

9. Additionally, Chiron Vaccines believes that the Government should extend its current age related influenza guidelines to those aged 50 years and over, and also to include children. There is strong health economic data to support these changes.8, 9 The US experience has demonstrated that public health practice tends to follow age-related vaccination guidelines rather than those based on risk factors. Gradual extension of the recommendations would enable all vaccine suppliers to build manufacturing capacity year on year, thereby increasing capabilities to face a pandemic, as well as providing the benefits of broader influenza vaccination.

What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?

10. There is uncertainty about which influenza strain will cause the next pandemic, and this will remain until the exact strain is confirmed by the World Health Organisation (WHO). However, it is still possible to undertake research and development work during the inter-pandemic period to identify and optimise potential pandemic vaccine formulations.

11. The European Agency for the Evaluation of Medicinal Products (EMEA) has established guidance regarding the requirements for licensure of a potential candidate pandemic vaccine, known as a “mock up” file or dossier. This provides a framework to undertake clinical trials to establish the optimum vaccine formulation, dosing regimen and antigen dose requirements. The aim is to facilitate the preparation of a “mock up” file, such that the “mock up” strain/vaccine can be replaced with the actual pandemic vaccine strain once it has been identified. The data generated will be extremely valuable in determining how naïve populations respond to the envisaged vaccine formulation. The estimated cost to develop such a mock-up file is between 11 million and 13 million euros per vaccine.10

12. Chiron Vaccines has considerable experience of working with potential pandemic strains such as H5N1 and H9N2, based on its research and development work with a number of governments at our sites in Italy and the UK. However, funding will be required to undertake the necessary clinical trials to establish the optimum formulation and dosage for a pandemic vaccine. Indeed, the Government stated in its response to the Lords Science and Technology Committee’s Fighting Infection inquiry in 2003, that it “would expect to be in the forefront of development of a suitable vaccine should a new influenza virus emerge with pandemic potential”.11

10 Influenza Preparedness: EVM Proposal for an action plan between European Vaccine Manufacturers and Members States with the support of the European Commission, February 2004.
13. Additionally, it is essential that clinical trials are undertaken to ensure that the product formulation is proven to have a good safety profile and is immunogenic in a naïve population. More than one vaccination and/or the addition of an adjuvant may be required to induce protective responses in un-primed individuals, and this can only be established in clinical studies.

14. Unless a mock-up vaccine is developed it is possible that, in the event of a pandemic, unlicensed and unproven vaccines would have to be used until enough data has been amassed to support formal licensure. If the UK Government is unwilling to invest in mock up file development, this could result in the need to use an unlicensed and unproven vaccine formulation on the UK population in the event of a pandemic. In this event, Chiron Vaccines would require indemnification from the UK Government so as not to be held liable for any vaccine that is released in such circumstances.

15. By definition, an influenza pandemic will be a global health emergency. Demand for pandemic vaccines will inevitably outstrip supply. A number of other governments, including the USA, Norway, France, Australia and Japan, have already initiated discussions to secure pandemic vaccine supplies and other Governments have initiated confidential discussions. Chiron Vaccines calls on the UK Government to demonstrate its commitment to the development and use of vaccines and to enter into negotiations or advance purchase agreements with manufacturers. Advance purchase agreements would go some way to demonstrate the Government’s commitment to the use of vaccines and to establish the necessary process that will support the delivery and access to vaccines.

16. The details of these agreements should cover a wide range of issues that impact on supply, including vaccine presentation, start-up time, availability of seed virus, Intellectual Property, public liability (third party claims) and costs. Tackling these issues now would help the Government expedite its response to an influenza pandemic.

**Memorandum by the National Institute for Biological Standards and Control (NIBSC)**

NIBSC is a key player in the global response network for pandemic influenza. It is one of only three laboratories worldwide tasked by WHO to develop and supply safe seed strains of virus for vaccine production based on emerging isolates of potentially dangerous pandemic influenza. For example in early 2004 NIBSC scientists rapidly created a vaccine seed based on the Vietnamese outbreak of avian influenza in humans and distributed it to manufacturers around the world. Several human vaccine trials are now underway using this seed strain. NIBSC is working closely with WHO, the Health Protection Agency, vaccine manufacturers and other stakeholders to help minimise the response time for vaccine development in an emergency through advance planning and preparation of materials.

This submission consequently focuses on the role of vaccine development, manufacture and distribution in responding to a pandemic.

1. Vaccine development and supply should be a key element in dealing with an influenza pandemic. Vaccines against seasonal influenza do provide protection against disease. In a pandemic setting, where the mortality rate may be high, even limited protection against disease or its most severe consequences would be highly valuable.

2. It will be impossible to be completely prepared for every possible influenza pandemic through either pre-vaccination of the population or by advance vaccine stockpiling because of the possibility that an emerging pandemic strain may differ significantly from the strain on which the prepared vaccine was based.

3. The time needed to move from identification of a new and dangerous isolate emerging in the human population to availability of sufficient vaccine to protect the population must therefore be minimized.

4. This period is dependent on a number of factors, but chief amongst them is manufacturing capacity. Global vaccine manufacturing capacity, based on current dosage requirements, appears wholly insufficient to meet vaccine needs in the time that would be required to deal with the first wave of disease. Capacity needs therefore to be increased as a matter of urgency.

5. This can be addressed to some extent by increasing vaccine coverage rates for seasonal influenza. This would in turn stimulate creation of additional manufacturing capacity by industry. A target of 33 per cent coverage has been recommended by some on the grounds that the capacity required to deliver this many doses of a three-component vaccine (the standard “trivalent” annual influenza vaccine) could deliver three times more “monovalent” vaccine against a pandemic strain, theoretically meeting total needs. In reality, however, this measure alone is very unlikely to be sufficient, since vaccine outputs against seasonal influenza can be planned over a six month period, whereas pandemic vaccine requirements will be compressed into a much shorter timeframe, perhaps as little as six weeks.
6. This problem is compounded by the fact that successful vaccination against a new pandemic influenza strain, using current vaccine technologies, is likely to require two doses at least one month apart, doubling the number of doses required to protect a given population. Furthermore a recent human clinical trial in the USA with an H5 avian influenza vaccine prepared using “standard” technology indicated that six times the usual vaccine dose was needed to generate an adequate immune response.

7. It is therefore unrealistic to imagine that demand for a pandemic vaccine could be met simply by investing in additional manufacturing plant. In order to meet demand it is clear that new and highly efficient “antigen sparing” strategies will be required, in order that a much larger number of effective vaccine doses can be generated in a shorter space of time from the manufacturing capacity that does exist.

8. Development of such strategies will require an urgent and extensive programme of clinical research and development using “mock-up” vaccines against potential pandemic strains of influenza. This needs to be funded by governments. It is unreasonable and unrealistic to expect vaccine manufacturers to divert large amounts of funds and resource into areas for which the market opportunities are far from clear. From the perspective of countries in Europe it would seem rational for this investment to be made through the European Union as well as at national level.

9. Given the scale of the potential threat from pandemic influenza, development of effective vaccine approaches needs to be done as a close and co-operative partnership between public and private sector with public health authorities, academic researchers, manufacturers and regulators working together to maximize the output from their combined efforts through co-ordinated planning and sharing of information. This would clearly be facilitated by direct government support to all parties including manufacturers.

10. This clinical development work should be complemented by research on vaccines manufactured using cell culture-based, rather than egg-based systems. Currently each dose of influenza vaccine manufactured requires one fertilized hen’s egg. While this system is tried and tested, and appears to represent the only viable option at present to produce sufficient vaccine on a global scale, in the long term the potential vulnerability of egg supply in an emergency represents a very substantial risk.

11. Another important preparation measure should be the advance development of a “library” of vaccine seed strains against potential pandemic strains. Though strains developed as part of the library may not turn out to be identical with actual emerging strains, they may be close enough to provide some protection, would quite probably provide effective immune “priming” (see paragraph 12) and could buy time for preparation of a more accurately matched vaccine. Availability of “ready made” vaccine seeds developed up to a point where they could be put directly into production by manufacturers would significantly speed up the overall response time.

12. A further crucial area for research in the short and medium term should be to explore opportunities for generating a degree of broad protection against pandemic influenza strains through advance vaccination. It is well recognised that the human immune system can react much more rapidly and effectively to an infectious assault if the system has been “primed” in advance through encounter with a similar agent. A vaccine that could be administered routinely and that would “prime” an individual’s immune system so that in the event of a pandemic outbreak he or she would enjoy a limited degree of protection, or would require only a single vaccine dose to achieve good protection, would be of great value. If this strategy proved effective, routine seasonal influenza vaccines could be regularly adapted to include one or more components in order to prime the population against potential pandemic influenza strains.

13. In the long term there should be investment in a vigorous programme of research aimed at identifying new approaches to vaccine development that would circumvent the problems associated with existing vaccine technologies.

26 September 2005

Memorandum by Roche Products Ltd

1. **Summary**

1.1 Roche is the manufacturer of the antiviral Tamiflu® (oseltamivir), with considerable expertise in influenza and committed to working as a responsible partner in pandemic contingency planning.

1.2 The manufacture of oseltamivir is a lengthy process involving significant lead times. Roche supports the recommendations of the World Health Organisation (WHO) that countries should stockpile antivirals as part of their process of preparing for a pandemic. We therefore welcome the decision of the UK Government to procure 14.6 million doses of Tamiflu as part of its Pandemic Contingency Plan. We consider that the UK
Pandemic Contingency Plan has put the UK in a position of preparedness in advance of many of its European neighbours.

1.3 There is no room for complacency in pandemic planning and Roche therefore welcomes the Committee’s decision to stage a short inquiry. Roche would wish to make the following recommendations:

— that the Government is congratulated on the levels of preparedness and pandemic planning that it has already put into place;
— that the Government is urged to continue to maintain, and where appropriate increase, its pandemic preparedness levels in line with changing domestic and international requirements;
— that the Government should be more clear about precisely which groups of the population will receive antiviral for prophylaxis and which group will receive antiviral treatment, thus allowing individuals who will not be covered to identify the need to protect themselves and their families from pandemic influenza;
— that the private sector (particularly key industries such as transport and utilities) should be supported and encouraged to develop pandemic plans for their own key workers, and integrate them into their existing business continuity plans;
— the UK Health Departments should plan transparently and early in their procurement policies, for both antivirals and vaccines, to assist vaccine and antiviral manufacturers appropriately address future capacity issues and minimize lead-in times.

2. Roche and Pandemic Planning

2.1 Roche aims to improve people’s health and quality of life with innovative products and services for the early detection, prevention, diagnosis and treatment of disease. Part of one of the world’s leading healthcare groups, Roche in the UK employs nearly 2,000 people in pharmaceuticals and diagnostics.

2.2 Roche is a leading healthcare company with considerable expertise in influenza and is the manufacturer of Tamiflu (oseltamivir), a neuraminidase inhibitor (NI) antiviral drug, which specifically attacks the influenza A and B virus, helping to stop it spreading and infecting other cells.

2.3 The House of Lords Science and Technology Select Committee requested responses to 10 specific questions. Roche has felt it qualifies to comment upon nine of the 10 questions and its submission to the committee is presented in that format as follows:

Question 1: How is the risk of pandemic influenza emerging in southeast Asia, and reaching the UK, being assessed; and how can this assessment be improved?

2.4 Effective surveillance and communication of influenza activity is critical for proper awareness of and preparation for influenza outbreaks, and for accurate patient diagnosis. General medical practitioners would therefore benefit from more timely local information on influenza. Accuracy of influenza diagnosis can be increased to more than 60 per cent when physicians know that influenza is circulating in the community and when they use a defined set of symptoms as diagnostic criteria.

2.5 According to the UK Health Departments’ Influenza Pandemic Contingency Plan, influenza A viruses mutate much more readily than type B viruses, infecting not only humans but pigs, horses, sea mammals and birds, and from time to time there is a major exchange of genetic material between different influenza viruses. Roche Products Ltd, through the Neuraminidase Inhibitor Susceptibility Network, is constantly monitoring to identify new influenza strains that might prove resistant to Tamiflu (virus susceptibility). Roche considers it important that measures continue to be developed, by both national and international organisations, to ensure that viral susceptibility and drug resistance indicators are closely monitored, data shared as widely as possible, and national pandemic plans updated as appropriate.

Question 3: How is the UK working with international bodies to: monitor the development of the virus; and reduce the risk of pandemic influenza emerging and spreading?

2.6 Both the World Health Organisation Communicable Disease Surveillance and Response Global Influenza Programme and the European Commission Health and Consumer Protection Directorate General maintain surveillance mapping programmes of potential pandemic influenza, including H5N1, and the UK Government should continue to develop a full and proactive role in these projects.
2.7 The UK Government should continue to pursue and progress the H5N1 agenda published by the World Health Organisation, particularly the following:

— improvement in the quality and coverage of virological and epidemiological influenza surveillance;
— improvement in the understanding of the health and economic burden of influenza, including benefits from epidemic control and pandemic preparedness.

2.8 The UK Government should continue to pursue and proactively build upon guidance provided by the EU, particularly the recent European Commission Health and Consumer Protection Directorate General advice as follows:

— review and update the contingency plans for avian flu already in place according to EU legislation;
— ensure that existing measures and controls at the EU’s external borders are fully applied as regards both commercial consignments and personal imports by individuals and particularly regarding pet birds.

2.9 The WHO states that the surveillance of potentially pandemic influenza is inconsistent or inefficient in many risk-prone countries where disease information systems and health infrastructure are weak. Accordingly, Roche would recommend that international organisations, particularly the WHO, should be supported in their rapid response preparedness to intervene in early outbreaks in at-risk countries to slow the spread of pandemic influenza at source.

2.11 Roche has been working as a responsible partner over the last four years with the WHO, key clinicians, international health authorities and national governments to encourage the implementation of the WHO Pandemic Plan and the stockpiling of Tamiflu. Roche recently donated three million treatment packs of Tamiflu to the WHO to be used as part of a Rapid Response Stockpile to target and slow the spread of influenza epidemics at the source of their outbreak. This Rapid Response Stockpile is not a replacement for domestic pandemic planning and stockpiling but will be a valuable supplement to this.

2.12 To encourage pandemic planning, Roche has substantially reduced the price of Tamiflu stocks compared to those for seasonal use, and has made the active pharmaceutical ingredient of Tamiflu—oseltamivir phosphate—available to governments, providing a cheaper option in the assembly of pandemic stockpiles.

Question 4: What is the current assessment of the likely impact of pandemic influenza on the UK (both in terms of health and on wider society, including the economy)?

2.13 The arrival of H5N1 avian influenza virus is imminent in the UK according to the World Health Organisation. Two of the three widely-accepted criteria for an influenza pandemic have already been met by the most recent strain of the H5N1 avian influenza virus in Asia and these are as follows:

— a new virus strain has emerged;
— this virus has spread to humans.

2.14 The only criterion for pandemic not yet proven is the transmission of the H5N1 virus from human to human and, accordingly, the WHO considers that the world has moved closer to a pandemic than at any time since 1968. According to the Department of Disease Epidemiology at Imperial College London the continuing spread of H5N1 highly pathogenic avian influenza in wild and domestic poultry in southeast Asia represents the most serious human pandemic influenza risk for decades.

2.15 When H5N1 has crossed species barriers to humans, it has been fatal in 70 per cent of patients infected to date. The WHO accordingly estimates that a pandemic will kill 8 million people globally, and that 30 million will be hospitalized. It is predicted that there could be more than 50,000 deaths in the UK alone.

2.16 It is difficult to predict the full scale of the impact that pandemic influenza, and its associated morbidities and mortalities, will have upon the broader infrastructure of the UK. However, in 1999 the WHO, recognizing the significant mortality that would occur as a result of an influenza pandemic and its effect upon societal infrastructure, issued a Pandemic Preparedness Plan to assist governments in their preparations to manage the next pandemic.

2.17 The UK Health Departments’ Influenza Pandemic Contingency Plan meets the core requirements of the WHO Pandemic Preparedness guidance, including the ordering of antiviral stockpiles to cover 25 per cent of the population. The UK Government should be congratulated on implementing this guidance in such a timely manner that the UK now finds itself in a significantly superior position of preparedness than most of its counterparts worldwide. Accordingly the UK is now well on its way to having in place measures that have the possibility of mitigating worst-case disruptions to essential services infrastructure.
2.18 Roche would, however, welcome greater transparency and clarity relating to plans for treatment and post-contact prevention use of Tamiflu for coverage of those designated “essential workers” with the UK pandemic plan. It would be helpful, if not vital, for the purposes of business continuity within the broader infrastructure industry (transport, utilities etc) to know precisely which groups of individuals will be covered under the UK Health Departments’ Influenza Pandemic Contingency Plan and which groups of the population will not. Such clarity would enable key infrastructure corporations to effectively plan for workers not identified for antiviral coverage by central pandemic planning, and make alternate arrangements where appropriate and do so in a timely manner.

2.19 It may be useful for the House of Lords Science and Technology Select Committee to invite the Office of the Mayor of London to submit evidence to this inquiry relating to the GLA’s subnational pandemic plan for general London workers. This may be a potential model for the private sector to follow when introducing pandemic preparedness into business continuity planning.

Question 5: Are the measures described in the revised UK Influenza Pandemic Contingency Plan adequate to minimise the effects of a pandemic? What more could be done?

2.20 The UK is one of several countries, including France and New Zealand, stockpiling antiviral drugs and participating in research to speed up the production of a vaccine against a future pandemic flu outbreak.

2.21 The WHO in its Pandemic Preparedness Plan has recommended that countries establish stockpiles of Tamiflu according to their governments’ pandemic management strategies. The UK has announced plans to procure 14.6 million courses of Tamiflu which will provide treatment for one in four of the UK population—the proportion most likely to become infected with the disease and the figure recommended by WHO for planning purposes.

2.22 Roche has agreed to deliver the UK order in full by 2007. In the interim, the UK Pandemic Plan has prioritised essential workers within the public services as early recipients of post exposure antiviral treatment. However, the Government has not yet provided clear details of precisely who will constitute essential workers and receive first access to antiviral treatment, and who will not.

2.23 Roche would welcome clarification relating to which groups within the broader health economy, if any, will receive antiviral prophylaxis and whether this would be prioritised in terms of the following:

— functionality (ie non-essential workers in key industries);
— clinical vulnerability (particularly children\(^{12}\) and the old);
— post-exposure treatment only, and no preventative programme beyond essential workers.

Question 6: How well prepared and coordinated are health, emergency and other essential services for responding to a pandemic?

2.24 The WHO has identified the UK Health Departments’ Influenza Pandemic Contingency Plan as a high quality plan and representative of the UK being at the forefront of pandemic planning. The Government is to be praised on how quickly it has amended and developed the UK response to possible pandemic influenza.

2.25 The Government has issued operational guidance for all Strategic Health Authorities and Primary Care Trusts, which requires that local NHS organisations should develop, maintain and periodically test multi-agency contingency plans to ensure that resilient arrangements are in place to respond effectively to an influenza pandemic. Local NHS organisations are also required to have in place an Influenza Pandemic Coordinator.

2.26 The current state of preparedness in the UK for individuals to gain access to treatments that might prevent an epidemic spreading is good. Patient pathways to access antivirals are, in the UK, now both rapid and innovative and the Government has worked in partnership with industry to ensure that barriers to vital medicines in the event of an outbreak are now minimal.

2.27 The National Institute of Clinical Excellence (NICE) has issued Schedule 2 guidance relating to influenza antivirals, which permits general medical practitioners to write private prescription of Tamiflu for treatment or prevention of Influenza to healthy individuals during NHS appointments. This means that individuals at risk from seasonal outbreaks of influenza can purchase their own Tamiflu without having to incur the expense of a private appointment with a general medical practitioner and without having to rely on NHS supplies of Tamiflu.

2.28 In order to help deliver an effective strategy for influenza patients, Roche has worked with a multi-disciplinary team of pharmacists and general medical practitioners to develop the first National Pharmaceutical Association-accredited Patient Group Direction (PGD). A PGD is a written protocol whereby a named prescriber (in this case a Pharmacist) is able to supply a medication in certain situations—for most of the PGDs developed this would be in the event of an influenza epidemic. As such, at-risk individuals age thirteen or over who have symptoms of influenza will no longer have to wait for a GP appointment and can instead visit their community pharmacist who, if s/he considers it appropriate, will be able to supply them with Tamiflu. A PGD is particularly suitable in the case of influenza treatments where the time from first symptoms to medication is very important and impacts on the effectiveness of the treatment.

2.29 Roche has now helped develop 12 such PGDs through which the influenza sufferer benefits because they have access to professional advice and support from community pharmacists who have a wealth of experience and expertise in dealing with winter ailments and are often more accessible in terms of location, opening hours, rapid access and immediacy than are general medical practitioners. Only appropriately trained pharmacists have the authority to supply Tamiflu under a PGD, and each PGD is specific to the locality of a Primary Care Trust alone.

2.30 Under NICE guidance on use of neuraminidase inhibitors issued in 2003, Tamiflu is available on NHS prescription for the treatment of influenza in at-risk adults and children (over the age of one year), and the prevention of influenza in at-risk adults and adolescents aged 13 years and over, who have been exposed to the virus. Accordingly, UK Health Departments have available to them an influenza treatment, effective against any clinically relevant influenza strain, that can be used to treat those in sections of society (children and older people) most vulnerable to secondary complications such as bronchitis and pneumonia.\(^\text{13}\)

**Question 7:** What is being done to ensure that the general public is aware of the risks and likely effects of a pandemic, and of how they should react?

2.31 The UK Government has now put into place some of the most comprehensive pandemic planning measures in the world. It has published its plans online and launched the UK Health Departments’ Influenza Pandemic Contingency Plan document widely and with much publicity including newspaper and television media coverage.

2.32 By October 2005 all general medical practitioners in the UK will have been provided with pandemic influenza packs. The packs are expected to include a copy of the Chief Medical Officer’s guide Explaining Pandemic Flu, as well as leaflets aimed at the general public.

2.33 There does, however, remain a deficit of transparency in the pandemic planning process and insufficient detail has been released relating to precisely who will be covered by the pandemic plan (specifically who constitutes the emergency workers that will receive early courses of Tamiflu). Individuals and the private sector will need to know who is excluded from Department of Health schedule of prophylaxis so that they can develop their own arrangement in the event of pandemic influenza. If the public does not receive timely and accurate information about who will and will not be covered by the 14.6 million courses of antivirals stockpiled by the Government it could create significant unrest and panic in the population when an outbreak of pandemic influenza does occur.

2.34 The current situation is that the private sector has been insufficiently encouraged to put into place pandemic recovery plans as part of business continuity planning. As the private sector is considered a partner in the UK pandemic plan it is clear that business should play a full role in mitigating the effect of pandemic influenza upon the broader UK economy.

2.35 Roche’s commitment to responsibly helping the UK prepare for a pandemic will not begin and end with our delivery of the UK pandemic stockpile. We will continue to work with all appropriate organizations with an interest in pandemic planning to help maximize the UK’s preparedness.

**Question 8:** Is the UK’s stockpile of antiviral treatments adequate, and how will it be distributed? What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?

2.36 Tamiflu is designed to be effective against any clinically relevant influenza strains. As part of pandemic preparedness, the efficacy of Tamiflu against new H5N1 virus has been investigated in vitro and animal models and has been shown to be effective.\(^\text{14}\) Tamiflu, the only available oral neuraminidase inhibitor, provides an immediate option for the treatment and prophylaxis of influenza from the outset of a pandemic. However, the


\(^{14}\) Balasingham S et al. Antiviral Activity of Oseltamivir Carboxylate Against a Human Isolate of the current H5N1 chicken strain. Poster 3839, presented at the InterScience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Washington DC, USA on 31 October 2004.
manufacturing process for Tamiflu is complex and takes approximately 12 months, making it vital for governments to prepare their stockpiles and place their orders for Tamiflu in good time.

2.37 In order to help meet domestic and international demand, Roche has doubled its Tamiflu manufacturing capacity in 2004 and 2005 and will increase capacity eightfold in 2006. Roche is also now producing oseltamivir in three forms as follows:

- capsule;
- suspension (Tamiflu is the only available oral neuraminidase inhibitor that is licenced for treatment in children aged one year and over,\(^ {15} \) and suspension allows for a more pleasant administration option for younger children);
- Active Pharmaceutical Ingredient.

2.38 The UK ordered its supply of Tamiflu earlier than most national governments and Roche has committed to completing delivery by 2007. However, the generally late decisions amongst governments worldwide to stockpile antivirals has meant that capacity planning to produce Tamiflu has been retarded. Accordingly, longer lead times will need to be considered by national governments, including the UK Government, when the stockpile of Tamiflu is due to be renewed after the present stockpile has expired. It is essential, therefore, that greater clarity be provided, sooner rather than later, about what plans are in place to replace current stockpiles (Tamiflu capsules have a five year shelf life and the suspension solution for children aged one year and over has a shelf life of two years). This will enable producers of antivirals to build sufficient early capacity to ensure no delivery lags occur.

**Question 9: What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?**

2.39 According to the WHO, vaccines and antiviral drugs are the two most important drug interventions for reducing morbidity. Vaccines are universally considered the first line of defence; but because their supply will be inadequate in every country at the start of a pandemic, antiviral drugs are now considered the primary early intervention in slowing the spread of an epidemic and reducing morbidity and mortality.

2.40 The difficulty in developing a vaccine is that the H5N1 virus has not yet developed into a virus that can pass from human to human. When it does it is unlikely that H5N1 vaccines developed in anticipation will be effective against the genetic makeup of the mutated virus. The WHO estimates that it will take approximately two months from an initial outbreak of circulating pandemic influenza to create a vaccine effective against the virus. Consequently stockpiles of antivirals will provide the first line of defence in the absence of a clinically effective vaccine and may be able to slow the spread of the disease. It is for this reason that Roche donated three million courses of Tamiflu to the WHO to be used as a “Rapid Response Stockpile” to be deployed at the source of potentially pandemic influenza outbreaks.

2.41 The Department of Health has placed a tender for two million units of a vaccine against H5N1 to be developed. However, two million (3.3 per cent of the UK population) is a figure that does not appear to refer to any obvious pandemic preparedness indicators. Roche would welcome clarity as to how a figure of two million has been arrived at when tendering for vaccine development programmes.

2.42 It should be remembered that vaccines were available for the 1957 and 1968 pandemic viruses, but were made available too late to have significant impact. As a result, great social and economic disruption was caused by these pandemics. If, as predicted by the WHO, the delivery of vaccines for a human to human mutation of the H5N1 virus were not available at the outset of a pandemic, then it is essential that the use of vaccines is planned alongside a robust framework of national and global pandemic planning that prioritises “rapid reaction” deployment of first line antivirals.

**Question 10: What is the long-term strategy for reducing the threat of pandemic influenza?**

2.43 As with any antiviral, a theoretical potential exists for an influenza virus to emerge with decreased sensitivity to the drug and this is known as virus susceptibility. Data collected from around 3,000 patients treated with Tamiflu demonstrate an overall incidence of resistant virus of 0.4 per cent in adults and 4 per cent in children aged one to 12 and this suggests that virus susceptibility relating to Tamiflu is currently low. Nonetheless, Roche Products Ltd constantly monitors potential resistance to Tamiflu through the Neuraminidase Inhibitor Susceptibility Network. Accordingly, Roche welcome increased surveillance efforts by national governments and international organizations.

2.44 The UK Health Departments’ current pandemic readiness is excellent, when compared with many countries around the world. However, it is clear that a best case scenario would be the stockpiling of sufficient antivirals to ensure that there would be coverage for prophylaxis in both essential workers, the vulnerable, and key workers not considered “essential” by the Pandemic Plan. This would significantly reduce the socio-economic impact of pandemic influenza in the months before effective vaccines could be deployed.

2.45 National governments need to provide clarity, much more quickly, of their plans to replenish stockpiles of antivirals. This has been particularly highlighted by lessons learned from the recent round of stockpiling in response to H5N1, which identified the importance of including lead times for antiviral development into any effective pandemic planning strategy.

3. Conclusion

3.1 The broad picture of pandemic influenza planning in the UK is very favourable, with the UK Government recognizing the risk and putting measures into place to mitigate that risk in a timely manner. Accordingly, Roche would wish to make the following recommendations:

— that the Government is praised on the levels of preparedness and pandemic planning that it has already put into place;
— that the Government is urged to continue to maintain, and where appropriate increase, its pandemic preparedness levels in line with changing domestic and international requirements;
— that the Government should be more clear about precisely who will be receiving antiviral for prophylaxis and the dosing regimen to be used, thus allowing individuals to identify the need to protect themselves and their families from pandemic influenza;
— that the private sector (particularly key industries such as transport and utilities) should be assisted and encouraged to develop pandemic plans for their workers and integrate them into their existing business continuity plans;
— that the UK Health Departments should plan early and transparently in their procurement policies for both antivirals and vaccines, which would in turn assist vaccine and antiviral producers to appropriately address capacity issues and minimize lead in times.

Examination of Witnesses

Witnesses: Mr Richard Stubbins, Chair, Pandemic Planning Sub-Group, UK Vaccine Industry Group, Dr Kevin Bryett, Managing Director, Chiron Vaccines, Dr John Wood, Principal Scientist, Virology, National Institute for Biological Standards and Control, and John Harrison, Influenza Therapy Manager, Roche Products Limited, examined.

Q32 Chairman: Thank you very much for joining us this afternoon. This is the second public hearing of the Science and Technology Committee’s short inquiry into pandemic influenza. We will report before Christmas, this being a short inquiry. I would remind witnesses that the meeting is being webcast and is being filmed by the broadcasting companies. I would draw the members of the public’s attention to the information note that is available that you can pick up, or may have picked up already, that describes the background to the inquiry. Before I ask the witnesses to introduce themselves, may I please ask them if they would attempt to be brief in their answers to questions because we have a long list of matters that we would like to ask you about and time is somewhat limited. So thank you very much for joining us, and if you would like, please, to introduce yourselves.

Dr Wood: Thank you, my Lord Chairman. My name is John Wood. I am from the National Institute for Biological Standards and Control, of Potters Bar in Hertfordshire. I am a principal scientist there in the influenza group and have responsibilities for control and standardisation of influenza vaccines. To put that more succinctly, I am a member of the WHO team that selects the annual vaccine strains. We supply those viruses to vaccine manufacturers on an annual basis, and we make and distribute the reagents to allow the vaccine manufacturers to standardise their vaccines. So we are involved at many different stages in the vaccine development process.

Mr Stubbins: Good afternoon, my Lord Chairman. My name is Richard Stubbins. I am the Chair of the UK Vaccine Industry sub-group on influenza, and the UK Vaccine Industry Group is made up of those companies that research, manufacture and supply vaccines into the UK. There are six companies who are represented by UK Vaccine Industry Group (or UVIG), and they are Baxter Healthcare, Chiron Vaccines, GlaxoSmithKline, Sanofi Pasteur MSD, Solvay Healthcare and Wyeth Vaccines. For the purposes of this hearing, these companies manufacture or supply 100 per cent of the flu doses.
which are used each year in the UK. For my part I am Managing Director of Sanofi Pasteur MSD here in the UK, and I have worked for the industry for about 13 years.

Dr Bryett: My name is Dr Kevin Bryett. I am Managing Director of Chiron Vaccines in the UK, and I am based at our influenza manufacturing plant, which is in Liverpool. I am a physician by background and was a general practitioner before coming into the industry. I have over 20 years of vaccine experience in both clinical research, commercial operations and global product operations.

Mr Harrison: John Harrison, representing Roche Products Limited in the UK. My position is Influenza Therapy Manager, and I have direct responsibility for Tamiflu, an antiviral which can be used for the treatment and prevention of influenza.

Q33 Chairman: Thank you very much and again thank you for coming to answer our questions. Let me start by asking if you would please describe the process, once a new strain of pandemic influenza is identified, for producing a vaccine. How long will each stage of the process take and what will be the rate of production once a vaccine is identified? Perhaps you could start, Dr Wood?

Dr Wood: First of all, if we assume that the newly emerging pandemic virus is highly pathogenic, like the H5N1 virus, then we have to attenuate this virus in some way; it is far too dangerous to give to vaccine manufacturers. There is a genetic modification process called reverse genetics that has been developed to attenuate this virus. So the first step is to obtain the virus by one of the laboratories such as NIBSC—and there are four such laboratories in the world that are capable of producing these attenuated vaccine strains by reverse genetics. So the first step is to obtain the virus and take it to a high containment laboratory. Secondly, to attenuate this virus by reverse genetics; then to test that virus to ensure that you have indeed attenuated it, to make sure that it is safe, and then to distribute this virus to vaccine manufacturers. So taking them in turn, it probably would take about one week to obtain the virus from a laboratory in Vietnam or Thailand. To genetically modify the virus it will probably take three weeks. Then the tests for safety take a little longer to do, about five weeks; then to distribute to vaccine manufacturers, a further one to two weeks. So we are talking about ten or 11 weeks for the whole process.

Q34 Chairman: Is there anything that can be done to accelerate this process?

Dr Wood: We are working closely with the Department of Health, with the Health Protection Agency and with vaccine manufacturers to try to shorten this process and one possibility is working with Defra and with the HSE, so that perhaps we can distribute this virus before the final safety tests have been done. You can do some very rapid in-vitro tests, laboratory tests, which give you a high level of confidence that in fact this virus is safe. Then with appropriate levels of containment by vaccine manufacturers it may be possible to distribute this virus before all of the five-week safety tests have been done.

Q35 Chairman: So you can initiate the manufacture, as it were, before you have completed those tests?

Dr Wood: Yes.

Q36 Chairman: Are there things we would have to do to lift regulatory barriers to allow that?

Dr Wood: I think it would have to be with the permission of Defra because Defra would possibly view this untested virus as a highly pathogenic avian virus, so we would have to confirm with Defra that this was indeed possible.

Q37 Lord Soulsby of Swaffham Prior: Does what you have just said refer in a way to the written evidence from Chiron and UVIG, which refers to the desirability of creating a “mock-up” file for a new flu vaccine? Could you explain how this process works and its advantages in the event of a pandemic? Finally, have you any commitment from the Government to assist in this work?

Dr Wood: I will give you my own view—I am not a vaccine manufacturer—and perhaps I could then hand over to those who do manufacture. First of all, it was realised by the European medicines Evaluation Agency (EMEA) two or three years ago that a pandemic vaccine is quite likely to be different from the normal seasonal flu vaccine; it probably will be one strain given in a two-dose schedule, at a different antigen concentration and possibly with an adjuvant. That means effectively re-licensing the influenza vaccine, which will take many months. So the Committee for Human Medicinal Products has devised procedures for rapid emergency licensing of pandemic influenza vaccine. This is a two-stage process: first of all, to license the strategy for each manufacturer of that pandemic vaccine, and this includes clinical trials. So this is where the mock-up pandemic vaccine comes in. The manufacturer selects a mock-up pandemic strain—it could be H5N1, it could be H2N2—and they make what they think will be the pandemic vaccine and they do the quality tests, they do the clinical trials and they submit the data to the EMEA, the licensing authority, in what they call a core dossier. Once this has been licensed, then if the pandemic subsequently starts it is a very rapid process to just update that—a matter of days. That is
the concept, but maybe I could hand over to my manufacturing colleagues?

Dr Bryett: Once we receive the antigen from NIBSC the manufacturing process for a pandemic would be essentially the same as we use for our inter-pandemic influenza. That is to say, we would incubate the virus in chicken eggs; we would harvest the amniotic fluid, purify, inactivate and prepare a monovalent bulk. For an inter-pandemic vaccine we would normally have three viral strains, but in a pandemic situation we would only have one viral strain to process. Once we have the monovalent bulk we would then formulate this to the correct strength and fill it. We would either fill it into pre-filled syringes or into vials. Now, for the sake of a pandemic this would probably be vials because our filling times would be significantly less. It is estimated that from the receipt of the antigen to the first product being available is about four to six months. There are two characteristics which are important in this time. The first is ensuring that we have an adequate supply of suitable hens’ eggs because clearly without the hens’ eggs the process cannot start. The second issue is defining the characteristics of the virus. The viruses grow in different ways; some of them produce large quantities, others produce small quantities per egg, and clearly the amount of antigen that we can get would limit how much product we can produce. The advantage of a mock-up file to the manufacturer is that the majority of the work defining how we will produce the product, how we will test the product and what clinical trials will be required, will all have been agreed in advance with the regulatory authorities. This means that once the pandemic starts that work will not have to be undertaken, we will know exactly what is required of us and we will have agreed this with everybody who is involved. From our viewpoint, to have a mock-up file is essential. The thing I would point out, though, is that it would be a mock-up file for each vaccine; it is not a question of a single generic mock-up file. Each manufacturer will have a different way of producing the vaccine and probably different testings, and this reflects the process that they use in their inter-pandemic vaccines.

Mr Stubbins: Perhaps I could just add to that? For the industry as a whole there are probably only about 10 different processes to make a flu vaccine. Of the vaccine companies that I represent for today’s hearing some have one, some have two, some have three current vaccines which are available for the annual flu production that we make. What we have estimated as an industry is that it would probably cost about €11 million—about £8 million—for different manufacturing processes to produce a mock-up vaccine, to go through all the procedures that we have heard from Dr Wood and Dr Bryett, and to get to the stage that we have a licensed vaccine. A licensed vaccine means that it has been determined by the EMEA as being safe and effective, and also of good quality. Once we have that licence and we know the strain of the pandemic virus we can then quickly do a variation to the licence and we would then be able to proceed with our production of a vaccine against the pandemic.

Q38 Lord Taverne: Could you comment on a report that appeared a few days ago in the Evening Standard that as a result of work done at UCL once a pandemic strain is identified it could be ready in days, say the makers, and enough could be ready in three weeks to protect the entire population.

Mr Stubbins: That would be extremely exciting if that were the case. I cannot comment whether it is or not; I do not represent the company that is making these claims. I think that we really have to concentrate on what we know well, which is how to produce flu vaccines, which we do with millions and millions of doses each year, and we need to go along the tried and tested route. This is the strategy that we have for the short-term. It may be in the medium and long-term that we can look at some of the changes that need to be made in the vaccine production process, and of looking at different ways of administering the vaccine, but I think at the moment it might be too early to be too optimistic with the suggestion that was being reported by the Evening Standard.

Q39 Lord Soulsby of Swaffham Prior: We do not know what a re-assortment virus is going to be, but can you give us best guess as to what it might be amongst, say, half a dozen potentials? There must be some where you say, “It is not going to come in that way, but it is likely to go in this direction.” Do you have any guess that you could make?

Dr Wood: Within the H5N1 virus?

Q40 Lord Soulsby of Swaffham Prior: Yes. Re-combining with the human virus.

Dr Wood: First of all there is no evidence of that. All of the human isolates so far are entirely avian-like, so there is no evidence of re-assortment yet. We just do not know how the re-assortment, if any, will take place. We know that it has occurred with past pandemic viruses and it could be a way of changing the transmissibility of the H5N1 virus this time, but we just do not know. I am sorry.

Q41 Lord Soulsby of Swaffham Prior: But that is the fear, is it not?

Dr Wood: That is the fear, or a random mutation which will allow the virus to attach to human cells much more efficiently than it does at the moment, for example.
**Pandemic Influenza: Evidence**

**25 October 2005**

Mr Richard Stubbins, Dr Kevin Bryett, Dr John Wood and John Harrison

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**Q42 Lord Patel:** Mine is a quick question that requires a yes or no answer. Have you agreed on the mock-up file? You need to agree on a mock-up file, you say, so that you are prepared once the strain is identified.

**Mr Stubbins:** The EMEA has set out a process for preparing the mock-up file. We have to follow that process and get a licensed vaccine. I do not think it is a yes or a no; they have set out how it is going to be done and we will follow that.

**Dr Bryett:** They have published guidelines which the companies will have to follow, but in order to prepare the mock-up file it will require a significant amount of work because we have to define exactly how we are going to manufacture the product, exactly how we are going to quality control it, and the ongoing research will feed into the mock-up file when it is prepared.

**Mr Stubbins:** My Lord Chairman, there was one part of the question which we have gone past, which was the rate of production, which you asked right at the start. Perhaps I might comment on that?

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**Q43 Chairman:** Yes, please do.

**Mr Stubbins:** At the moment it is said that we do not really know what the pandemic strain would be, we do not know when it is going to start and we do not really know when it does start what the capacity will be of the vaccine industry. However, I think everyone ought to understand that the capacity of the industry is inextricably linked to the use of inter-pandemic flu, i.e. the flu that is used every year. In 2005, for instance, the total production for the European vaccine industry was 300 million doses of trivalent vaccines. That means that we would theoretically be able to produce something like 900 million or a billion doses in a 12-month period of a monovalent vaccine. Of those 300 million doses about 90 million are used in the whole of Europe, of which the UK uses just 12 million. So the UK orders only four per cent of the industry’s total production; the remainder is exported to the rest of the world. What we heard last week, from the announcement made by the Chief Medical Officer that there will be an Advance Purchase Agreement, for which we have not yet seen the details—we would very much like to see the details as to how this would work. What they have said is that they would like to immunise the whole of the UK population, that is 60 million people, and they are working currently on the basis that there will need to be two doses given to each person, so that is 120 million doses. So what they want to do is to give those doses over an eight-week period, so therefore they would need 15 million doses per week. At the moment the industry only supplies 12 million doses for the whole of the flu vaccine season. That is the challenge that we have been set: of trying to meet the requirements of the UK Government and no doubt other governments as well. It certainly shows that we have a lot of work to do to bridge the gap between what undoubtedly will be an impressive amount of demand, not just from the UK, not just from Europe but around the world, because this is a global issue that we are talking about for the pandemic flu.

**Q44 Chairman:** Are you suggesting that that might not be possible without alternative means of manufacture? Would one be able to do that with eggs?

**Mr Stubbins:** I am suggesting that we have to work very closely with government and their agencies to find ways of increasing the production of the industry in as short a time as possible. At the moment, as I said, supply is inextricably linked to demand. I think it would be unreasonable for the industry to build additional plants around the UK and Europe and then just mothball them. We would have to have some sort of link. We ought to increase the usage of vaccines in the inter-pandemic period; we ought to be working with the Government to see how we can do that. There are various ways. We ought to be talking to them about increasing the current coverage rate of those people who have the vaccines at the moment—people aged over 65, people with chronic conditions, people with diabetes, carers of those people and so forth. We ought to look to increase that to a 75 per cent coverage rate, which is the target which has been set by the WHO for all governments. But even that will not be enough. On top of that we also need to consider very carefully extending the recommendation for flu vaccination. There is good and compelling data which suggests that you could reduce the age recommendation to 50—

**Q45 Lord Patel:** I think we are digressing here, Chairman.

**Mr Stubbins:** I beg to disagree. The critical issue is capacity. We have talked about the mock-up vaccines, this is important, the dossiers, and we need to undertake that work. But capacity is absolutely critical.

**Q46 Lord Patel:** I thought the point that was made was if we were to increase the capacity for the threat of the pandemic flu there has to be the need to use this increased capacity in the future for ordinary flu. That is the point you are making?

**Mr Stubbins:** That is the point I am making.

**Lord May of Oxford:** But there are other ways of doing it. Having the excess capacity deal with an emergency is a classic example of something that ought to be a public good and the private sector will not in fact deliver effectively. So if we are going to go
down that digression we are going to have to widen the discussion beyond what we are trying to do.

Chairman: I think we had better proceed with the questions before us and I think this is a topic that we might return to. But thank you for that. Baroness Finlay.

Q47 Baroness Finlay of Llandaff: Can I ask you what progress is being made towards the incorporation of an adjuvant to reduce the dose required? Linked to that, I would like to ask you how you foresee being able to have enough eggs, given this is avian flu, and if there is a shortage of eggs how do you anticipate coping even with the current capacity?

Dr Bryett: Shall I outline where we are with an adjuvant within Chiron and then I will hand over to Dr Wood to widen it out? Chiron already has an adjuvanted influenza vaccine; it has been available for many years throughout Europe. It uses a proprietary adjuvant called MF59, and we have produced in excess of 20 million doses and it is currently approved in a number of European countries. Starting in 1997 we have undertaken work using MF59 with an H5N3 virus. Now, I am aware that that is not the current virus that is causing concern but it was the one that was available in 1997. What we have shown is that this adjuvant will be dose sparing, so we have shown in clinical studies that by adding the adjuvant you can reduce the amount of antigen that is required to produce an effect. We looked at three different dose studies. We have also looked at a booster effect.

Q48 Baroness Finlay of Llandaff: By how much can you reduce it?

Dr Bryett: We looked at 7.5, 15 and 30 microgrammes, and we showed that it was effective at the lowest dose. We have also shown a booster effect after 16 months, but, more importantly, we have revisited the sera that we took in during this study and looked at it against H5N1s that have been circulating in the period from 1997 to 2004, and we have shown that it is effective against the drifting of the H5N1. This data has all been published in journals such as *The Lancet* and *Vaccine*, so it has been published in peer review journals. We are currently looking at both the dose-sparing elements of an adjuvant in clinical trials, both in Europe and in the US, and we are also looking at how effective this is in the drift element that may be around.

Dr Wood: That study was a kind of groundbreaking study, and there have been two further studies done by GlaxoSmithKline in Germany. The problem with the MF59 study is that the MF59 is a Chiron adjuvant and it can only be used by other companies subject to a license. What GSK did was to use the very simple alum adjuvant and to see how low you could take the antigen content and still get an immunogenic response, and they used the H2N2 virus and the H9N2 virus as potential pandemic candidates. They found with two doses of vaccine that they could reduce the antigen content four-fold and still get a satisfactory immune response, a response that would pass current licensing criteria. They were very small studies and some would argue that they were not very well defined studies, but they do indicate the possibilities, and really there is a great need for more studies like this.

Q49 Baroness Finlay of Llandaff: Is there a hold-up in the production of adjuvant in the event of Chiron being asked to share it with other manufacturers?

Dr Bryett: Chiron at the moment is reviewing the capacity for the adjuvant very actively.

Q50 Lord Soulsby of Swaffham Prior: The Government has recently ordered 2.3 million doses of vaccine against the H5N1 bird flu virus, but what is your assessment of the likely effectiveness of this vaccine in the event of mutation or a recombination of that virus? Would it give some degree of protection?

Dr Wood: There have been some animal studies that have indicated that even if the pandemic virus has mutated from a vaccine that you hold as a stockpile there could be protection against the worse consequences of a pandemic—that would be serious illness and death. Animals did survive after a heterologous challenge, but we really do need to obtain more data to have some security in knowing whether a stockpiled vaccine would give you any protection.

Q51 Lord Soulsby of Swaffham Prior: But it is a wide route to go, to have lots of vaccine for the H5N1?

Dr Wood: Yes, that is right. We just do not know whether the ultimate pandemic virus will have mutated or, if it does, how far it will. So we can only postulate really.

Q52 Chairman: While we are talking about and the virus modifying itself, are there means of monitoring that as it goes on, or does one have to wait until you have seen human-to-human transfer? Are there means of looking at the virus itself as a molecule to detect whether that change has taken place?

Dr Wood: This is a process that is ongoing throughout the world, both looking at the human viruses and the avian viruses, and the work is coordinated by the WHO and the OIE, the animal equivalent of WHO. So there is a constant surveillance for human and avian viruses, so there will be a very early warning of any changes.
Q53 Baroness Sharp of Guildford: My question brings us back to this issue of capacity, and it really is what steps should be taken in order to increase vaccine manufacturing capacity? Perhaps we can come back to that and you can tell us a bit more about what we might do?
Mr Stubbins: I would probably have to repeat myself, but we have to look at ways of improving the coverage rates of those who are currently recommended for immunisation and also to look at extending the recommendation to other groups—this would be those aged over 50 and perhaps children. The JCVI’s sub-group for flu is also looking very carefully at the idea of immunising children as there is evidence to suggest that more deaths occur in children than we had previously thought, and that they also act as a reservoir of infection which can then be passed on to others who may be more at risk from influenza.

Q54 Baroness Perry of Southwark: This takes the issue about capacity further. You mentioned earlier that the manufacture of the vaccine still requires culture in fertilised eggs. Is this a major constraint in capacity? And a further thought that we have had is that the supply of hens’ eggs might be threatened by an outbreak of avian influenza itself amongst poultry. Is there any research going on to try other techniques besides the culture in eggs?
Dr Bryett: Yes, there is ongoing research. At the moment the future lies in something called flu cell culture. Basically, instead of using a chicken’s egg you use a culture medium. Chiron is working on this actively and we announced today that we have started a study in the US and we have completed a phase 3 study in Europe. So this is a process where we are currently building the production facilities actively in our plant. Flu cell culture clearly is the way forward. In the short term hens’ eggs are the only way to produce the product. There are a number of bio-security steps that we can undertake. For example, we receive our eggs from a large number of suppliers who are scattered throughout the UK; each of those suppliers have the facility to keep the chickens inside, if that is necessary. Obviously in each of our farms there are already bio-security steps in terms of the staff and everything else. Also, eggs can be transported, so even if one of our suppliers was unable to supply we could obtain eggs from other countries and move them into the plant in Liverpool. So in the extreme case, yes, eggs could be an issue, but we feel that we have in place a large number of alternatives to ensure that we could supply eggs to the plant.

Q55 Baroness Perry of Southwark: Could I press you on the question of cell cultures? You said that research is going on; what is its timescale?
Dr Bryett: At the moment we have just completed enrolment in a phase 3 study, so that means you are probably looking at about a couple of years until we would be looking to have the product available. So we are very well advanced with the flu cell culture and, as I say, we announced today, at lunchtime, that we have started studies in the US as well. So this is a very active process for the Chiron company.

Q56 Lord May of Oxford: I do remember when I was Chief Scientist I put together a little group to ask why, in the name of goodness, in an age of molecular biology we are still doing this with hens’ eggs, and I never really felt that I got a satisfactory answer. Am I right or wrong in thinking that when we finally have moved on to cell culture that we will be able to grow things in large quantities quicker, or is that a misapprehension?
Dr Bryett: Certainly it will enable us to respond more quickly to a pandemic because we will not have the delay of getting the hens’ eggs into the system. In terms of being quicker, it will probably be a little quicker, but the basic time is the culture of the virus and the processing of the virus, which will remain unchanged whether you have hens’ eggs or a cell culture. So in terms of being able to produce products, it will take out the delay of building up the egg stocks, but the process will continue in a very similar way.

Q57 Baroness Sharp of Guildford: The process that seems to be being developed at UCL is based on the culture of bacteria. Peter Dunhill is reported here as saying that it is a very quick process. You know nothing of this, is that correct?
Dr Bryett: I can speak personally. This is a proprietary process being developed by another company, with which I am certainly not involved. Perhaps the Committee would like to speak to them at some point. I am certainly unable to comment on another company’s processes or claims.
Mr Stubbins: Perhaps I could comment that Chiron’s description of what they are doing with cell lines has also been replicated by a number of other companies that are currently involved in flu manufacture. So I think we will be seeing in the medium term some move away, if possible, from cultivation in eggs to the cell-based line that you were referring to.

Q58 Lord May of Oxford: And not before time. Coming to the question I was going to ask. If and when a pandemic were to arrive there is going to be a global demand for a vaccine, and I wonder what discussions you have had with the UK Government
regarding the distribution of vaccine as the production comes online, both within the country and, more importantly, internationally?

Dr Bryett: I think this is a very key point. Chiron and indeed all the other manufacturers are global suppliers and, as such, we are in discussions with a number of governments throughout the world. We believe that the way forward is to look towards Advance Purchase Agreements of the type which the UK Government has announced in the last couple of weeks. They have announced the intention to have an Advance Purchase Agreement but so far we do not have any details of that. If we are going to supply a global issue we must have discussion and collaboration with as many governments as possible. This would save valuable time and the Advance Purchase Agreement would allow us to discuss issues such as liability, supply, quantities, mock-up files well in advance of the issue happening. Once such an agreement is in place it is important that all of the governments and all of the manufactures respect that agreement and hold to it. So we welcome the Government’s intention to have an Advance Purchase Agreement, but to date we have not seen the details of that.

Q59 Lord May of Oxford: Do you have any other Advance Purchase Agreements with other governments?

Dr Bryett: We are in discussion with a number of governments worldwide.

Q60 Lord May of Oxford: Once these things come on line and there is the demand are you going to do it on a first come first served basis, or what?

Dr Bryett: If we have in place agreements with governments we will respect the agreements that are in place. That is why I am emphasising the importance of an Advance Purchase Agreement.

Mr Stubbins: Perhaps I could just comment? About 18 months ago the European vaccine manufacturers did put out a pandemic action plan, in which they came up with six points that needed to be addressed. The aim in that plan was to try, as far as possible, to distribute vaccines as equitably as possible, but also taking into account those contracts which the industry would have across the world, and maybe one way of doing this would be to provide vaccines on a proportional basis, based on a government’s purchase of the vaccines in the inter-pandemic period. So if we are looking at the UK, with the 12 million doses that they buy at the moment, if you multiply it by three for a monovalent, then a proportional supply it would be 36 million doses, assuming everything else being equal, and the yields being the same as for an annual flu vaccine.

Chairman: Thank you. Let us move on to antivirals.

Q61 Lord Patel: First to clarify, Mr Stubbins, I would agree in a different context that we ought to widen the prophylaxis against influenza to a wider age group, and I am trying to concentrate in particular on the procedures in an emergency pandemic, so I would agree on that point. But I will go on to antivirals and I have several questions about this. First of all, everybody is trying to stockpile antivirals, particularly Tamiflu. Secondly, how far therefore, is the industry going to meet this demand? Next, how far ahead are the order books—how full are they and how far ahead are your order books? Is there enough supply of raw material for the production of Tamiflu? Is there a possibility of others in the industry being able to help with the production and, if so, I understand that the production method is quite complex and, if that is correct, how quickly can they be ready? The most important point is, can Roche on its own be certain that on their own they can limit the human suffering? Remembering by use of Tamiflu in the event of a world pandemic, which will cause a lot of suffering?

Mr Harrison: There are several questions there and what I might do is to start with your last point on Tamiflu. Effectively what is it? It is an antiviral; it is presented in capsule form. It can be used for both treatment and prevention, so if somebody develops symptoms of influenza then they will take a five-day course of the drug, which would actually help reduce the severity of symptoms and also the length of the infection. More importantly, it can actually reduce the complications, like pneumonia, associated with influenza.

Q62 Lord Patel: My question was: can Roche on its own be sure?

Mr Harrison: Let us turn to that one. Perhaps if I explain the capacity that Roche has? In effect we have obviously five years’ experience in manufacturing Tamiflu. We actually forward invested, if you like, in manufacturing capacity in 2004, ahead of notice of a pandemic. We have doubled manufacturing capacity in 2005 and we intend to double it again in 2006, so that will effectively be an eight-fold increase in capacity. In real terms we now have four factories manufacturing the oseltamivir, the active ingredient, and we have two factories capsuling it, with a further two factories that go on line mid next year. In terms of resourcing governments’ plans, we are currently resourcing the pandemic plans of over 30 governments. The UK pandemic plan, in fact we entered into an agreement with the Department of Health in March 2005, and we started resourcing their pandemic plan for 14.6 million packs in August. Currently the stocks that the Department of Health hold are 2.5 million packs. We were due to complete that order in December 2006, but as a result of
increasing capacity, streamlining our processes, we have actually now brought that forward to September 2006. So we will actually complete the plan in September 2006. The specific question you raised was around capacity. One thing that Roche has done is to reconfirm, in fact last week, our willingness to talk to other governments, manufacturers in terms of their either sub-contracting certain parts of the process—and it is a complicated process—or in fact wholly contracting that out to other manufacturers. Up until last month we had no approaches from other companies; we have now received approaches. I can tell you that the process to convert it to the raw ingredient to the active substance is a 10-stage process. We actually already use and contract out three steps in that process, so we have tried to be as efficient as we can in contracting out to specialist companies. But, as I say, Roche is willing certainly to talk to governments or other manufacturers in terms of either sub-contracting or contracting out the process. But the key thing I would say is that I think those manufacturers need to supply the drug to the quantities needed; it needs to be to the right standard in terms of the product; and obviously it needs to comply with the regulatory authority requirements around production and quality control. I am not sure if I have answered all your points?

Q63 Lord Patel: I think you probably have. The important part is that you have the increased capacity; that you are prepared to talk to others on a contractual basis for an increase in capacity; that you realise otherwise the responsibilities that Roche alone would otherwise have, which is to limit the suffering that lots of millions of people would have.

Mr Harrison: We have also actually donated three million courses to the World Health Organisation.

Q64 Lord Patel: Have you any idea how that will be used or how you are going to supply that?

Mr Harrison: It is part of the emergency response plan. The idea is that if you can stem outbreaks in the Far East early on then you can actually slow the spread of the disease worldwide. It is not intended to be a plan on its own but it is actually an emergency response plan.

Q65 Lord Patel: Suppose that emergency response was satisfactory and there was a need for more than three and a half million doses?

Mr Harrison: Roche has a continuing dialogue with the World Health Organisation, and in fact we have already made other donations to countries like Turkey, for example, as part of an emergency response there. So we have made initial donations to Turkey and one other country, and clearly we will keep that in mind.

Q66 Lord Patel: And there is no problem about supply of raw material?

Mr Harrison: That was the other question. The actual raw ingredient, the starting point for oseltamivir is called staranise. It is actually a seed, basically, which is produced in four provinces in China, and we currently use that as the starting point. However, we are looking at other ways of producing the raw ingredient, shikimic acid, and one of these is actually a derivative of E-coli by a process of biosynthesis. I am not an expert on that but we are looking at more efficient ways of making the starting ingredient, shikimic acid.

Q67 Lord Taverne: Everyone is relying very much on Tamiflu. I believe there has been one recorded incidence of resistance to Tamiflu developing in the H5N1 virus. How serious is that concern?

Mr Harrison: The class of drug is a neuraminidase inhibitor and they are actually designed to be active against all strains of influenza A and B. We have good laboratory data to suggest that Tamiflu is active against H5N1. There is also a worldwide group of experts, the Neuraminidase Inhibitor Susceptibility Network, who monitor resistance, and in fact to date that group has examined over 3,000 strains of influenza, including H5N1. The recorded cases of resistance in adults was 0.4 per cent and therefore very low; in children it was just 4 per cent. The specific case you refer to was a case reported in Nature in October. It was actually not a new case, it was originally identified in February. It was the case of a 14-year old girl who seemed to have caught influenza from her brother, who was hospitalised. In fact she was actually treated with half the appropriate dose of Tamiflu, ie a sub-optimal dose, because she was already exhibiting symptoms of influenza. In fact she made a full recovery, as did her brother. So I think the fact that she was treated with a sub-optimal dose may have actually led to some degree of resistance. What we do know about Tamiflu is that where we do see resistance that the virus in some way seems to be disabled so that it has a reduced pathogenicity and a reduced transmissibility. So in some ways it does not, if you like, have the disease causing effect of what we would term “wild type virus”. I think the important thing is that the group in question, that I mentioned earlier, is continuing to monitor resistance and clearly that is something that is important.

Lord May of Oxford: If I may just say, it is important to remember it is not a question of whether resistance will appear, it is just a question of how long.
Q68  Lord Howie of Troon: I would like to apologise to the witnesses because I am by training a structural engineer, and therefore I am at home with Newtonian physics, which does not seem to me to be appropriate to this discussion. However, I have one or two supplementary questions to ask before I get to my real ones. The first is this: being over 65 I am a keen adherent to the anti-flu vaccine and I had mine the other day, on Thursday. However, last year I had my anti-flu vaccine and a week later I got pneumonia. I do not know if these were connected in any way, but my question is this: are there any side issues connected with your vaccines?

Dr Bryett: If I can put my former doctor’s hat on? Because the British Government has been so successful in its influenza vaccination campaign it is inevitable that in the days and weeks following influenza vaccine people will develop diseases, and this is not related to the vaccination as such, it is purely a temporal relationship. So the fact that somebody had an influenza vaccine and subsequently developed pneumonia, the pneumonia probably would have happened anyway and was not connected to the vaccination. In general terms, the influenza vaccine is a very straightforward vaccination. The side effects are generally limited to local side effects, occasionally some sore arms. Modern vaccines are very much better than the other ones. They are totally disrupted viruses, so the commonly held view that you can get influenza after the vaccine is not a scientifically sound basis. So overall influenza vaccine is an extremely effective and basically very safe vaccination to give, and I am very sorry that you were ill but I do not think it was the vaccine.

Q69  Lord Howie of Troon: It was fairly mild. I am happy to say I survived it. I thought the Conservatives were after me! I have one other quite important question—and I apologise, Chairman, I am going to turn to it throughout this investigation. Your job is to produce things and you do this in response to governmental demands. But at the back of your mind there must be a question, and that is: how real is the problem? What I have in mind is such things as mad cow disease and triple vaccine whatnot. It is an unfair question, I realise that, but to what extent do you think that this a real problem?

Dr Bryett: I think I would defer to the NIBSC on that issue.

Dr Wood: Do you mean the current state of alertness?

Q70  Lord Howie of Troon: Of course. I mean, 100 people died; it is not a lot—four died in their kitchen yesterday.

Dr Wood: I think there is the potential there, that is all we can say. There are human cases, they are still going on. The potential is, I believe, not any greater because avian flu is on our doorstep, and I think the media are really responsible for creating something from that.

Q71  Lord Howie of Troon: Of course. Thank you for that. I will come to my real question. Should the UK be looking at alternatives or supplements to Tamiflu, especially after what Lord Taverne asked, for instance Relenza or something else?

Mr Harrison: Perhaps if I can respond on that? I obviously cannot respond for GSK.

Q72  Lord Howie of Troon: You can do it in general terms, you need not name any names.

Mr Harrison: There are two antivirals currently available and endorsed by the National Institute for Clinical Excellence. One is oseltamivir or Tamiflu and the other clearly you have just mentioned.

Q73  Lord Howie of Troon: Is there any other?

Mr Harrison: There is a drug called Amantadine.

Q74  Lord Howie of Troon: So there are three rather than two?

Mr Harrison: Yes, although Amantadine was not endorsed by the National Institute for Clinical Excellence. I think the difference that has perhaps been prompted by the Government, in terms of choice, relate to things like Tamiflu being indicated in both treatment and prevention; it can be used in treatment right down to young children, for example. So there may be some differences around its indications, how it can be used and in whom it can be used. Also Tamiflu is available as a capsule. So there are differences in the drug delivery and aspects like that.

Q75  Lord Howie of Troon: Should the pandemic turn out to be real and not a feature of the media, would the third or other remedies be appropriate?

Mr Harrison: I cannot really answer that. I can only say that the National Institute for Clinical Excellence did look at the antiviral Amantadine. I think there were various reasons why they felt perhaps that they could not endorse it for routine use. I think one of them might have been resistance, but clearly we are represented with colleagues from the Health Protection Agency who I am sure can offer advice on that later.

Q76  Lord Howie of Troon: If people started dying do you think they might extend the range of possible remedies?

Dr Wood: I think it is always good to have a variety of antivirals but so far the only ones effective against H5N1 have been the neuraminidase inhibitors, and that rules out Amantadine.
Pandemic influenza: evidence

25 October 2005
Mr Richard Stubbs, Dr Kevin Bryett, Dr John Wood and John Harrison

Q77 Lord Howie of Troon: You think there are only the two?
Dr Wood: Yes.

Q78 Chairman: We have talked about vaccines and we have talked about antivirals but there is another potential way of controlling flu that arose at a meeting of the Academy of Medical Sciences, and that is the suggestion that the fractionation of plasma from convalescent patients could provide antibodies that could prevent or attenuate infection in others. At present I understand that this approach appears to be precluded by precautions against vCJD transmission. I wondered whether you might comment on this Dr Wood?
Dr Wood: That is quite correct, that the current CJD precautions preclude the use of UK or indeed French plasma for fractionation, so if we are going to obtain plasma it has to be sourced elsewhere. At the moment it would be difficult to understand where we could obtain convalescence serum. It is certainly extremely difficult to obtain even blood samples in Vietnam and Thailand and other affected places. So this would have to be if and when the pandemic starts presumably.

Q79 Chairman: But you would still feel that the potential dangers of transmitting CJD are severe enough.
Dr Wood: There would have to be a risk analysis given the emergent pandemic. But at the moment the regulations preclude it.

Q80 Lord Patel: It would be true to say, though, that in the UK you cannot obtain the convalescent plasma until the pandemic starts, and if you did have permission to collect those plasma it would still be too late to do the fractionation to produce antibodies to give them?
Dr Wood: It would be too late but it would be quicker than making vaccine.

Q81 Lord Soulsby of Swaffham Prior: Chairman, could I just return to the Tamiflu resistance? What is the evidence with antiviral substances that, as with bacteria, you can have a bacteria-inducing resistance to unrelated organisms so you get antibiotic resistance? What is the situation in antivirals? If there was resistance developing to Tamiflu with H5N1 virus could that virus genetically transfer back resistance to other H5 organisms?
Dr Wood: I can only echo what my colleague has said, that so far the Tamiflu resistant viruses have been less fit to survive, so they would be unlikely to pass on that resistance to progeny.

Dr Wood: That is quite correct, that the current CJD precautions preclude the use of UK or indeed French plasma for fractionation, so if we are going to obtain plasma it has to be sourced elsewhere. At the moment it would be difficult to understand where we could obtain convalescence serum. It is certainly extremely difficult to obtain even blood samples in Vietnam and Thailand and other affected places. So this would have to be if and when the pandemic starts presumably.

Chairman: Let me thank you very much for your evidence; it has been very useful in the answering of our questions. We have gained a lot of ground here and thank you very much.

Memorandum by the NHS Alliance

Evidence is presented by Jan Hutchinson, Director of Public Health, Bolton PCT, on behalf of the NHS Alliance, a multidisciplinary body representing Primary Care Trusts (PCTs) and clinicians, managers and lay people working in PCTs, and on behalf of the Association of Directors of Public Health.

Members of the Alliance were asked for their comments on three key areas:

1. Preparedness of Front Line Staff for Pandemic Flu

Many PCTs are updating their existing major incident plans to reflect the need for more detailed business continuity planning and are in the process of further updating in the light of DH and HPA guidance on pandemic flu. Some have carried out table-top exercises using pandemic flu as the scenario to help in identifying where there will be capacity problems, additional information and training needs. There is a concern that GPs may be unwilling to take part in such training unless payment can be arranged to enable locum cover while they are away from their surgeries—an additional financial pressure for PCTs struggling to maintain financial balance.

In some PCTs GPs have expressed concern about the lack of advice to date (although this should have been rectified through the distribution of information to GPs from DH at the end of last week). Some GPs are anxious about the provision of personal protective equipment. Some feel that the algorithms for access to antivirals contained in the guidance are difficult to follow and there is a desire to see simple, practical guidance.
PCTs with prisons in their areas are concerned about the impact of flu in confined settings and need specific guidance to support their planning. Prisons in parts of the north of England are planning desk top exercises to test existing plans.

There is an anxiety that the full impact of pandemic flu is not being fully recognised in relation to community and primary care services. Many patients with existing health problems would be unable to receive hospital care during the pandemic and would require some input from primary care, hospitals would be under pressure to discharge early—in addition to patients becoming ill with flu plus flu affecting NHS staff and their families. PCTs need reassurance from DH that current access targets etc would be dropped during the period of the pandemic. There are additional concerns associated with PCT reconfiguration under Commissioning a Patient Led NHS which are dealt with at point 2.

The main concern from front line staff centres on the availability of antivirals and vaccine. GPs have seen an increase in demand for flu vaccine this autumn, particularly from individuals who fall outside of the risk groups who are currently targeted for the vaccine. Speedy access to antivirals for front-line staff is seen as essential; questions have also been raised about the availability of antivirals for the immediate families of such staff.

2. CONCERNS THAT RESTRUCTURING UNDER COMMISSIONING A PATIENT LED NHS MAY HAMPER PCTS ABILITY TO RESPOND

Strategic Health Authorities have recently submitted proposals to DH for the reconfiguration of PCTs in their areas, as required by Commissioning a Patient Led NHS (CPLNHS). This may result in radical change in some areas with the merger of small PCTs and mergers of Strategic Health Authorities (SHAs). The scale of the proposed changes varies greatly across England; some PCTs are anxious that the importance of the emergency planning function in PCTs may be overlooked. Emergency planning requires strong relationships at the local (borough) level and large PCTs covering a large population, and several local authorities, may struggle to maintain the appropriate links at a senior level. Some PCTs are concerned about a lack of health protection expertise at the local level, a problem experienced in some areas after the last NHS reorganisation in 2001–02 and the creation of the Health Protection Agency, which removed specialist health protection staff from PCTs and located them in large health protection units at a county level.

There is a need to clarify the emergency planning responsibilities of the proposed new SHAs alongside the responsibilities of existing Regional Public Health teams linked to government offices in the regions.

In some areas there are proposals to merge smaller police forces—which could result in completely new arrangements for emergency planning and major incident management at a regional level between health services and the police and potential disruption to relationships at that level in the short term.

Commissioning a Patient Led NHS also sets out plans for the transfer of existing provider services in PCTs, such as district nursing and health visiting, community based therapy services etc, to other organisations. This has caused much concern for PCTs because of fears that there would be difficulties in mobilising staff and resources in a separate organisation in the event of a pandemic.

3. RELATIONSHIPS BETWEEN LOCAL UNITS OF THE HEALTH PROTECTION AGENCY AND PCTS

The strength of working relationships between PCTs and the local units of the HPA varies across the country. Some PCTs still feel the local HPA is too distant, operates at arms length and does not provide adequate input at the local level. In other areas working relationships are strong and there is clarity on roles and responsibilities. In planning for a pandemic it is essential that issues such as these be clarified.

23 October 2005
Examination of Witnesses

Witnesses: Professor Pat Troop, Chief Executive, Professor Maria Zambon, Head of the National Influenza Laboratory, Deputy Director, Virus Reference Division, Centre for Infection, Dr Nigel Lightfoot, Director, Emergency Response, Health Protection Agency; and Mrs Jan Hutchinson, Director of Public Health, Bolton PCT, NHS Alliance, examined.

Q82 Chairman: Thank you very much for joining us. I think you had been in the room during the previous discussion so I do not need to go through the routine of telling you that we are being web cast, et cetera, but let me thank you very much at the beginning for coming and for submitting the evidence that you have already and perhaps I can ask you each to introduce yourselves.

Professor Zambon: Maria Zambon, Head of the National Influenza Laboratory and Deputy Director of the Virus Reference Division at the Centre for Infection, Health Protection Agency. My overall responsibilities are influenza surveillance in the United Kingdom, biological surveillance, and a clinical research programme associated with the development of improved diagnostics.

Professor Troop: I am Professor Pat Troop, Chief Executive of the Health Protection Agency so I have overall responsibility for the organisation.

Dr Lightfoot: Nigel Lightfoot, Director of Emergency Response and lead of the Pandemic Influenza Programme Board in the HPA, which brings all of the activity of the HPA in influenza preparedness together.

Mrs Hutchinson: I am Jan Hutchinson, Director of Public Health in Bolton Primary Care Trust and I am here on behalf of the NHS Alliance and the Association of Directors of Public Health.

Q83 Chairman: Thank you. Let me kick off then and ask you if you can outline the HPA’s key responsibilities regarding infectious disease in an interpandemic period?

Professor Troop: For those who are not aware of us, we are an integrated specialist health protection service with a network of local services and a number of specialist centres. In particular in this context we have our Centre for Infection at Colindale where we have our National Surveillance Programme and our National Reference Laboratories of which Professor Zambon is head of one. We have another Centre for Emergency Preparedness and Response at Porton Down where we have the lead for emergency planning and preparedness and, in particular, a lot of model work that we have done in this context. The way that I would perhaps set out our responsibilities is to do it in the context of how we would tackle an infectious disease and therefore how we would apply that to influenza. To control infectious disease we look at a number of levels of activity. One is preventing the infection arising in the first place, secondly, preventing people from getting it, thirdly, preventing it from spreading, and then, fourthly, treating it and controlling the outbreak. If we look at each of those very briefly, we would try and prevent an infectious disease by, on the one hand, working with international colleagues, who work a lot with WHO. We have agreements with other countries, we are part of an international surveillance network and so on, and we would do exactly the same with influenza. We have had colleagues in Vietnam and China trying to support their activities. We work with other agencies such as Defra and the Veterinary Laboratory Agency so if they identify an animal disease we would try and see if it has human implications, and we have done the same for influenza. For specific prevention you have picked up the issue of vaccines. The main way of stopping people getting a disease would be through a vaccine programme and we do a range of work on early vaccines and then on testing and monitoring vaccine use. We have a role then in picking up any new infectious disease. We do this through different kinds of surveillance programmes and for this particular situation we have put in place protocols and algorithms for clinicians, particularly if they see returning travellers. For any new disease we would develop new diagnostic tests and then we would train other people to use those diagnostic tests, which is what has happened for H5N1 influenza. We then have a range of surveillance programmes to be able to monitor diseases. We have them for the early stages of any infection. We have a case management system so we can follow up all the contacts and in that way you can try and contain the early stages of infection, but we have a range of other surveillance systems which is of course enhanced for influenza that we have been developing and building up in preparation for a pandemic. We do that through NHS Direct, we do a lot through primary care and, of course, we do a lot through our laboratories. We have modelling systems so if we have any infectious disease we can model how it is working, how it is spreading, and how we might control it. We do a lot of modelling in advance of the situation to see if we can understand how diseases move. We have, of course, done that for influenza. We do a lot of training and we are running a lot of training now for people in relation to influenza. We produce guidance for the rest of the NHS on infection control, and we have again done that for influenza. We work with others on providing treatment guidance and again we have been doing that for influenza. We work with all our local colleagues in the primary care trusts, the hospital trusts and the local communities on how we might control an infectious disease once it comes. Finally,
we give a lot of guidance to the public and we give out a lot of public information and of course we have got a very active web site. They are examples. We are a very large and complex organisation and there are many other things I could have pulled out, but I hope that gives an overview of the picture of the work that we do for infectious disease and how we are applying it to influenza.

**Q84 Lord Howie of Troon:** Chairman, I do not want to sound like a high court judge but I wondered what an interpandemic period is and when it happens?

**Professor Troop:** We are in an interpandemic situation at the moment. It is when we do not have a pandemic.

**Q85 Lord Howie of Troon:** You mean it is in between the last one and the next one? You mean just kind of now?

**Professor Troop:** Yes.

**Chairman:** It is all the time we do not have one.

**Q86 Lord Howie of Troon:** Thank you very much. I got awfully worried.

**Professor Troop:** We have had several pandemics.

**Lord Howie of Troon:** I know but it is these techno terms that get me all flummoxed, thank you.

**Q87 Chairman:** How well does the HPA work with health authorities?

**Mrs Hutchinson:** With Primary Care Trusts?

**Q88 Chairman:** Yes.

**Mrs Hutchinson:** I think there were some considerable changes in the health protection function with the change from health authorities to Primary Care Trusts and indeed with the formation of the Health Protection Agency. In some parts of the country I think there were some short-term difficulties where the relationships which had existed previously had been passed from the health authority and health protection function was then one step removed in the new health protection unit. We have moved on considerably from those times and I think now relationships work extremely well at the local level. I think there are very good working links between the Health Protection Agency and its units covering strategic health authority areas and the Primary Care Trusts within that area. I do not see that there is a problem now.

**Q89 Earl of Selborne:** I would like to ask about the preparation of contingency plans. The Health Department has produced a Pandemic Influenza Contingency Plan, the Agency has its own plan and indeed of course in the Government’s plan the Agency has a large role. Likewise at the local and regional level there are contingency plans. Whose job is it to co-ordinate all these plans and is there coherence between the plans? Perhaps you could also refer to it at the European Union level as well. Are we involved in planning at that level?

**Professor Troop:** If I give the initial response and I will then ask Dr Lightfoot to pick it up. Firstly, at the European level we work very closely with the European Centre for Disease Control. In fact, one of our senior members of staff has been seconded there and he has taken the lead on influenza so we have a very strong relationship there. There is a European network and there are other European mechanisms whereby we are all planning together. In fact, the Health Protection Agency has been commissioned by the European Union to run an exercise across the whole of Europe in the next few weeks. We have not set a date, to keep it private when it is going to happen, but all the Members States and the WHO, the Commission and the industry are all going to be involved in this Europe-wide exercise, so we are working very closely with colleagues. We have worked extremely closely with the Department of Health. We have been contributing to their plan and we have been doing ours at the same time, so we have been doing it in partnership so that they were and have been complementary and will continue to be so. As they update theirs we update ours. For our plan we are making it consistent across the country. All our regions are developing plans and we have a local and regional services implementation group to make sure that we are implementing that plan in a consistent way across the country, working in partnership with people at the regional and local level. That is an overview, if the others would like to put more detail on it.

**Dr Lightfoot:** The WHO plan sets the overall global strategy and approach and sets the phases which all countries are expected to follow, and they all do. We have worked within the G7 group of nations comparing the G7 countries’ plans against each other and against the WHO and found good harmonisation and a lot of agreement. The areas where there are differences are areas you might expect which are about what to do about social distance measures, and we may come to that later. Having done that, the DH’s plan sets the strategy for the United Kingdom, then the HPA plan underneath that sets the operational elements of how it is done. These are all passed down to the local level and at local level they have to prepare their plans, mainly based on the HPA plan and the elements of the DH plan which state this is how to distribute antivirals, this is our vaccine strategy that you will have to implement eventually. So it is done at local level. At local level they have always worked together over legionnaires’ disease and everything else. They are used to getting on with this. A lot of work has been
done. I do not think there is duplication and confusion. At the bottom those plans—the Guidelines for Control of Infection in Pandemic Influenza, which are on our web site, and the Clinical Treatment Guidelines, which we prepared with the British Thoracic Society, give all the information locally as to what they need to do in GPs' surgeries and in hospitals. Furthermore, we have been running exercises around the country. These exercises bring everybody together—the PCTs, the local authorities, the Ambulance Service, even the police—to exercise what would happen at a local level. Those have been very valuable in checking the plans at local level and making them work.

Mrs Hutchinson: If I could just add to that. We are having an exercise of that nature tomorrow involving a whole range of people. The important role for us within PCTs is that we have all the information and guidance we require, and our job is to put that into place, so for example there is plenty of guidance about the storage of antivirals. We have to make our decisions and make arrangements about where that should be stored within our localities. It is very clear how the plans all nest within one another.

Dr Lightfoot: My Lord, you did mention the European plan. There is a European plan but it basically says not what each country should do but what the European Commission should do in conjunction with each country.

Q90 Lord Patel: I was going to ask a supplementary. I thought today's discussion was not around this fact but now that you have brought it up I will ask a question about it. You said that you are doing the exercises that are necessary but in a pandemic we might be talking about 100,000 people a day or more requiring attention?

Dr Lightfoot: Yes.

Q91 Lord Patel: How would you get the drugs to them?

Dr Lightfoot: That presents one of the big challenges. In exercises you push people to the limit and they will respond by giving the way they would deal with a particular situation. If they are tabletop exercises, people tend to say, “We will do that” and then you say to them, “It is going to take you seven hours to do that,” and there is that assumption, so you are quite right, so we recognise that. Mass treatment centres become an important part of any response in the United Kingdom. Earlier this year we ran a live exercise where we did it for real with the public in Worcester PCT to get antibiotics to people who had been in a simulated biological agent attack. That went very well. We had the police involved and there was a big car park because it was a rugby club. It is that sort of lateral thinking to get medicines rapidly to people in those situations that means you can reach those targets of having to treat lots and lots of people.

Q92 Chairman: You plan this by asking for volunteers. So you lined up hundreds of people—

Mrs Hutchinson: No, it is a tabletop exercise.

Q93 Chairman: Yours is a tabletop.

Mrs Hutchinson: We are not playing for real.

Q94 Lord Howie of Troon: Is this anything like the response to natural disasters which of course are a little bit different because national disasters break up roads and bridges and so on and they take a little bit of time, understandably, to get into action. Is it anything like that?

Dr Lightfoot: The same questions come out.

Q95 Lord Howie of Troon: Of course they do. It is about food supply.

Dr Lightfoot: It is a different context, it is the infrastructure.

Professor Troop: Can I say that in the HPA we have taken it as a major disaster. Dr Lightfoot heads our programme for handling major disasters and so the teams we have got helping to plan and support this and running the exercises are the same people we have running the exercises for a bio-terrorist attack or natural disaster. We work across government with the Cabinet committee who also handle those kind of issues so we are trying to apply the lessons from those into these situations.

Q96 Lord Howie of Troon: It is slightly different. In natural disasters bridges are broken down, which is not the case here, or sewage systems are destroyed, and all that kind of thing. So you are asking a different body of people to respond, are you not, a different body of territories and all that kind of thing? Is that not right?

Professor Troop: You are but then we still could have big problems with utilities because so many people are off sick, if you have 25 per cent of the population affected, so the infrastructure issue is still a major issue and therefore the whole of the country having business continuity plans is still quite important, although there are, as you say, other players of course in this situation.

Q97 Lord Patel: Are we running the risk that we might be too confident about being able to deal with what is likely to be a really serious problem?

Dr Lightfoot: I do not think there is any over-confidence whatsoever. What we have done has helped us along the way to being prepared.
**Professor Troop:** I think that we are absolutely far from complacent and one of the messages we give out all the time is that whilst we should put as much planning in place as we can we should not underestimate the impact a pandemic will have. I started off by saying with any infectious disease you should try and stop it coming. We are not going to stop it coming. We might internationally slow it down a bit, which would help everybody prepare a bit more, and in the UK we might be able to slow things down a little bit here or there so that we can prepare, but if it comes it will be devastating. What we have been trying to do is put in place as much as we can to mitigate the effects of a pandemic, but none of us, I can assure you, is complacent or confident that the whole thing is going to be totally under control.

Q98 **Lord Taverne:** Have you got the resources that you need? Having regard to the fact there have been many institutional changes in the Health Service, have these changes in any way hampered your planning?

**Professor Troop:** Perhaps I will ask my PCT colleague to comment in a moment. Certainly from our perspective having the HPA has helped with delivery of stability for the last two or three years because at least having the Health Protection Agency we have been able to continue the work of our planning in a consistent way, and hopefully that has been very supportive. It is always a worry when changes happen around you, whether or not that will have an effect, but most of the people we are working with are people we have worked with over a number of years, no matter where they have been sitting, and the NHS has changed around them, and the key thing is maintaining the strength of those relationships. There is obviously a concern that we have that people will take their eye off the ball but my colleague from the PCT is going through the middle of that change.

**Mrs Hutchinson:** I think there is a question about resources for the PCTs—in trying to identify the resources to pay for training, for doing the sort of exercises that we are needing to do at the moment, particularly about how best to involve GPs and primary care staff. That is proving to be quite a challenge for us and additional resource to help us with that would be great. The second question with regard to changes happening around the NHS, the main concern is about the timing of those changes, that we may see new Primary Care Trusts coming into existence round about this time next year which may not be a good time to have new organisations coming into existence. The important thing that throughout all of the changes that are happening is to emphasise the importance of emergency planning as a key function of PCTs. Whether it is emergency planning for pandemic flu, or any other emergency,

it is a very important function of a PCT. We need to continue to maintain the high profile of that function. I think the stability of the Health Protection Agency helps enormously with that because they are not changing.

**Professor Troop:** No we are not. We are trying to strengthen our front-line rather than anything else. Perhaps I might add one thing, though, which is that although we have been stable by being the same organisation now for two and a half years we did go through a major review last year through the arms’ length body review process in which there was a review of all the arms’ length bodies, and we came under extreme scrutiny and had our budgets squeezed. That process of squeezing budgets has not gone away so it does make planning for an influenza pandemic quite challenging. We do get small amounts of money for specific activities but most of this has been found by internal efficiencies, and while influenza is a priority of course all the other infectious diseases do not go away whilst we do this. So it has not been straightforward, but I think we are rising to the challenge. If somebody said “there is some extra support” we would not say no.

Q99 **Lord Patel:** Are you suggesting in the least having the Health Protection Agency we have made these changes in any way hampered your planning? You have not said anything about these changes in any way hampered your planning?

**Professor Troop:** Yes. What we are trying to do is put in place as much as we can to mitigate the effects of a pandemic, but none of us, I can assure you, is complacent or confident that the whole thing is going to be totally under control.

Q100 **Lord Soulsby of Swaffham Prior:** One brief thing. From what I hear, the HPA and regional health authorities are in good shape and well prepared. What you have not said is anything about the relationship of what you are doing to the VLA. Are you working closely with the VLA in Defra?

**Professor Troop:** Yes we work very closely with Defra colleagues. In fact, we have signed a memorandum of understanding with Defra to make sure that we do work closely together. We have established something called the Interlab Forum, which is all the government laboratories like the Central Science Laboratory and the VLA and ourselves, to create a network of government laboratories. This is a group of us initiated so that should there be a big problem we would provide mutual support, and that has never been agreed before. We do work closely with our colleagues in the VLA and again we have a memorandum of understanding with them. Obviously when everybody is incredibly busy you have to catch up with each other, but that is the natural way of things rather than a lack of will. But, Maria, you have worked with them.
**Pandemic Influenza: Evidence**

25 October 2005  
Professor Pat Troop, Professor Maria Zambon, Dr Nigel Lightfoot  
and Mrs Jan Hutchinson

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**Professor Zambon:** Perhaps I could comment on that. We do work closely with our veterinary colleagues, particularly with respect to the influenza biology and structure and function and the sharing of the strains and the exchange of information. That is essentially a scientific process which is not impeded by organisational barriers, and it has been good for many years.

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**Q101 Chairman:** Following on a little about how serious all of this is going to be, we note that a case fatality rate of 0.37 per cent only has been used in the HPA’s pandemic plan, giving 50,000 excess deaths. This is the rate from interpandemic years but yet the 1918 flu pandemic is estimated to have had a case fatality rate of up to three per cent. We cannot help but note that the death rate of those people who have contracted the bird virus has been very much higher than these numbers. Is the HPA’s estimate realistic when providing guidance on planning for an H5N1 pandemic?

**Professor Troop:** If I can ask Dr Lightfoot to pick up on the specific modelling work and perhaps Professor Zambon will pick up on the nature of how the virus changes when it goes from avian to human form.

**Dr Lightfoot:** In our guidance we provided a range of estimates and you are quite right the one we have used responds really to that observed in interpandemic periods. The 1918 pandemic had rates of around 2.5 per cent and some of the reports go up to eight per cent in closed communities, so there was much more excess death. The 1957 pandemic was significantly lower, the death rate was 0.1 per cent. So our model has looked at seasonal influenza, looked at the previous pandemics and it came out with a set of parameters and inputs into their model and came out with the death rates that you see in our plan. Our modellers have not been working alone however. They have been working with models at Imperial College—Neil Ferguson—and we do have a modelling group that works together. We are looking continuously at these scenarios. In fact, you can never predict what it is going to be. It is more like a guess based on previous experience and trying to get some order to the thinking. The important step is that you do have a model and when the virus begins to emerge those clinical details about the first cases will be so important because you feed them back into the model and re-do it so in a few weeks you are talking to decision makers and saying, “It is now beginning to look like this.” That is the starting point and that is the reason why those figures are there. We do recognise what you have just said about it but we are working on it the whole time.

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**Q102 Lord May of Oxford:** Can I just say very quickly and very pedantically and rather sniffily that it is the use of two digits that irritates some. It is a good answer and I am happy with your answer, but to say it is a sort of guess and then you write 0.37 suggests that the person who wrote it did not really understand what they were doing. I just say that in passing.

**Dr Lightfoot:** I take your point.

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**Q103 Lord Howie of Troon:** I quite understand why you have got to do this kind of thing in your line of work but was it sensible to make this 50,000 deaths public as was done the other day? That can only lead to unease. I would say, at a time when 100 people have died. Maybe this is not your department.

**Professor Troop:** I will ask Professor Zambon to look at the shift in how that change can happen in the level of fatalities amongst those at the moment now. I think people want to see that we have planned for a pandemic and then people ask on what basis have you done that planning. Therefore we put out, as we have done, a model of what we think the impact might be, and then put out a range of scenarios to say it is on this basis we are doing the planning. otherwise it is very hard to justify we need this amount of antiviral, we need this amount of vaccine. My own view is what should be in the public domain is all the information and evidence on which we have based our findings.

**Lord Howie of Troon:** I am not so sure about that. It is totally sensible that people who have got to work this thing have got to know that, that is quite true. However, as soon as a figure of that sort becomes public the papers get hold of it. Our view is what should be in the public domain is all the information and evidence on which we have based our findings.

**Lord Howie of Troon:** I am 300 percent against. The previous pandemics and it came out with a set of parameters and inputs into their model and came out with the death rates that you see in our plan. Our modellers have not been working alone however. They have been working with models at Imperial College—Neil Ferguson—and we do have a modelling group that works together. We are looking continuously at these scenarios. In fact, you can never predict what it is going to be. It is more like a guess based on previous experience and trying to get some order to the thinking. The important step is that you do have a model and when the virus begins to emerge those clinical details about the first cases will be so important because you feed them back into the model and re-do it so in a few weeks you are talking to decision makers and saying, “It is now beginning to look like this.” That is the starting point and that is the reason why those figures are there. We do recognise what you have just said about it but we are working on it the whole time.

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**Q104 Lord Howie of Troon:** I have been on my own many, many times and it does not bother me one bit!

**Professor Troop:** Under the Freedom of Information Act—

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**Q105 Lord Howie of Troon:** Oh dear, never mind that.

**Professor Troop:** If somebody contacted us and asked us for this information—

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**Q106 Lord Howie of Troon:** You would have to tell them.
Professor Troop: We would have to tell them.

Lord Howie of Troon: I know. You have won, you have won.

Q107 Chairman: I am going to ask Professor Zambon to get back to the topic.

Professor Zambon: At the moment we see an approximately 60 per cent case fatality rate where there has been transmission of H5N1 from birds to humans but it is important to remember that that is essentially zoonotic transmission. The virus is pretty much at a dead end in humans. If the virus changes, evolves, mutates to become a virus capable of human-to-human transmission it is likely, I think, that we would see a reduction in the case fatality. By definition you are then looking at a virus which is rather more adapted to humans and I think evolutionary history teaches us—

Lord May of Oxford: That is not true. That is one of these canards you find in every medical textbook. We have to look beyond that.

Lord Howie of Troon: I should mention a mea culpa, in that I understand newspapers because I am a life member of the National Union of Journalists!

Chairman: I think we should pursue this one a little further. You are saying that it is not true, Lord May?

Q108 Lord May of Oxford: It is not true. It is a thing that you will find in any medical textbook that says successful pathogens evolve to become less harmful. In fact, what successful pathogens do is co-evolve with the host and they are trading off, and doing things that transmit themselves against the damage. More commonly than not it trades off to go to some intermediate level. The one really clear experiment is myxoma in Australian rabbits where there is a really elegant analysis where people laid down reference strands of the virus and of the rabbits, backtested them against each other, and you see a quick diminution in the virulence of the myxoma virus to an intermediate degree beyond which if it had got nicer it would not transmit as many things but it was nastier, and so it goes. In general, that is true but not always. As I say, smallpox appears to have had a case mortality rate of something like 30 per cent from when it was first reported.

Professor Zambon: Absolutely. You cannot be absolutely sure about what will happen but it is likely that it is going to become rather more attenuated.

Lord May of Oxford: Yes, but do not invoke evolution.

Chairman: Again I will not challenge any of these experts and I am not a structural engineer, I am a microelectronics engineer, but what is the highest death rate that one has seen for a flu-type pandemic?

Q109 Lord Patel: Spanish flu.

Professor Zambon: I think the best example would be the 1918 influenza outbreak.

Q110 Chairman: That was again 15 per cent or something like that?

Professor Zambon: It was overall 3 to 4 per cent, I think.

Chairman: 3 to 4 per cent? So it was very low.

Lord May of Oxford: And in a very stressed population.

Q111 Lord Taverne: Can I ask about the perception of danger because I understand that the number of fatal cases in South East Asia has been decreasing. On the other hand, there also seems to be an increased worry about it at the moment and disturbing reports from the United States that the actual strain of avian flu is one with increased pathogenicity. Is the situation looking more serious or has it recently looked a little less threatening because the number of cases of deaths has been decreasing?

Professor Zambon: We heard from our colleague Dr John Wood earlier on that really the situation is unchanged in many respects. The H5 continues to circulate in birds. The risk of that virus transmitting to humans is essentially unchanged. What we have seen, though, is evidence of the virus being distributed perhaps more widely in wild birds, which is the aspect which has changed. The evidence for pathogenicity comes mainly from some animal work and what can be said there is that the currently circulating (that is the 2004–05) influenza viruses appear to be more pathogenic or virulent in animal models than those circulating in 1997–98. That is, if you will, evidence of change in the properties of the virus. The implication of that for humans is difficult to work out. Our understanding of pathogenicity in influenza virus depends on animal models and we do not really properly understand what makes an influenza virus virulent for humans.

Q112 Lord Taverne: Increased pathogenicity does not mean therefore that the death rate might be higher if it mutates to humans?

Professor Zambon: No because the description of pathogenicity relates at present to pathogenicity in an animal model. It is important not to draw inferences directly from that into the human situation.

Q113 Chairman: But if we look back at the death rate during the Spanish Flu pandemic, was the three per cent number an overall average? Did that change or at the beginning of the pandemic was it much higher?
Professor Zambon: My understanding is that that is an overall average and that there was some change over time. In fact, that might be an evidence of, if you will, the virus changing as it enters the human population.

Lord May of Oxford: It is a pretty soft number. The overall estimate for global mortality ranges from 20 to 50 million so it is a factor of three.

Q114 Lord Howie of Troon: Was it 3 per cent of Britain?
Professor Zambon: I think that is right, it was actually.
Dr Lightfoot: It is important to note—
Chairman: Let’s move on a little now.

Q115 Lord Patel: This is more to do with surveillance and therefore directly to do with the Health Protection Agency. The whole strategy is going to work if we are sure of identifying the first case that we get and then the spread from it, okay? So how confident can we be that whatever strategy is in place that you have got in the health system it will work efficiently to identify the first case of H5N1?
Professor Troop: Some of it will depend on the speed and how widespread it comes in the early stages. We have put a whole series of issues in place. Obviously one is clinical guidance because some of the ways we pick things up is through vigilant clinicians who are aware of something. We have got guidance out so if people see something which they think may be influenza there is a process to go through, so that that also helps to identify it. We have a surveillance system around NHS Direct which is actually a very sensitive measure. We measure it on a daily basis and as soon as you start seeing things, you see the measures of people phoning in advance of where you pick it up in primary care, so that is quite a sensitive measure that something is beginning to change. Also, of course, we have got the new diagnostic test which has been developed so if people do identify a problem we should be able to diagnose it. That is all there in preparation. Having said that, of course, it is then reliant on reports and it is reliant on clinicians reporting and so on and unless we have that obviously we do not know it has come.

Q116 Lord Patel: To avoid a higher death rate at the initial phase of the pandemic what would be important is that the people are given the treatment that is required at a very early stage even though in some of those cases, and I might be using the wrong words, the implication is that you are “overtreating” the person.
Dr Lightfoot: We have worked this scenario through and the key step is the recognition of the first importation. We really rely on astute clinicians and we work on that as much as we can. Once that happens it is how we deal with it and that is written down. We have got algorithms for dealing with it on our web site. It means the household contacts of the first case are almost certainly going to become cases themselves, so the HPA is recommending that you use the antiviral prophylactically in those few people and with the next cases. That might just slow it down for a few weeks which gives us time.

Q117 Lord May of Oxford: When you say a diagnostic test, is this sent out to a lab or do you mean you are developing a dipstick test that you can do bedside?
Professor Zambon: I think there are a couple of things to say. Currently, the main plank of the diagnostic strategy of the United Kingdom is the availability of high-quality molecular diagnostics devolved into a number of regional laboratories. There are at present no dipstick tests for H5N1 specifically. There are plans for some to be developed but there are not any available now and probably not for within six to 12 months.

Q118 Lord May of Oxford: But you are making that a priority?
Professor Zambon: Yes, that is part of the research diagnostic development plan.

Q119 Baroness Sharp of Guildford: You have stressed the importance, so to speak, of communication between the field and what is happening there. I wonder whether you are confident that with the devolved nature of the Health Service now, and the breaking down into primary care trusts on the one hand and then the hospital trusts on the other, you are going to get this information through and whether it will be able to work on the ground? There has been some concern expressed that you may not be able to have effective central control in these circumstances.
Mrs Hutchinson: From my perspective in the PCT the information comes to us very straightforwardly and it is very clear what our responsibilities are and what action we need to take. Although, yes, there are many PCTs (there are going to be less in the future) there is that chain of command and the way in which information comes down to us works very well.

Q120 Baroness Sharp of Guildford: I suppose, as with SARS, in a sense when the first cases come through here there will be a high alertness to people who have been travelling abroad and things like that?
Mrs Hutchinson: Yes and we have very good arrangements for cascading information to our general practitioners and accident and emergency centres. We use those systems all the time for a whole variety of information so they are well-tested routes.
**Dr Lightfoot:** Similarly in the Health Protection Agency you have 31 health protection units around the country and information goes directly down to them to work across at a local level and from our regional offices at a regional level. I suppose you could say the United Kingdom is the envy of the others in that it has a National Health Service.

**Q121 Baroness Sharp of Guildford:** Highly centralised.

**Dr Lightfoot:** That is quite right and a national protection service from the top right down to the units delivering on the ground.

**Q122 Baroness Sharp of Guildford:** Are you confident that there is the capacity in hospitals to cope with influenza beds and this sort of thing? We know that even in an ordinary winter there is great tightness of acute beds in hospitals, particularly of the intensive care beds. Are you confident we will be able to cope with the demand for these sorts of beds?

**Mrs Hutchinson:** I think it is something you have got to plan for very carefully. Clearly, we would have to stop doing a lot of the routine work that we do now and that is something we need to work closely with our strategic health authorities in order to have permission, if you like, and the guidance as to when we can take that step. In my own area, there are particular concerns about access to paediatric intensive care which is an issue we are looking at anyway. Yes, it is something we do need to plan for very carefully and to consider the impact that therefore has on what happens within primary and community care, because clearly if people are not able to be admitted to hospital for something quite different to influenza then they are going to require care from somebody, and that is where we have to think quite creatively about the way in which we provide that care, not through the more traditional routes we do it now maybe.

**Q123 Baroness Perry of Southwark:** In your evidence as the NHS Alliance as opposed to speaking about your own PCT in Bolton, you do express some very major concerns about the impact of reorganisation, do you not? You talk about the removal of some of the expertise from the PCTs from the local level to the regional level and you talk about the impact of the 2002 re-organisation followed straight away by the 2005 reorganisation, and the fact that at the same time in the police force some units are being merged and changed, and you do present a much more gloomy picture in your evidence about the anxiety that your colleagues up and down the country have obviously expressed. Do you feel that is being addressed?

**Mrs Hutchinson:** I am sure that people who are likely to experience a lot of change in their locality are more likely to have got in touch with me over evidence for this particular inquiry. There are parts of the country where the sorts of changes that are being proposed will have very little impact at all. Greater Manchester is one of those places where there is very little change being proposed for the PCT. The fact it varies so much across the country makes it very difficult to give a single answer to that question. I think it is something that the strategic health authorities have sought to take into account in their proposals that were submitted on 15 October in relation to the reconfiguration of PCTs and I hope that when the Department of Health looks at those proposals that they also will consider what impact the proposed changes on PCT boundaries will have on emergency planning in that area. I think it is particularly important that where larger PCTs are being proposed that there is sufficient public health expertise left at the local level and at the borough level, and indeed that is what is now being suggested in the more recent guidance that has come out from the Department of Health which is talking about having an executive director of public health covering a large PCT, but then an associate director of public health in each borough. Provided we have that sort of arrangement in place there will be sufficient senior officers in place to continue with the work that needs to happen locally. I think there are safeguards in place but it is something that we need to continue to monitor.

**Q124 Baroness Perry of Southwark:** But your evidence also does mention—and again I recognise it is only in some areas—the possibility of district nurses and health visitors being removed out of the PCTs, which obviously would be a very key factor in any pandemic, and these are the people who would be picking up very early these cases, would they not?

**Mrs Hutchinson:** Although the Secretary of State for Health made an announcement, I think last Tuesday, on this issue, which indicated that the proposals that were set out in Commissioning a patient-led NHS regarding the provider services of PCT being put into a separate organisation are now being softened, and it looks as though PCTs will be able to continue to directly employ those staff, so this may not now be the concern it was at the point when I was putting the evidence together. Things change very quickly in the NHS.

**Q125 Baroness Perry of Southwark:** Obviously during a pandemic it will be very important to be able to carry out research activities to monitor the effectiveness of the treatments that you are using to
Professor Troop: Firstly, the Health Protection Agency does some research but we do it in partnership with many other organisations and we are very pleased that the MRC has called a convenor meeting to bring people together to look at the research that might be needed. We hope that they will also look at some other issues as well. Firstly, there needs to be rapid access to research funds if we identify urgent questions that need to be addressed. That was very difficult to achieve in SARS despite us approaching a number of organisations. Secondly, there need to be rapid methods for being able to have research approved. We have a tight regulatory system in this country and it takes quite a long time to get research approved. Then, thirdly, for other areas we often need licences, for example. Again in SARS we wanted to do some animal modelling work but it took a very long time to get the Home Office licences and therefore by that time we were almost too late. I think there are these issues to be addressed as well as the actual questions. I think if those issues are addressed collectively with academic partners, ourselves, and others, we have a lot of capacity for research. Maria is one of the people who was trying to carry out those studies at the time of SARS and faced many of these frustrations.

Professor Zambon: I think Professor Troop has said pretty much what I would like to say on that point which is that there is a necessity for some planning ahead in certain ways, in particular to engage the research councils and ensure that there are rapidly responsive mechanisms for funding research proposals and ethics approvals.

Chairman: I am afraid we will have to suspend the hearing for ten minutes.

The Committee suspended from 5.24 pm to 5.39 pm for a division in the House.

Chairman: We are reconvening please and I am going to ask Lord May to ask the next question which is to do with antivirals.

Q126 Lord May of Oxford: One of you said in response to an earlier question that you can use the antivirals both to treat people now that they are infected but also, to a degree, preventively, so you would treat people, perhaps the relatives, the household, and so on. I would frame my question this way: when you do the calculation of trying to get 15 million courses by the end next year, what proportion do you see being used to treat infected people and what proportion do you see being used for targeted antiviral prophylaxis? More generally could you say a word or two about the use of antivirals for prophylaxis?

Dr Lightfoot: I think the Department of Health strategy that they have stated is to use it for treatment in the first phase and that is the 14.6 million doses.

Q127 Lord May of Oxford: That is a assuming that a quarter are going to be infected?

Dr Lightfoot: On that assumption, and that is all it is. We looked at prophylaxis in the Health Protection Agency some while ago, to make some decisions about what we should do to make sure we could still operate that and we have purchased antivirals to use for our laboratory workers, those people like in Maria’s laboratory, who will be working with high titres of the virus during the beginning of the epidemic and helping to get the strains organised. Those people will be given antibiotic prophylaxis for the duration of that period of time in the first wave. That might amount to three months’ use of prophylaxis.

Q128 Lord May of Oxford: We are touching on something really important here because to put it in exaggerated form this is like saying if smallpox comes into the country we will treat the people with smallpox but we will not produce quarantine rings. As you know, the modelling work on how we could hope to control this thing in South East Asia, if it breaks out there, and we are quick enough, is based on slightly extended TAP. You are taking the view, are you, that if you start getting cases in the United Kingdom it will already be too late to do anything other than just treat the sick people rather than identify the cases and try and go for targeting?

Dr Lightfoot: No, as in my response to the earlier question, the HPA view is that we should be using them for post-exposure prophylaxis around the early cases. Because of the transmission characteristics of the influenza virus, which we expect to be by droplet transmission, that means close contacts, it does not mean people who have passed on the bus those first cases. In South East Asia the work done both by Longini and by Ferguson, you are very well aware of those papers, demonstrate by modelling that if you do snuff out the early beginnings of the bird flu virus adapting to humans, and it will go much slower the first few jumps it makes, probably—

Q129 Lord May of Oxford: We have discussed that. That is by no means certain.

Dr Lightfoot: It theoretically demonstrates that you can—

Q130 Lord May of Oxford: So your plans do not involve specifically targeted antiviral prophylaxis in the UK?
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Dr Lightfoot: They do.
Professor Troop: For those early cases it is for all the contacts, like the ring you describe.

Q131 Lord May of Oxford: Why do you not want more courses available by the end of next year?
Professor Zambon: I think we have heard the limitations on global capacity.

Dr Lightfoot: I do not think it is that. If you look at using it as prophylaxis the question then is how long do you give it for and it is an enormous number of people, it is the whole population, and it would to my mind be the wrong use of antivirals, very wasteful of a particularly useful drug that can be used for treatment.

Q132 Lord May of Oxford: So the real answer is not because you think it is enough to cover a quarter of the people infected; it is because that is what you can get, which is a good answer?
Dr Lightfoot: Until you stop taking the last tablet.

Chairman: What is the lifetime of the antiviral in terms of helping with the—
Dr Lightfoot: The shelf life is currently about—
Professor Zambon: —It is about five years.

Q133 Chairman: But that was not quite my question. My question was more to do with if you take a dose prophylactically how long will you be protected for?
Dr Lightfoot: Treatment is a five-day course of one tablet twice a day. If you take it within 24 hours to 48 hours of the symptoms developing, the idea is that it will reduce the effects of the illness and reduce the morbidity, ie, the complications and deaths so that you reduce the impact on the Health Service.

Q134 Chairman: From the moment you take the last dose, so you have got five days.
Dr Lightfoot: Treatment is a five-day course of one tablet twice a day. If you take it within 24 hours to 48 hours of the symptoms developing, the idea is that it will reduce the effects of the illness and reduce the morbidity, ie, the complications and deaths so that you reduce the impact on the Health Service.

Q135 Lord Soulsby of Swaffham Prior: And transmission?
Dr Lightfoot: We think it may affect transmission but we are not certain. At the end that person will be immune.

Q136 Baroness Perry of Southwark: And prophylactically do you also take it for five days only?
Dr Lightfoot: Prophylactically you take it for the period of time that you will be exposed to the virus which should be three months in the first case, we think, we do not know, in the first wave.

Q137 Baroness Perry of Southwark: Because one of our witnesses told us that it had never been tested for longer than 60 days. Is that right?
Professor Zambon: The licence currently available for Tamiflu is for six weeks. I believe the companies are trying to submit finals to extend the prophylaxis licence, so that would mean at the moment you could give it for 42 days.
Chairman: Let us move on.

Q138 Baroness Perry of Southwark: Assuming all this happens and you have got somebody who has got this disease and you have identified it, how long would it take to develop the appropriate vaccine which dealt with the disease which he actually had, and after that how long would it take for the industry to produce the amount of stuff you require?
Professor Zambon: I think we heard from the previous speakers very concisely the time limits that we have. It is 10 to 12 weeks currently to develop a vaccine seed and then there is four to six months to develop mass doses of vaccine. Following the description of trying to reduce the initial 10 to 12 weeks, if successful, we may be looking at more like five months, but I think it is unrealistic to expect millions of doses of vaccine much before five to six months.

Q139 Lord Howie of Troon: As I understand it, and I may be wrong here, the HPA plan assumes that the majority of the population would be vaccinated by the time of a second wave three to nine months after the initial outbreak; is that right, or am I havering as usual?
Professor Zambon: I think it is possible to assume that some vaccines will be available. Vaccine will start to come on stream really as the first vaccine becomes available.

Q140 Lord Howie of Troon: We are talking about the majority of the population.
Professor Zambon: I think that would probably be longer than the first figure you gave.

Q141 Lord Howie of Troon: It will be nearer nine months. Might it be even more than nine?
Professor Zambon: Much nearer nine.

Q142 Lord Howie of Troon: Good, that is fine. One last question. As I understand it, the Government has ordered a certain amount of H5N1 vaccine. What is that for?
Professor Zambon: I am not entirely sure.

Q143 Lord Howie of Troon: That is a very good answer; neither am I!
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Professor Zambon: In the sense that the Government has contracted a supply of vaccine but I think it has been clear from the previous session on vaccine development that we do not have many candidate vaccine strains. So one possibility is that if you make two million doses of vaccine with the candidate vaccines today, you may well have suboptimal protection against the real pandemic strain as it emerges. The way in which that pile of vaccine could be used may actually depend on the situation as it evolves.

Q145 Lord Howie of Troon: Do you mean to be rationed in some way?
Professor Zambon: Clearly if you have two million doses and you have 50 million people who want a vaccine then there will have to be some degree of rationing applied to it.
Lord Howie of Troon: Are the House of Lords a priority?

Q146 Lord May of Oxford: At least they come under the age category!
Dr Lightfoot: To add to what Maria has answered, I think it is important to remember that the manufacturers making the H5N1 vaccine will be going down a route, a mock dossier, for the production of this vaccine so it will make it easier to produce a vaccine using those methods with a different strain but using the same process and safeguards when pandemic influenza comes, so from that point of view it is a very good move.

Q147 Lord Howie of Troon: Do you believe that the pandemic is actually going to happen?
Dr Lightfoot: Yes.

Q148 Lord Howie of Troon: You think it is going to happen. You would not tell me when so I could flee the country?
Professor Zambon: I think if it was a pandemic there is not a lot of point in fleeing the country.

Q149 Lord Howie of Troon: I was thinking of Ayrshire. You are sure it is going to happen?
Dr Lightfoot: You can never be sure.
Professor Troop: In public health I would never say sure.

Q150 Lord Howie of Troon: Would you advise me to put a fiver on it?
Dr Lightfoot: You can never be certain.

Q151 Lord Howie of Troon: Of course you cannot, but I have in mind things like the triple vaccine and "mad cow" disease and all these things. Is it another one of them? You will say no; you must.
Professor Troop: I think there is a probability that we—

Q152 Lord Howie of Troon: I am not going to ask this question again, Chairman, because I see that rationing applied to it. other people are not as au fait with it as I am.
Professor Troop: I think when one is preparing for something like this where we think there is a very definite risk of it happening, the concern is then should it happen it would have such a major impact.

Q153 Lord Howie of Troon: The Cold War was like that.
Professor Troop: On that basis therefore it is very sensible to, yes, hope for the best but plan for the worst and therefore we are planning, because if the risk is sufficient and the potential impact is likely to be very high it is very prudent to do that planning.
Lord Howie of Troon: I am actually convinced this is why people continue to live in San Francisco where an earthquake will certainly happen quite soon.
Chairman: I think we are all agreed that the risk is sufficient that if we can take actions we have to take those actions, and I think what you have told us today is that you are taking many of these actions. I would just like to thank you for coming and talking to us and for submitting evidence. I would also like to say to you that should anything additional occur to you that we have or we have not discussed, then of course we are open to receive input from you, either orally or in writing, so thank you very much for coming to talk to us today.
Memorandum by the Royal College of General Practitioners

1. The College welcomes the opportunity to comment on the House of Lords Science and Technology Select Committee inquiry into Pandemic influenza.

2. The Royal College of General Practitioners (RCGP) is the largest membership organisation in the United Kingdom solely for GPs. It aims to encourage and maintain the highest standards of general medical practice and to act as the ‘voice’ of GPs on issues concerned with education, training, research, and clinical standards. Founded in 1952, the RCGP has over 23,000 members who are committed to improving patient care, developing their own skills and promoting general practice as a discipline.

The Risks

3. According to the World Health Organisation (WHO), influenza experts are agreed that another pandemic is likely to occur but are unable to specify when. Given the continuing outbreak of highly pathogenic H5N1 avian influenza in South East Asia since December 2003 there is a justifiable international concern that this could provide the potential for a pandemic in humans, were co-infection with avian and human flu viruses to occur.

4. The principal body involved with assessing the risk of pandemic influenza emerging in South East Asia and reaching the UK is the Department of Health, advised by the Health Protection Agency (HPA).

5. International veterinary and human disease surveillance activities are critical to both assessing the risk and to responding to the emergence of a pandemic. The UK provides one of the four collaborating centres that form the WHO surveillance network, along with the USA, Australia and Japan. The European Union (EU) also has an influenza surveillance scheme and the UK is part of the 23 country collaboration.

6. The UK is further a member of the World Organisation for Animal Health (OIE). This has adopted a new chapter on avian influenza in the Terrestrial Animal Health Code in order to “improve transparency and control methods of the disease, protection of human health and provide greater protection for countries importing poultry and poultry products while eliminating unjustified barriers to trade”. We imagine that Defra will be providing evidence to the House of Lords Committee on this matter.

7. There is a concern that for modelling strategies of containment at source in South East Asia to be successful there will need to be early diagnosis and verification of cases. However this is unlikely to be achieved in practice in many parts of South East Asia. Moreover Sudden Acute Respiratory Distress Syndrome (SARS) has demonstrated the ease with which international air travel can lead to rapid intercontinental spread of infectious disease.

Contingency Planning in the UK

8. The WHO has set out its role and recommendations for national measures before and during pandemics in the WHO Global Influenza Preparedness Plan. GPs and the Primary Care sector will have to play a critical role within this. Our position statement on major incidents and disasters calls for GPs to be engaged in contingency planning with Primary Care Organisations (PCOs).

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9. The Department of Health invited comment on its pandemic plan and has reported that GP responses included concern about when GPs would receive training and also how single-handed practices would be supported.

10. The Department of Health also issued guidance for health service planners in March 2005. This places responsibility on Primary Care Trusts (PCTs) and Strategic Health Authorities (SHAs) to “develop, maintain and periodically test multi-agency contingency plans to ensure resilient arrangements are in place”. The Department of Health and the HPA are probably best positioned to assess progress in this regard. Currently there seems to be only limited awareness amongst other services of the impact pandemic flu would have on their own ability to function and the challenges this would present to health. Further there have been some comments in the media in regards to preferential use of antiviral treatment for ‘essential services’; this has led to questions as to what health plans are in place to achieve this. We would be concerned if Primary Care suddenly were faced with providing occupational health services to the “essential services” given the pressure GPs would be already under. Guidance is required for essential services on this matter.

11. Both the Department of Health and the HPA have usefully provided information for the public in a question and answer format. The public will need clear guidance in the event of a pandemic and NHS Direct has a very important role to play in providing this along with the media and thereby relieving pressure on general practice. Contingency plans should include effective and clear communication strategies to include the media, virologists and politicians. With pre-prepared material that can be made available in the event of a pandemic.

12. Advice for the professions will need to be consistent, timely, relevant and achievable. However, as yet there is no knowledge among GPs as to what is pre planned or what Primary Care input has been.

13. The Department of Health has announced that Roche will supply 14.6 million doses of Tamiflu over the next two financial years. Clearly were a pandemic to occur by April 2006, there would be a shortfall as only half of the purchase would have been obtained. Effective logistics are critical to ensuring that those who require vaccine and Tamiflu countermeasures at the Primary Care level receive them. GPs will want to know how this will happen for their patients. There will be a huge issue surrounding rationing and delivery of the antiviral therapy and we need to be clear what role Primary Care will play within this.

14. Low nasal swab for flu could help to identify those who need isolating. Given that the overall sensitivity of the NPT is low (30–50 per cent), those who test negative are those who are shedding little virus, so it is an ideal indication of those that need to be isolated.

15. GPs are at the centre of NHS and Department of Health plans to deal with pandemic flu and have a history of providing a large part of the medical response to previous outbreaks. However there is a concern in Primary Care about the huge potential workload any pandemic would engender. We are confident that many in Primary Care would want to provide additional support to health needs over and above their normal duties. The contract system however that GPs currently work under, with large numbers working part time or to fixed levels of patient available time, may reduce GPs abilities to expand their responses as had previously been the case.

16. GPs will not expect to provide extra capacity without reward. Furthermore it is not clear yet how many GPs will want to take out of hours work during a pandemic when normal duties may be taxing enough. In addition GPs will need to have their quality targets in other areas protected if the workload due to a pandemic affects their performance in these areas.

17. There seems to be a real problem here in the need for people to self-isolate at home and the ability of GPs to provide home based care on this scale.

18. Given these factors it has left questions to be answered about the surge capacity of NHS Direct and Out of Hours services when faced with a pandemic.

19. Expectations about additional GP deputies coming from abroad to help build capacity seem optimistic given the situation they would be working in and the situation likely to be occurring in their own country’s health care system.

20. There needs to be planning for how GP resilience could be tackled. This seems to be an important omission, and whilst individual PCTs may have some thoughts about this few seem to be engaging with practices to find out how they perceive their role, or how much support they will be able to give and will need in turn given a pandemic.

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21. In a pandemic situation many smaller practices may suffer greatly due to staff illness; however, it is not clear that any support for provisions of masks for either GPs or their staff will be forthcoming from PCOs or central government. In the absence of a strategy few practices are committing to buying any form of mask and the risks are that practices will lose more staff and GPs in the first few weeks and months of a pandemic than would be the case if they could be protected.

22. We are further concerned that the figures in the NHS plan around excess GP consultations may be misleading as they qualify the number of excess consultations that will be due to influenza at 2.4 million. However in previous pandemics of “flu like illnesses” consultations rose from 1 million to 6 million i.e. a 5 million excess. GPs are unlikely to be able to differentiate with much certainty between flu and flu-like illness therefore there will be a need to assess them both with equal rigour. If antivirals are available for the treatment of the sick then it may be that GPs will have to give treatment to those with flu like illness rather than those GPs can be certain have flu. This process will be made more difficult by two factors, antiviral stocks are not yet at levels that make it clear how much will be available for treating patients and secondly, it is unclear how distribution to a point where patients can access it will be achieved. We would also like to note that the assumptions on which the figures are calculated are subject to wide margins of error and that although based on previous virus behaviour, plans could be an order of magnitude out in reality, and this should be recognised in the planning stages.

23. There needs to be a clear guide line on Primary Care’s role in vaccination policies and their role in reducing other hospital admissions during a time of a pandemic.

24. In addition the impact of infrastructure collapse on Primary Care (utilities, fuels and schools) needs to be further understood.

25. It is important that, in the event of a pandemic, good will exists between Department of Health, PCOs and GPs. It is important that GPs are highly involved in discussing and preparing for a pandemic and practical support measures taken in advance of a pandemic will help in maintaining good will. There is not much evidence of this happening at present.

26. There needs to be a clear research plan in place to ensure that any management lessons are quickly learnt after a pandemic or epidemic so that we are not in the same situation after the outbreak as we were before it. As it is difficult to gear up research quickly we need an emergency research plan as well as an emergency management plan and this research needs to be led by GPs as well as lab and health doctors.

27. Secondly, there needs to be a firming up of the evidence surrounding the role of antibiotics in managing flu so that we can issue clear guidance on antibiotic use and make sure we have a sufficient supply.

28. Primary Care has a long way to go if it is to be able to meet the challenge of influenza in the 21st Century. Moreover there are some concerns that the previous ability of Primary Care to adapt and expand its capacity to respond to surges in demand may have been lost due to changes in GP contracts. We feel the revised Influenza Contingency Plan does not accurately reflect the increases in GP workload that could be expected and could engender some complacency. It is possible to identify strategies that might improve resilience but few are being implemented systematically and require political decisions to be made before PCOs will commit to any spending.

29. Primary Care has a problem in itself that it has little experience in resilience and emergency planning for disease, catastrophe, or attack. Given current global conditions this will need to change and will require work from both government and professional organisations.

Memorandum by the Intensive Care Society

The Problem

1. A recent paper from the Intensive Care Society\(^1\) used a model provided by the US Center for Disease Control and Prevention (CDC)\(^2\) to estimate the impact of an influenza pandemic on critical care services in England.

2. Using plausible inputs for this model (a 25 per cent attack rate and 8 week pandemic duration) we estimated bed occupancy for Level 3 critical care beds that exceeded 200 per cent from the pandemic alone. This scenario does not account for prevailing high occupancy rates in UK ICUs in the absence of a pandemic (typically 85–90 per cent).

3. Current ICU resources would be overwhelmed if the assumed 15 per cent ICU admission rate and 7.5 per cent ventilation rate for hospitalised patients were to materialise. These are not outlandish figures—there is a clear problem
4. However, the exact magnitude of this problem is difficult to estimate, given the paucity of data for ICU admission rates with influenza. Some data are available for the surrogate of community-acquired pneumonia, but there are wide variations in both ICU admission rates (3–20 per cent of hospitalised patients) and mechanical ventilation (37–88 per cent of ICU admissions). The available evidence suggests that inter-institutional variations in provision of ventilatory support are less than those for ICU admission. Since the need for artificial ventilation is a hard outcome in terms of health economics and resource requirement, this may be a better end point to focus on.

5. Best North American estimates for community acquired pneumonia suggest ICU admission rates of ~10 per cent overall, with about half of these requiring ventilatory support.

6. However, these figures need to be viewed with some caution in the light of the high incidence of primary viral pneumonia and reported mortality of > 50 per cent for recent human cases of H5N1 infection in the Far East. The current strain of the virus would seem to be extremely virulent, suggesting a higher rate of admission to intensive care and need for mechanical ventilation. In addition, the need for ICU facilities may be significantly modified by the propensity of the virus to cause exaggerated cytokine responses. Indeed, in past episodes, the morbidity and mortality have been related to these aspects of viral pathogenicity.

7. In the event of human-to-human transmission with a virus of this virulence and high infectivity, intensive care colleagues in Hong Kong (population 7 million) are bracing themselves for 2 million infected subjects with a 10 per cent ICU requirement (200,000 patients). Many hospitals in Hong Kong have expanded ICU isolation facilities. When the Hong Kong Infectious Diseases Centre is finished next year it will have 12 purpose built ICU Isolation Rooms with negative pressure ventilation (Buckley T, Personal Communication). The whole centre, which consists of 108 beds, will have negative pressure ventilation. The total number of ICU beds with negative ventilation in Hong Kong is reported to be in the hundreds (this is not fully substantiated).

8. It has been reported that no patient who has been infected by the avian H5N1 strain in Vietnam, and has required ventilatory support, has survived. There may be questions regarding the promptness and quality of critical care delivered to these patients. However, if these issues are clarified and the report is confirmed, then we need to think carefully about when and where we deploy scarce critical care resources. Indeed, informal reports from the Far East and Australia suggest that they have at least considered conceding that it would be impossible to provide conventional intensive care in this context. At the very least, we may need to develop robust triage systems.

9. Unlike ICUs in Australasia and Canada (which experienced the SARS outbreak), UK intensive care units have little experience of dealing with, or even preparing for, an infectious disease outbreak of this magnitude. There needs to be close attention paid to infection control education and enforcement—including and up to the designation of enforcement officers who ensure that precautions are adhered to.

10. The availability of staff for ICU expansion, or even running current levels of capacity, may be severely compromised by staff sickness (25 per cent) and fear of coming to work. Indeed, a recent publication suggests that less than 50 per cent of nursing staff would be able to or willing to report for work in such circumstances, because of staff sickness, sickness in family members, or the fear of acquiring and transmitting the disease. It is important to recognise this latter factor, and make attempts to assure the safety of staff, as far as is possible, by providing protective equipment, antivirals, and the best immunisation available at the time. It may be important to find hospital based accommodation for key staff who are exposed to high risk of infection, so that they can minimise the risk of taking infection home to their families.

11. These problems of inadequate critical care would be worsened by variable resource availability, which may be appropriate for current casemix, but not necessarily for pandemic geography.

12. We also need to consider the impact of disease specific epidemiology—clustering in urban areas or near regions where disease entry into the country is likely.

Potential Responses

1. The ICU community needs to be involved in contingency planning (the ICS has specific individuals with responsibilities for these issues).

2. We need better modelling with hard UK data to address the magnitude of the problem and the extent of available solutions. Dr Menon and the ICS have begun to address modelling with UK data as part of a dialogue with the DoH (collaboration with Daniel Wood and Peter Grove, with potential involvement of David Harrison of the Intensive Care National Audit and Research Centre (ICNARC).
3. There are potential means of expanding ICU capacity temporarily, which have been explored in published contingency plans. In the UK setting, this may be initially achieved by converting Level 2 to Level 3 beds, and creating temporary critical care resource in operating theatres and recovery areas.

4. Individuals who work in these areas (recovery nurses and operating department assistants) have the requisite clinical and technical skills to support critical care staff. It is essential that we accelerate rotation of non-ICU staff through ICU areas to build up a larger cohort of staff that could be called on to help in the context of a pandemic.

5. There is likely to be a fine balance between useful ICU expansion (with preserved basic care standards) and over-expansion (to an extent that the care systems, clinical skills, and discipline inherent in critical care are lost). There is no point in admitting patients to expanded “intensive care areas” if they do not get a higher standard of care. Discussions with colleagues in Hong Kong with experience of the SARS epidemic suggest that a 50 per cent expansion may be tolerated, but this will vary from hospital to hospital.

6. We should consider, on a hospital-by-hospital basis, the development of critical care services in isolation/infectious disease wards. If this is thought appropriate we need to organise the services that will be required in these areas—piped oxygen, suction and air, and protected power supply.

7. Non-NHS (eg private sector) critical care resources should be logged and quantified. The NHS should develop agreements that will allow us to use these resources in the event of a pandemic. Consideration should be given to using these facilities, where adequate and appropriate, as centres for “clean” (ie non pandemic related) essential clinical activity.

8. We need to have clear central triggers to move from standard to crisis mode—ideally as a staged escalation. This will avoid any confusion about when current priorities (eg waiting lists etc.) can be set aside to deal with the pandemic.

9. We need to create and maintain libraries of critical care equipment in hospitals. Equipment shortages may also be addressed (at least partly) by dialogue with industry and imaginative resource expansion schemes. For example, it may be possible to induce vendors of clinical monitoring, ventilation, and infusion devices to increase their stock levels. This would provide equipment that was available for rapid deployment. Increases in stock levels may require the payment of a relatively small retainer.

10. Such ICU expansion is not compatible with continuing adherence to conventional clinical standards and targets—public education is essential to manage expectations.

11. There need to be clear plans at a hospital level, including rapid access to protective equipment for staff (perhaps chemoprophylaxis for carefully defined subgroups of key hospital workers). We also need to stockpile antibiotics (especially antistaphylococcal antibiotics) for the treatment of secondary infections.

12. Regardless of preparations, resources may be overwhelmed in many hospitals, and we need to consider two options (both may be required, and should certainly be explored):

   a. transfers will occur, and we need to make provision for this;
   b. we may need to bring skilled staff to hotspots, rather than transfer patients.

13. We need to make plans for the recovery and aftermath—catching up with waiting lists etc.

14. It may be prudent to consider whether current indemnities will provide adequate cover, both in terms of individual life insurance (if clinical staff voluntarily go into areas with high infection risk) or organisational responsibility (where the NHS utilises staff working at the margins of their clinical competence).

**Potential Opportunities**

While an influenza pandemic may be clinically devastating, it may also offer unique research opportunities. There is a strong argument for identifying research funding, developing research protocols, and applying for regulatory authorisation to conduct such studies now, so that we are prepared if and when a pandemic strikes. This process needs to be urgently undertaken, and should involve (but not be limited to) epidemiologists, public health physicians, virologists, immunologists, general physicians and intensivists.

We should plan to get regulatory approval from MREC that covers issues relating to the Mental Capacity Act (the sickest patients will be unable to provide consent), EU Clinical Trials Directive (to assess antiviral drug and vaccine efficacy and safety), the Human Tissue Act (research will almost inevitably involve blood samples), and the Data Protection Act (to allow clinical data collection and processing). I would suggest the following actions:

[a] We define a minimum clinical dataset from all patients that would be used for epidemiological analysis, and could provide data for use across many studies. This would be best designed as a series of nested
data collection instruments, with increasing complexity of data collection as the severity of disease increased. NHS Direct are keen to provide the base for this, and I would see them collecting basic data on demographics, comorbidities and symptomatology. A proportion of patients would present to GPs, either directly or via referral by NHS Direct, and could have additional data collected on these topics, as well as information about vaccination and antiviral drug use. A smaller number would present to hospital, where detailed clinical and laboratory data could be collected. Finally, we expect a small proportion of hospitalised patients to come into ICUs, where additional data will be available. It is essential that we have good quality outcome data for the hospital and ICU segments of the populations, including length of hospital stay, treatment and mortality.

[b] It would be ideal if we could achieve such data collections within the framework of existing administrative datasets. As far as the ICU segment was concerned, the perfect framework would be the ICNARC Casemix Program, which provides high quality audit for the vast majority of ICUs in England and Wales (including data on disease severity and organ failure quantitation and 28 day mortality). The additional resource required to obtain data of specific relevance to the pandemic have not been quantified, but are likely to be small. We should explore the use and expansion of similar administrative datasets in less acute settings.

[c] We should identify a matrix of GP surgeries, hospitals and critical care units wishing to participate as stakeholders in a research collaboration that pursued a range of pre-specified studies. A collaboration covering 2 million individuals (~2 SHAs), would result in an estimated 100,000 GP consultations, 3,000 hospitalisations, 1000 ICU admissions, and 2,000 deaths (based on HPA estimates).

[c] In the subset of the NHS identified in [b] above, patients could be involved in more detailed studies. In these patients we should bank a sample of blood for DNA extraction, and store acute and convalescent blood samples to assess host responses, including the development of immunity. Possible synergies with the UK Biobank initiative that should be explored.

Two potential research areas are described below as examples. I have listed studies at two ends of the research spectrum to provide a view of the range of opportunities available:

1. **Clinical trials of antiviral therapy and vaccination in the early phases of the epidemic**

   When the pandemic first strikes we will be using neuraminidase inhibitors and/or novel vaccines with an extremely small (or possibly nonexistent) evidence base. Rapid processing of results from early in the epidemic may allow more optimal use of a range of therapeutic options in subsequent pandemic waves, or even later in the course of the first wave of the pandemic (especially if it is prolonged). Similar considerations apply to the use of protective measures. Assessing the efficacy of barrier protection and antiviral chemoprophylaxis in hospital staff at high risk of infection might provide important early pointers for the use of these interventions in the general population. We need to identify the key interventions that we wish to evaluate now, but provide enough flexibility in funding and study organisation to respond to unexpected challenges and opportunities.

2. **Genotype and outcome from major illness**

   There has been much interest in how genetic regulation of the innate immune response affects survival from critical illness. At one extreme, an inadequate proinflammatory cytokine response may result in high mortality from infection. At the other extreme, an excessive proinflammatory host response may, in itself, predispose to multiple organ failure and death.

   The ability to define critical components and optimal levels of the immune response that enable survival could allow risk stratification and selection of patients for intensive monitoring and specific anti-inflammatory therapy. However, clear understanding in this area has been limited by small patient numbers in most studies, and by the heterogeneity of critical illness (in terms of aetiology, disease severity, therapy, and host variability).

   An influenza pandemic presents a unique opportunity to address these questions in situations where a large number of individuals (potentially up to 25 per cent of the UK population) have a stereotyped biological insult, have similar therapy, and clear outcome measure (mortality). The data that result from a genetic study which involved only a fraction of individuals in this setting would be immensely valuable, not only in the context of influenza, but also for other infections and for non-infectious critical illness.
**ACTION POINTS:**

1. Complete the ICS/ICNARC/DH calculation of ICU admission rates for seasonal flu like illness.

2. Individual hospitals to run Flusurge 2.0 for their practice, with a range of inputs decided after the ICS/ICNARC/DH simulation exercise.

3. The DH should talk to the independent sector nationally, and encourage individual hospitals to do the same on a local basis. It is important to identify the ICU facilities that are available in these hospitals, and agree on ways in which these can be used in the event of a pandemic.

4. The DH should talk to medical equipment manufacturers and define current stock levels. We should also explore ways of rapidly making additional equipment available (eg by increasing stock levels).

5. Published infection control measures need to be cascaded down to ICUs, and their preparedness audited (both in terms of knowledge and availability of equipment).

6. Critical Care Medical and Nursing leaders to identify areas in which non-ICU staff can provide useful support—can be within the auspices of the Critical care Contingency Planning Group. Similarly, the Intensive Care Society should identify core medical skills that will allow expansion of ICU medical staff.

7. Hospitals should undertake evaluation of the ability to expand or upgrade the physical space available for critical care. This may require a specific simulation exercise which should be funded. Such expansion will include conversion of Level 2 to Level 3 facilities, and utilisation of operating theatres and recovery areas. Where geography is favourable, individual hospitals may consider expanding infrastructure for critical care (medical gases, suction and protected power supply) to infectious disease wards.

8. Initiate hospital based cataloguing of spare ventilatory and monitoring equipment. When operating theatre and recovery ward equipment are taken into account, every hospital ought to be able to expand ICU capacity by 50 per cent if elective surgery is stopped. Consider the case for purchase of small amounts of additional equipment.

9. Identify the theatre and recovery staff theatre would be freed by above changes. These staff would be the first port of call for the ancillary ICU training identified by #3 above. See if this can allow expansion of ICU nursing numbers to allow staffing of 150 per cent of current capacity, even if there was a 25 per cent sickness/absenteeism rate in both cohorts of staff.

10. The DH should provide additional funds for medical and nursing staff to undertake core critical care medicine training, and find ways to ensure their willingness to be called in the event of an emergency (eg payment of a retainer to undergo initial and refresher training, and be available in the event of an emergency; these would be the equivalent of the Territorial Army for the hospital’s critical care services).

11. There needs to be explicit statement and restatement of the principle that staff involved in the care of patients with influenza will receive the best available personal protection, in terms of vaccination, antivirals and personal protective equipment.

**REFERENCES:**


27 October 2005

Examination of Witnesses

Witnesses: Professor Nigel Mathers, Chair, RCGP Research Group, Dr Richard Jarvis, BMA Council member, consultant in health protection, Ms Lynne Young, RCN Primary Care lead, Professor David Menon, Intensive Care Society, and Ms Helen Young, Executive Director of Nursing/Clinical Director, NHS Direct, examined.

Q154 Chairman: May I welcome our five witnesses to this session this morning and members of the public and the media who are attending. This meeting is being webcast and the webcast may be filmed by the broadcasting companies as well, so this is very much a public meeting. An information note is available for everybody. May I ask the witnesses to be as concise as you can in your answers because we have a number of questions and, with five of you, we would like to hear from you on these issues and time will slip away? Will you each introduce yourself for the record?

Dr Jarvis: I represent the British Medical Association today. In my normal work I am a consultant in health protection in Cheshire and Merseyside working with the Health Protection Agency.

Professor Menon: I am Professor of Anaesthetics at Cambridge. I am working as an intensive care doctor and representing the Intensive Care Society today. I am a working as an intensive care doctor and representing the Intensive Care Society.

Professor Mathers: I am Chair of Research at the Royal College of General Practitioners. I am also Professor of Primary Medical Care at the University of Sheffield. I am a general practitioner, working in inner city Sheffield.

Ms Lynne Young: I am a primary health care adviser at the Royal College of Nursing, so I am a community nurse by background. I am not a scientist but very much in touch with nurses who will be dealing with the programme.

Ms Helen Young: I am the Executive Director of Nursing for NHS Direct. I am also Clinical Director for that organisation.

Q155 Chairman: Thank you. I start with the first question, which is directed to the ICS. Can you outline what impact you would expect a flu pandemic to have on your work?

Professor Menon: The impact is going to be critically dependent on how virulent the virus is. There is a whole range of possibilities. We know that avian flu infection, the one that is transmitted from chickens to people but not between people, has a mortality of about 50 per cent, so you could expect about half of the patients who come into hospital to require intensive care. At the other end of the spectrum, we would be able to cope with about 50 per cent of the patients who come into hospital to require intensive care. What we did was to use some software developed by the Centre for Disease Control in Atlanta to try to estimate what the impact on intensive care would be in the event of a possible pandemic. They have assumed a 7.5 per cent requirement for mechanical ventilation—the need to go on a breathing machine. With that, at peak epidemic, we would anticipate that bed occupancy would be 230 per cent of our current intensive care capacity. Clearly, that could be mitigated by things like antivirals, or we could increase that capacity temporarily. Those are things we may want to discuss later.

Q156 Chairman: Could we hear from the others on this general question?

Dr Jarvis: The BMA recognises there are a great number of uncertainties relating to the pandemic flu: whether it will happen at all, what the attack rate will be, what the mortality rate is likely to be. It estimates that the effect on society as a whole will lie somewhere between major and catastrophic. However, we want to make the point that the planning that is being undertaken at present has our full support and is as good as that of any country in the world in order to meet this particular threat. This does not get past the major hurdles that we have in meeting the possible pandemic. Those are: an increase in the number of patients requiring treatment by the NHS, by general practitioners, by secondary care trusts; a decrease in the number of staff available due to illness
themselves; and, finally, the generalisation which has to do with the condition.

Q157 Lord Patel: May I ask a supplementary to Professor Menon? I am pleased to hear that there is some thinking being done and contingency plans developed based on that thinking. The thinking, to a degree, is pessimistic in terms of the numbers we might get, which is probably good too. Yes, the beds might be available but what about the equipment? Professor Menon: In simple terms, if we have an increased load of intensive care patients, we need three things: somewhere to take care of them; equipment with which to take care of them; and people to take care of the equipment and the patients. In terms of space to take care of patients, one possibility is for us to utilise the space that would otherwise be utilised for other things. For example, normally, operating theatres have ventilators, monitoring equipment and so on, as do operating theatre recovery areas. You would anticipate that in a pandemic those would not be used for elective operating lists. We have made the suggestion that hospital trusts look very carefully at how they could expand those areas and that would, to some extent, also provide us with essential equipment. The difficult thing is going to be people. We are going to be limited in terms of nursing and medical staff. I should preface all of this by saying that most intensive care units in country, in the absence of a pandemic, run at about 85 to 90 per cent occupancy, going up to 100 per cent from time to time. In an intensive care expansion scenario, the problem is, just as 25 per cent of everyone in this room will become infected, 25 per cent of the staff in intensive care will become infected. There has been some work done in the States where they went and asked nursing staff, “Would you be willing or able to come in to work in an emergency?” At one end of the spectrum, if there was a building collapse and a lot of people died, all the nurses said they would turn up. At the other end of the spectrum, if there was a snowstorm and all the roads were blocked, none of them would be able to come. With a pandemic or a bio-terrorist surge in demand, the problem is that some nurses may not be able to come because of transport. In addition, others may not be able to come in because many of them will be naturally scared, either for themselves or for their families. I think we ought to say that either because of sickness, or fear, or inability to get there because the infrastructure has collapsed, we should anticipate that we will lose 20 to 50 per cent of our nursing staff in ICU anyway. We have to expand from there to the normal level and beyond. There are ways we can do this. What we have suggested to the Chief Medical Officer’s colleagues is that we train nurses who normally work in wards and operating theatres in some of the core clinical care skills so that they can actually come and support critical care nurses, and do the same with doctors. That is something we have to put in place now. We are trying to work out a core curriculum for both medical and nursing staff and how we can try to implement that.

Q158 Lord Howie of Troon: I think Dr Jarvis said that if an outbreak were to occur, it might be either major or catastrophic. My question really is this: is the planning which is being arranged now aiming at major or catastrophic? Dr Jarvis: A number of assumptions are made in the plans, based on realistic estimates of attack rate and mortality rate. The planning assumptions derived from those are based on middle of the range estimates. I think we have to plan for what is reasonably foreseeable at a level that is reasonably foreseeable.

Q159 Lord May of Oxford: You have said that case mortality in the people who have contracted it directly from the animals they work with is about 50 per cent, or 60 out of 120. I wonder whether in the dominator there of 120 there may be many people who have been infected but not seriously enough to be recognised in the system. I am ignorant on this but there are quite a lot of zoological studies of people who work with poultry, and I think about 1 in 1,000 show antibodies to H5N1, which suggests some sort of reaction. That adds up to quite a lot of people. I wonder to what extent that 50 per cent may be slightly higher than the real number. Professor Menon: I think that is a very fair point. Happily, it is not something that we have to deal with. What we have concentrated on asking is: if patients are sick enough to come to hospital, what proportion of those would require intensive care services? That, I suppose, is the crucial test as far as we are concerned. That, at least, allows us the luxury of dealing with harder data.

Q160 Chairman: Coming back to this general questions, could I ask Professor Menon and the others how it will affect your work if we have a pandemic? Professor Mathers: I would preface this by saying that we think in the College that the Department of Health has done a good job with the contingency planning as far as they can go. There is still quite a lot to be done but I think we have time to do that. That would be our general view of the planning that has gone on so far. As far as the impact on general practice and Primary Care is concerned, there is a series of issues. One is our surge capacity: can we cope with the additional workload? Another is service continuity and resilience. Another is supporting
essential services and links with PCTs and NHS Direct. There is the question of communication with the public and the issue of smaller practices and the impact on our performance targets of managing a flu pandemic. There is a whole range of issues which still remains to be addressed, including the position of our surveillance unit. The Royal College of GPs has run an influenza surveillance unit for the last 40 years. That has a well-deserved, international reputation as being the gold standard in surveillance. There have been some issues with our contract, which I would like to talk to you about at some point this morning. My Lord Chairman, I am not sure whether you want me to take each of those in turn or whether you would like me to focus now on one particular issue.

Q161 Chairman: Perhaps you could help us a bit with what you are doing for GPs individually? Have GPs been given the opportunity to express their concerns and how have these been addressed?

Professor Mathers: The consultation which we have undertaken as a college has been of our members of the College. We have 23,000 members; they have had the opportunity to comment on how general practice could contribute to managing of a flu pandemic. At the moment, the base line figure is that we have some 30 consultations per week for influenza-like illness per 100,000 population. That is size of a PCT. In a normal flu pandemic we would have about 250 consultations per 100,000. In a flu pandemic, the contingency plans call for 5,000 to 10,000 additional consultations per week per 100,000 of population, which means that our surge capacity would not be able to cope with demand like that and that we would need some alternative provision.

Q162 Chairman: Have you thought about what that provision might be?

Professor Mathers: Certainly we would have to work very closely with the Primary Care organisations, such as the PCT; we would have to work very closely with our nursing colleagues; we would have to introduce triagings systems; we would have to have a huge, very sophisticated media campaign as to self-management and keeping away from practices unless you are one of the unfortunate number that has complications. We would have to teach people about self-management, about when to see the doctor, and employ every health worker that we could to spread the message and to provide the treatment, but we would have to work very closely with our PCTs. One of the questions on the list that we were given was, “Has the NHS current organisation impacted on preparation for the pandemic?” I think, from our point of view in the College, this is clearly the case. PCTs at the moment are being reorganised. There are issues around that reorganisation because there is planning blight and it is very difficult for PCTs actually to focus down on one particular topic, such as the flu pandemic.

Q163 Chairman: In terms of a media campaign, have you thought of the needs there? Have you prepared a brief, as it were, for the media?

Professor Mathers: We have not prepared a brief but we would be very pleased to contribute to such a brief because it would not just be the College but us working with other partners in the health care sector. It would have to have a lot of content in terms of when to visit the doctor, when to visit the practice, how a nurse triaging system works. It is a very complicated picture and there would have to be a whole series of instructions, not only for practices but also for patients.

Q164 Lord Patel: If I heard you correctly, there would appear to be a concern about the ability of Primary Care to carry out the surveillance that would be required to see where the disease starts and how the disease is progressing. Have I picked you up correctly?

Professor Mathers: There are two separate concerns. One is our capacity to deal with the numbers of ill people who are likely to be involved in a pandemic. The other is a concern about the continuation of our research unit, the influenza surveillance unit. Those are issues around our contract with the Department of Health. As I said earlier, we have had a contract for many years with the Department of Health. We very much wish to improve the service that we provide. However, for the last 18 months we have been trying to get some formal agreement for continuing support. As it currently stands, our contract runs out in April 2006, which gives us problems with the continued employment of the staff. It is almost as though there is a planning blight. Although we understand the Department is very supportive and wishes to see the service continue, we do not have any formal arrangement, and we have been trying to do this for the last 18 months. That is my concern around surveillance.

Q165 Chairman: We take that on board. Perhaps we could move to Ms Lynne Young?

Ms Lynne Young: There are several issues here, given that we are dealing with huge uncertainty, but, even with the good news, we could safely anticipate a lot more nursing work. I think it is really important to step outside the setting of intensive care in the hospital. I could give you the district nurse as an example. District nurses may nurse older people at home who are very fragile and very frail. All it takes is for many of those older people to have a heavy dose of flu and the workload of the existing district nurse
workforce will just rocket and may be unsustainable. We have issues about looking at the population and not just those who are severely ill and will need an intensive care bed. We could safely say that most people will not need that but will need extra nursing in the Primary Care setting. The College is working very closely with the Department of Health to make sure that all the Department of Health information is circulated to the nursing population, and we will continue to do that and give all the support we can. I think we do need to start thinking about if it does become pretty bad, we could put a call out, for example, to recently retired nurses, nurses who have actually chosen to leave the profession but would be very keen to come and help, should the population require that, but that would take quite a lot of work. There are issues in terms of nurses who have been out of work a little while and whether they are safe to practise and what kind of support they would need. A lot of co-operation will be required in terms of Department of Health organisations, such as the Royal College of Nursing, the Royal College of General Practitioners and community organisations. That is quite a challenge but the RCN is very committed to doing what it can to limit damage. Even without a lot of newly ill people, there is again extra nursing work in terms of delivering a mass vaccination programme. That also has to be taken very seriously indeed.

Q166 Chairman: Have you looked at the actual numbers of retired nurses who might be available? 
Ms Lynne Young: I do not have those figures available. I can find them. We do know there are about half a million nurses on the NSU register, some of whom are not working, so there is an opportunity there to seek those nurses out if we need to do that.

Q167 Chairman: Do you think it would be feasible to give them a briefing update, as it were, just on flu? Would that be a feasible thing to do? 
Ms Lynne Young: Yes, we can do that. In fact, currently at this moment, we are preparing a briefing that would help with very basic simple information to nurses to help them know what to do: not panic, not be anxious, but help to become involved and deliver effective care and management.

Q168 Chairman: Perhaps Ms Helen Young could tell us about NHS Direct? 
Ms Helen Young: NHS Direct has worked in collaboration with the Department of Health and, based on modelling that the Department has done (and our contingency plans are based on those figures) we are estimating that a potential of 3.2 million clinical cases would appear between week six or week seven of an outbreak. On that basis, our understanding is that all of those people will need access to either antiviral treatment or, at the very least, clinical triage. We believe that we would be capable of being the gateway that my professional colleagues have referred to for patients who have been affected. In order to do that, there are a number of contingency plans that we would switch to. It is clear to us that if we do that, we would be unable to continue with what we call the core business, the business that we currently do. The plans would be to become a potential gateway for patients or those affected by a flu pandemic to receive information and clinical assessment to aid my clinical colleagues in the community so that those who actually need to have face-to-face consultation are given access to a face-to-face consultation and those that do not and might receive information, i.e. the worried well or those who might be able to self-care, are directed to our existing self-care channels. Members of the Committee may be aware that we already have a successful website, an on-line service, on which information around the flu pandemic currently exists, but there is also information around bird flu on that website, as are our self-help guides actually on-line. For those who are not able to access on-line services, we currently run a digital television service. Again, we propose to keep current the information about the two, both the flu pandemic and bird flu. We are able quite rapidly to change information on both those channels to meet the demand. The telephony service that we run, which traditionally NHS Direct is known for, would therefore seek to take calls from those who have been directly infected by the flu. We would, through messaging, be able to divert those who could not get information elsewhere to our other channels. We would seek to triage, or to assess, or speak to those people who felt they needed to speak to somebody. We would clearly seek to outsource some of the call handling. For instance, we would use all of the NHS Direct staff currently employed to deal specifically with the flu outbreak, and we have geared our staff up to know that is exactly what we would expect them to do. We would be able to outsource, through the virtual technology we have, the call handling. That basically means that for those people who would call us and we would get demographic information from, et cetera, and assess, we would outsource that. All of that is predicated on us being part of a multi-system planning, which the Department Health is engaged in doing at the moment. My points around capacity are that, yes, I believe that NHS Direct would be able to cope with the capacity; it would be a big challenge, but we have plans in place to be able to do that. We would seek to take as much of the public demand for information to our alternative channels, such as digital television and on-line, and also our self-help guide, which is in
the back of the Thomson Local Directory. There are 18 million which already have access to that. We would probably seek to triage appropriately those patients who need face-to-face consultations with someone in Primary Care and en bloc that will stop the panic that might ensue for those who feel that they need to have a face-to-face consultation.

Q169 Lord Patel: May I ask a supplementary at this stage, my Lord Chairman? I think that sounds pretty good. The problem would be that when a pandemic starts you would get, as you describe it yourself, hundreds of thousands of calls, each one of them describing symptoms that are akin to flu symptoms, and each one of them expecting immediate access to drugs, such as Tamiflu. How would you deal with that?

Ms Helen Young: Calls to NHS Direct would clearly be triaged. We would seek to do what we normally do, which is to triage the most severely infected cases. The information about what drug therapy is available, when you might expect to receive it, and where to go to get it, would be available through the on-line services, through the information in patient leaflets and through the information that is available on digital television.

Q170 Lord Patel: That would tell you exactly who they are and where they would get the drugs?

Ms Helen Young: We have a knowledge management system, as you may well know, which basically has a list of all the areas, both GP contacts and walk-in centres, clinics, pharmacies, et cetera. The Department and ourselves would work together to ensure that that knowledge management system, that database, was fully up-to-date to show people and help people on where they would be able to receive face-to-face treatment, information, and where they would be able to get access to the drugs. That is our planning.

Q171 Lord Howie of Troon: As I understand it, and you will tell me if I am wrong, a pandemic would start fairly slowly and then peak quite sharply before it is over. You have obviously done a good deal of work. At what point on the first bit of the curve do you become convinced that a pandemic has actually started?

Ms Helen Young: I feel, as I am a non-scientist, that may not be a question that I can personally answer. May I refer to colleagues on the panel?

Professor Mathers: The Department of Health contingency plan described six phases and four alert levels, depending upon the cases which are reported. I understand, though I have no direct experience of this, that a pandemic portal has been created by the Department of Health whereby all the sources of information about outbreaks, care and the rest of it can be collected into one dataset so that we can get up-to-date information. The other point is that under our surveillance unit, the Royal College surveillance unit, we have at the moment a twice-weekly return service. There are 75 practices plus another 31 just coming on line across the UK from which twice a week information is automatically downloaded from their computer system into the one central research unit so that we can monitor cases and see the rate at which the cases are increasing because you have to reach certain criteria to move on to the next phase. The Department of Health would be responsible for issuing alerts depending on how many cases were being detected.

Q172 Lord Howie of Troon: I am wondering where this portal is that you mention. How many cases are there?

Professor Mathers: As I said earlier, the base line is around 30 consultations per week per 100,000 population, peaking at about 250 in normal seasonal flu. Once we get beyond 250 additional consultations per week per PCT population, then we begin to start moving through the phases, but there are other sources of data as well.

Q173 Baroness Finlay of Llandaff: I apologise for being late and also if perhaps this question has already been asked. When you were talking about triage, I wondered what the criteria are by which you will put people into the different categories and how do you then safeguard against exaggeration of Department and ourselves would work together to safeguard against exaggeration of the risk and potential risk of having a telephone consultation with people who do exaggerate their signs and symptoms. I guess to a certain extent we cannot particularly stop that, but with the information that is made available to people and the information that we would make available to people about what alternatives they have, we can trust very much on our nurses’ ability to be able to make the triage and be able to get information from them and give information. A lot of it is based on our experiences with the public when they use us currently, that they are genuinely quite honest with their clinical answers because they want to be in the right place at the right time. I do believe there is public information and public education, and that is exactly what our nurses would do. I cannot give any guarantee that we would get it right 100 per cent of the time. We would use our best clinical judgment and our best clinical decision making, which, based
on current evidence and current experience, we are reasonably successful at doing.

**Q174 Baroness Finlay of Llandaff:** Do you have those algorithms up already?

**Ms Helen Young:** Yes, we have algorithms available currently for a flu outbreak. We have algorithms available for a potential flu pandemic. We are also working on system contingencies to see that, if there are any technical failures in our system, we can use a stand-alone system; in other words, we can operate that system also.

**Q175 Baroness Finlay of Llandaff:** What are the criteria for triggering a referral or obtaining advice?

**Ms Helen Young:** I am very happy to give you the information for the algorithm and I will pull it out. I do not have that information at this point. I am happy to share the algorithm with you.

**Q176 Lord Soulsby of Swaffham Prior:** From the answers you gave to the first rather extended question, it seems to me that you are reasonably content with the plans that each of you in your various professions has of dealing with an endemic flu outbreak. There is always a gap somewhere. Is there a gap? What more needs to be done to be assured that we could handle the thing? The second point is: have you tested your plans, either collectively or individually? Firstly, what more needs to be done?

**Professor Mathers:** From our College’s point of view, there needs to be a lot more detail as to how Primary Care would respond to the challenge. Some of the issues are around service continuity. For example, the contingency plan suggests that if you develop influenza-like symptoms in the middle of a pandemic, then you should go into voluntary quarantine. If you are in a practice of, say, four receptionists, two nurses and three doctors, then if you have someone in a practice who is going to follow the guidelines, very rapidly you are going to close down the practice. That is one issue which needs to be progressed. The other is resilience. If we are dealing with patients during a pandemic, then of course there is the usual core business still to be done. That needs to be addressed as well because that, of course, will have an impact on our performance-related contracts. If for three or four months we may not be able to deliver on the core business because we are dealing with the pandemic. The other difficulty is around how we support essential services. In the plans it recommends that we support essential services, but it does not actually define what that is. Does that mean we give priority to health care workers for antivirals, for example, or consultations? We are not sure about that. Also, there is the particular problem with smaller practices. If you have a practice of, say, four or six people and one or two or those go down with influenza, then there is a problem about continuing to manage the service. There is also the issue about how we manage our visits. My colleague Lynne Young has suggested that some of the issues are going to be that the workload will increase exponentially if people are ill and told to stay at home and require a visit; that may be from a nurse or a doctor. That is an issue which has not been resolved satisfactorily yet.

**Ms Lynne Young:** I think we need to acknowledge that in many areas community nursing is actually under pressure right now; it is struggling very hard to meet even very essential demands. Because of the demand very rapidly to make savings within the Primary Care trusts, agency, part-time staff, bank staff perhaps have been told that there is currently no work for them. That therefore puts more pressure on existing services. That is very important. I think we have to take very seriously indeed the fact that if we suddenly get a large number of people who are newly ill and can be cared for in the community, the essential services that are currently being carried out will have to be put on hold. We will need to be very clear about priorities and emergencies making a different set of priorities. The front line of nurses and doctors will need a lot of support from their organisation, and indeed from the Department of Health, in order that they do not come under increasing pressure from a very disgruntled public who, even for the short term, are not receiving the services that they are used to receiving.

**Dr Jarvis:** I think the overwhelming feeling is that the flu pandemic plans in this country are very good. As you intimate, there are holes and problems with that. The areas where we think there are adequate plans already in place include: vaccination and provision of antivirals for vital staff; alerting mechanisms, both international and national; cascading of professional advice; and production of public advice. I think more preparation is needed in a number of areas, particularly organisational plans both within the NHS and in the wider private community. We need to be able to provide effective triage systems. I think these will change as the course of the pandemic progresses. I think we also need time-sensitive flu management algorithms for front-line staff. Most of all, there are major challenges that a flu pandemic throws up for which it is actually very difficult to plan and particularly in service-wide demand management. In a system that runs at very high levels of efficiency, it is very difficult to provide surge capacity and also maintenance of adequate staffing levels when staff are likely to be unwell. To answer the final question, which was about exercising and making people aware of these things, exercises are taking place and they are very useful, but, by the
nature of these things, although it is possible to include most of the organisations involved in flu pandemic planning in the exercises, it is very difficult to involve individual practitioners at the front line, and they express a need to be involved in this. It is difficult to bridge that gap.

Professor Menon: The answer is in two parts. The published pandemic plans from various sources really make no mention of intensive care. There is a very big gap. What has been heartening over the last two weeks is how much involvement there has been with the Department of Health. While the gaps have not been filled, at least there is a recognition that the gaps are there. There are specific issues that worried me and which we need to address quickly. The first thing is to make sure that monitoring involves intensive care admissions, as does surveillance. We have suggested to the Department of Health that the Intensive Care Research and Audit Centre in London, which essentially audits 80 per cent of the ICUs in England and Wales, provides surveillance and monitoring so that we can take account of the full spectrum of disease. We have also taken on board a lot of the capacity issues. I believe Bruce Taylor, who is sitting here representing the Intensive Care Society, is chairing the Department of Health Critical Care Contingency Forum, which is addressing some of the capacity issues. Finally, we have made some suggestions about research in the context of the pandemic, which I think is both a necessity and almost a duty but also a huge opportunity. I hope that we have a chance to discuss that at some stage during this hearing.

Lord Soulsby of Swaffham Prior: May I return to one matter, my Lord Chairman and that is the commentary about personnel, the shortage of personnel and personnel being under pressure? Are there any plans to recruit people from parts of the Commonwealth, say Australia and New Zealand, and to draft in people to help out at the peak of a pandemic?

Q177 Lord May of Oxford: Assuming they do not have it! Professor Menon: I suspect they are going to have it. Australia in particular may well see this before we do because they are closer to the most likely focus of outbreak. I think a major problem is that I suppose the establishment, which includes all of us, has in dealing with public expectations is both ways. First of all, I think people need to realise that we cannot prepare for the catastrophic scenario; it is simply not possible because it is unlikely and we would not be able to put in place the resources. However, even if a less severe pandemic does happen, they need to be attuned to the fact that we will not be able to deliver services as usual. All the people sitting on this side of this room have made it clear that we are doing our best and we are putting in place plans to deal with some medium-scale scenarios. However, if things are really bad, we will not be able to cope and may be unable to deliver the same standard of care. The second point is that in the medium eventuality, your hip operation is going to be delayed, elective surgery is going to be delayed and lots of things are going to have to wait. People have to realise that that is a fact of life. There is no getting away from that.

Q178 Chairman: Do you want to go on and talk about the research that you would like to do here? Professor Menon: Yes, and in two aspects, one being the general area of research. The reason why we are not as prepared as we would like to be is because previous pandemics have not been subjected to the rigorous research that modern research techniques allow. The first thing I would say is that we need to get together our data collection mechanisms and decide how to do it most efficiently. It would be ideal to have a minimum clinical dataset so that every patient who presents to the help lines has some information collected from them, that when they present to the GP and additional information that is collected; and if they come to the hospital, further additional information is collected; and if they come into intensive care, there is still more information. Second, especially for people who come into hospital and into intensive care, we really need to know what the outcomes are. There is no point in our saying a drug is a good drug unless we know it saves lives, and in order to know whether this is the case we need to have clinical outcomes on all of those patients. Those minimum clinical datasets need to be decided now. Third, there are also regulatory issues. I am told that in the great epidemic of 1918/19 people dropped dead on the street. They probably would not drop dead now because ambulances would bring them in. Many people would come in unconscious. There is a whole set of regulatory hoops that we have to jump through, and we have to do this in advance. We have to get Ethical Committee approval. Many of these patients may come in incapacitated and so we need to go through the provisions of the Mental Incapacity Act. We need to address issues of data protection. Many of the studies we want to do urgently in a pandemic to tell us how best to use the interventions we have would have to be done under the aegis of the Clinical Trials Directive, and so we need to put those in place. All the regulatory issues need to be dealt with now. I understand that the MRC are chairing or co-ordinating this kind of initiative. As far as intensive care is concerned, as soon as the first patient comes into intensive care, we owe it to that patient and to the patients we are dealing with at the end of the pandemic to make sure that we deal with them as
part of the scientific protocol-driven study. If we are going to use antivirals, we need to know: does it make a difference when the patient came in whether the antiviral was given on day one or day four? If, on day four, it was making no difference to the severity of the illness, then that makes a difference to how we treat people at the end of the pandemic. We need to know, for example, whether what is killing them is the disease or whether it is the host response. To explain, if you get a serious infection and you do not produce a good immune response, you die because of the infection. If you have just enough immune response, then you fight the infection and, hopefully, survive. In modern medicine with antibiotics and hopefully effective antivirals, you treat the infection but may experience an exaggerated host response. An excessive immune response which may be genetically-driven may actually cause you to die because that inflammation kills you. There is a case to be made for trying to understand the genetics underlying how badly people do or how well they do. As I have said, this is not only a duty but also an opportunity because it will inform our understanding of a lot major illnesses both infectious and non-infectious. There are generic things that we can put in place, and that we have to put in place now, that will advance our understanding, not just of the disease, which would be very useful, but also more generally on how we deal with pathogens in general.

Q179 Lord May of Oxford: Are you satisfied that this is being done?
Professor Menon: I do not know. The announcement about the MRC convening this group was recently announced. When I spoke to the Department of Health this morning, I said that we would very much like to be involved. We have also made that obvious through a submission that we put through the Academy of Medical Sciences. All of that has been fed in. I think it would be sinful to miss this opportunity.
Professor Mathers: To add to that, some important research also needs to be done in general practice and Primary Care, for example in diagnostic testing. If you do a swab from the nose, can that help you decide who is infectious and who is not? There is some evidence but we do not know how effective such early diagnostic tests would be in the early part of a pandemic.

Q180 Chairman: To your knowledge, there is no dipstick test, as we have described it, for this at this stage?
Professor Mathers: The sensitivity—that is the chances of being right—would depend a bit on how common the disease is. The sensitivity is around 30 to 40 per cent of a nasal swab. That means that you are less likely to be shedding the virus if it is negative and you are less likely to be infectious. That could be, but that is a pretty low sensitivity and will be affected by prevalence as well.

Ms Lynne Young: On the issue of regulations, there are one or two regulations in place that need to be confronted if we are to do what is required. It may not be an issue but there is a regulation on the use of unlicensed drugs. I would like the committee to be aware of that. If nurses and others are to give mass vaccinations and other drugs within what is called patient group directions, which prevent the use of an individual prescription for each patient, the unlicensed drug matter would have to be dealt with. Am I clear with that? You cannot give an unlicensed drug within a patient group direction. That is the issue.

Q181 Lord Taverne: May I follow up on the question of research? Obviously any research that has to be done has to be done very quickly; it is very urgent. Are there any regulatory obstacles that have to be overcome to ensure that you can do the research quickly enough?
Professor Menon: There is a question of time because we deal with pathogens in general. It takes a certain amount of time. In our experience, because of the issues about the Clinical Trials Directive, if you wanted to assess, for example, whether steroid drugs which reduce inflammation are helpful in the most sick patients, that would have to be run as clinical trials. It takes three to four months to go through the regulatory hoops to get approval for a clinical trial. This may be quite appropriate, but the point is that we need to do it now. Generally, there is an issue of time. We need to get started now. For specific groups of patients, again there are issues, for example, with children. I have not addressed the issue of children. We have been talking about ICU expansion. It is important to realise that many children may become infected with this agent. If we have to expand paediatric ICU facilities, that raises a whole different series of problems. Maybe we should talk about that separately. Children are one issue. People who get so sick that they cannot provide consent to research are another issue. Finally, the whole issue of taking blood and keeping it for DNA so that we can look at the genetic associations to determine which patients get the sickest and which patients, if they get the sickest, survive, will all mean that the requirements of the Human Tissue Act will have to be fulfilled. Some of those are not in place as yet. The regulatory framework is not in place yet. We need to reach an accommodation that allows us to proceed with this research if we want to do it.
Q182 Baroness Finlay of Llandaff: May I follow up on that, Professor Menon? Are you implying that there is a need for a new statutory instrument to be brought in, in the event of there being a pandemic, to override some of the bits of legislation which are in place at the moment which are impeding immediate research on patients who lack competence to give consent and whose families cannot give consent in relation to things like the Human Tissue Act?

Professor Menon: I think that would be very valuable, provided we have the safeguards. We have to take the public along. We need to make clear that providing patients are not being harmed, and providing for the issue of confidentiality, we should undertake such research because then the greater public good demands this. However, we have to have the safeguards to say, "You are not going to be harmed". This is important. God knows, the medical profession has a record of not communicating well. We need to get that right, but, if we do, I think the public would be supportive.

Q183 Lord Patel: My question relates to the current organisation activity that is going on in the NHS or reorganisation, that you partly referred to early on. The whole ethos of that is to devolve down the responsibility. Do you think that kind of devolution of responsibility is going to be effective in delivering proper care in a pandemic situation? That takes you away from a pandemic situation where you want central command and control.

Professor Menon: That would be precisely the issue that I raised earlier. In such a situation of a flu pandemic, you would need command and control. It would not be enough to leave it to individual practices, or even individual PCTs, to deliver the necessary care.

Q184 Lord Patel: Are you currently addressing that issue?

Professor Mathers: We are in the College. We prepared a major incident and disasters plan two years ago in which there are details of how such a command and control system would operate.

Q185 Lord Patel: Are you addressing that with the Department of Health?

Professor Mathers: The Department of Health has been part of that, yes.

Ms Lynne Young: I would like to make a point about the state and robustness of the Primary Care Trust at this time. The reality is that there is complete pandemonium out there. For example, in the north-east of England, 16 Primary Care Trusts will go down to two. This is causing huge anxiety and huge distress. For very understandable reasons, I think people are looking at their jobs and where they will be in the next few months rather than keeping the eye and the focus of attention on what local people require from health services. I think that has to be taken very seriously at the highest level. That is how it is at the moment. We are hearing from our nurse members every day about what utter chaos and confusion there is in Primary Care Trusts at the present time.

Professor Mathers: My Lord Chairman, I would support that.

Q186 Baroness Finlay of Llandaff: I am a great fan, of course, of GPs, having been one myself. What authority does the College of General Practitioners have nationally to take command and control? Is that being recognised by the Department of Health?

Professor Mathers: I would not suggest that the College took command and control at all. I think our role is to inform and certainly encourage our members as to best standards and what is appropriate. We work very closely with partners. I think command and control lies with the Primary Care organisations, whatever they happen to be.

Q187 Baroness Finlay of Llandaff: At that level and not higher?

Professor Mathers: We would input higher up but I do not think we would want the College to be in the position of being in command and control. There is also the whole question of rationing. If there is insufficient antiviral and it is effective, then in the College we would not want individual doctors to be engaged in deciding who was treated and who was not—dispensing, for example.

Q188 Lord May of Oxford: As a supplement to that, are you happy that you have been consulted as an institutional body adequately? In particular, we keep using the word “pandemic” and talking about just the UK, but it is very likely that by the time we come to be talking about the UK, there will have been a great deal of experience elsewhere already. In the light of that, could I also ask you, while we are dealing with that: are you happy with the degree to which the plans assume that the public will behave calmly and will not be badgering you unduly, particularly as they will be well aware that Tamiflu can be used both to treat people who are diagnosed but also as targeted prophylaxis? Are you happy that the current plans that it would just be given to people who are sick are going to stand up when people in the same house or the same school class are going to be pressing you for it?

Professor Mathers: My Lord Chairman, this is a key issue. We are very heartened by the response of NHS Direct, who I think will play a crucial and critical role in the necessary information campaign. There need
to be very clear guidelines as to what your doctor or your nurse can and cannot do for you, how antivirals should be used in the community, if at all, and who should make the decision. Those issues are not clear from the current pandemic contingency plans.

Q189 Lord May of Oxford: May I ask the others how they feel about that? It is going to make your life very difficult.
Professor Menon: Clearly there are going to be issues about rationing of intensive care if this gets as bad as we hope it does not. We have some basis for doing this. The natural thing that is trotted out is age, but the key factor is not age; but the presence of pre-existing co-morbidities—diseases in other organs. Patients may have a bad heart and bad respiratory disease and then, if they get an acute flu infection, their chances of survival are going to be quite small. Those are issues which have to be discussed, I suppose, at some stage. Again, it would be useful to have this discussed nationally rather than each individual intensivist having to make the strategic rather than the tactical decision. As far as experience from abroad is concerned, there are two areas where we have had a lot of discussion. One concerns the Far East, and colleagues in Hong Kong have been very helpful. Tom Buckley, one of the intensivists there, has been in communication with us. They may have the scar of SARS on their experience, and it is going to be very difficult for us to try to get up to their levels of preparedness. For example, his intensive care unit in one hospital has nine negative-pressure isolation rooms. The number of negative-pressure isolation rooms over Hong Kong for a total population of a couple of million runs into several hundred. These are ICU negative-pressure isolation rooms. We would be very lucky if we had that within the UK for a much larger population base. The other set of people we have talked to a lot are the Canadians, again because of SARS. We have learnt a lot from their publications and talking to them has provided added value. In answer to your question, yes, we are talking to them.

Q190 Lord May of Oxford: Would you feel that the institutions you represent are adequately involved?
Professor Mathers: As of the last couple of weeks, yes. Ms Lynne Young: You may not know about this but the United Kingdom National Influenza Committee has just been set up. That is due to meet in the next couple of weeks. We will be involved, as, I imagine, will all the organisations. Obviously sub-groups will be set up under that umbrella. We will be very involved with that and that is good news. May I say this, and it may be a depressing note on which to finish, that we also have to acknowledge that if there is a great acceleration in deaths, that will have to be handled. I think it was three winters ago, when there were was a flu epidemic, there problems disposing of bodies in a dignified way. We have to talk about prevention and management but there will be more deaths. We have to manage that, too, with dignity.

Ms Helen Young: In response to a question in relation to whether we have been consulted as a national organisation within the NHS, yes, I can give a reassurance that we have been consulted and we have played a role both nationally and with the Department of Health and other colleagues, but we have also been consulted and involved regionally and in some of our regional areas also locally with partners. I have mentioned already the role that we all play in public information, public health and education. We are additionally working with the Department of Health on an advertisement campaign that is a pre-runner to any potential outbreak or pandemic, which will give the public information specifically on all signs and symptoms and access to the emergency services. We are fully aware, as a national organisation, of our gateway role and the need to be both resilient and robust in order to protect other parts of the NHS. I can give some reassurance that we are aware of gravity and scale. We are planning to do everything we possibly can both in advance, during and in a protective role to help the elements of the NHS that will need to be utilised for face-to-face consultation.

Dr Jarvis: On the question about being consulted, the BMA has been relatively poorly consulted up until the last two weeks, but we have encouraged the Chief Medical Officer to set up multi-agency stakeholder meetings to address this issue as a matter of urgency. Regarding overseas co-operation, the virology and epidemiology aspects in this country are led by the Health Protection Agency Centre for Infection, in Colindale. There are very good links through the World Health Organisation with all other countries very lucky if we had that within the UK for a much larger population base. The other set of people we have talked to a lot are the Canadians, again because of SARS. We have learnt a lot from their publications and talking to them has provided added value. In answer to your question, yes, we are talking to them.

Q191 Lord May of Oxford: I perhaps folded too many bits into the question, but could you say a little bit more about how you feel about what is (as best we could gather the other day) the current idea that if one person in a household is infected they get Tamiflu but that it is not currently envisaged, and it would have to be a very deliberate thing, to offer it to others, when your information system will have told other people in the household that there is a prophylaxis purpose and I can even see parents with flu giving their children their drugs if you do not give it to them. To what extent, particularly as a GP, do you envisage handling that at the surgery?
Professor Mathers: That is a very difficult question to answer individually.
PANDEMIC INFLUENZA: EVIDENCE

27 October 2005

Professor Nigel Mathers, Dr Richard Jarvis, Ms Lynne Young,
Professor David Menon and Ms Helen Young

Q192 Lord May of Oxford: Generally?
Professor Mathers: From my own point of view I think that it would be sensible to restrict Tamiflu to treatments and not to prophylaxis because the Department of Health plans include 14.6 million doses which is enough for 25 per cent of the population.

Q193 Lord Patel: Are you suggesting that is inadequate?
Professor Mathers: If it were to be used as prophylaxis then you would need a dose for everyone in the country which I think would be unreasonable because there are suggestions, although I am no expert in this area, that should a pandemic occur then its virulence will diminish in order to facilitate transmission person-to-person. That is my understanding, in which case it would seem logical to me that Tamiflu should be restricted to those who actually do have the disease rather than those who have been in contact. The Department of Health calls for voluntary quarantine for those. I think it is an issue that needs to be discussed.

Q194 Chairman: But is it your recommendation or would you support the relatively small number of doses of Tamiflu that have been ordered? Would it not be a good idea to order more?
Professor Mathers: Not everybody, as I understand it, and again this is not my field of expertise, will catch the flu. Lord May was saying earlier there are people who are asymptomatic and in the cases that have been reported the 50 per cent mortality may just be the tip of the iceberg. There may be plenty of other patients out there who have had the disease and not come to the attention of the surveillance procedures or the surveillance mechanisms. It is still full of uncertainties.

Q195 Chairman: Is it consistent to be ordering 120 million doses of vaccine and only 14.6 million doses of Tamiflu?
Professor Mathers: I think that is a question for the Department of Health to answer.

Lord May of Oxford: Very quickly on this. First of all, the roughly quarter is a very soft number, you understand. For example, Imperial College modelling of what they think is the most likely, but with a wide range of possibilities, beginning in South East Asia, is assuming that in the absence of intervention two-thirds could be infected, it is a very soft number and it could be fewer and it could be more. Secondly, all these plans are assuming that everybody behaves in a quiet way rather than getting very upset. Thirdly, the notion—and the evolution of virulence in infectious disease actually happens to be one of my academic subjects—that you can rely on it becoming less virulent as it goes on is a very out-of-date notion and a very frail read to depend on in the opinion of the informed frontiers of the subject community.

Q196 Chairman: Just one more point from each and then we are going to have to wrap this up.

Professor Menon: I would just make the point that if you are using Tamiflu for targeted prophylaxis you would not need 60 million courses, you would need much more than that because the pandemic is going to go on for eight to twelve weeks so you will need eight to 12 times the population.

Q197 Lord May of Oxford: Depending on the extent to which we could be effective in containing the foci by using targeted antiviral prophylaxis.

Dr Jarvis: Just to return to something I said at the outset, which is there is a great deal of uncertainty about this, and I think the numbers of vaccines and the amount of drugs that are purchased is based upon planning assumptions which may vary from what happens in reality. The second point that I would like to make is that when we are considering who should be given the vaccine and who should be given the antivirals, it will depend very much when in the pandemic, when in the epidemic curve we are actually at present and how much of that medicine is available. So where I draw that to is that the algorithms and the decision aids that we would use to assist GPs and nurses actually doing this would change during the pandemic. My absolutely final point is that under no circumstances can we let individual GPs and nurses on the frontline have to make decisions of that magnitude; it needs to come from the centre.

Q198 Chairman: Alright, thank you very much for your evidence. Did you want to make just one more point?

Professor Mathers: Just one last point. I think that we have made a good start with this contingency planning and I think we have got time to continue the work.

Chairman: Good. If you have other points you would like to make, we are always open to that input so get in touch, write to us, submit more if you have more to say. Thank you very much indeed for coming this morning.

Supplementary evidence by the British Medical Association

The British Medical Association (BMA) is a voluntary, professional association that represents all doctors from all branches of medicine across the UK. About 80 per cent of practising doctors are members, as are nearly 14,000 medical students and over 3,000 members overseas.
Introduction

1. The BMA welcomes the actions that the Department of Health has undertaken to prepare for an outbreak of pandemic influenza in the UK. Good planning and preparedness might mitigate the enormous consequences of a pandemic, and this opportunity must not be missed. However, even with good planning, an influenza pandemic could potentially have major implications.

2. The timing and the impact of pandemic influenza are the greatest uncertainties, and could therefore make planning extremely difficult. Despite the commendable efforts that the Department of Health has made, there are a number of areas that still need to be addressed.

Can you outline what impact you would expect a flu pandemic to have on your work?

Wider NHS:

3. It is anticipated that there would be a large increase in demand for primary and secondary care, although the exact degree is difficult to predict. As the NHS normally runs at very high efficiency there is little surge capacity.

4. The increased workload giving vaccines and antivirals is likely to be concentrated on Primary Care.

5. There would be a reduction in levels of NHS staffing due to flu related illness but staff shortages can be mitigated to a certain extent by selective use of vaccination for staff. However, vaccination is unlikely to be available in the first six months of the pandemic because production cannot begin until the exact form of the pandemic strain is identified, and because inherent characteristics of the production process means maximum production is not achieved for several months.

6. In summary, the impact on the NHS would be substantial. The increased demand and reduced staffing may force reassessment of the normal assumptions about triage systems and waiting time for emergency treatment. Moreover, elective work is unlikely to be sustainable.

General Practitioners and Primary Care:

7. There would be a need to develop practice contingency plans, although uncertainty about a pandemic frustrates effective planning. General Practitioners (GPs) will need guidance in developing their practice contingency plans. This would be primarily from Primary Care Trusts (PCTs) and strategic health authorities, with technical advice and support from the Health Protection Agency.

8. The normal weekly workload for GPs could be expected to increase dramatically. For example, home visit requests may increase 10 fold or more. It is estimated that GPs may expect to see 1,000 new cases per 100,000 of the population per week, which would rise to 5,000 per 100,000 per week at the height of the pandemic. The large numbers of the “worried well” could have an effect on GP workload whilst the impact of staff illnesses could be higher for small practices. There could also be the probable suspension of all “routine services” with the risk of practice closure unless temporary staff cover is available.

9. Due to high numbers of those infected, there may be the inability to admit sick cases to hospital because of bed unavailability.

10. GPs will need specific advice on prevention, diagnosis, management and treatment of flu cases. In addition, GPs will require specific information to pass on to their patients.

Public Health & Health Protection:

11. There is some difficulty in engaging some PCTs in the planning process, as senior personnel are occupied with other priorities such as NHS reorganisations and achieving targets. In addition, there is a current lack of dedicated emergency planning posts in PCTs.

12. Engagement with GPs has also been difficult, as it is challenging to achieve a balance between providing sufficient detail on an uncertain and changing subject to a busy audience. Furthermore, exercises can cover most of the affected organisations but cannot reach more than a few staff or GPs.

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7 UK Health Departments (October 2005) *UK Influenza Pandemic Contingency Plan.*
13. The modelled impacts of an influenza pandemic vary and this contributes to uncertainty in gauging the exact amounts of antiviral or vaccine to stockpile. Furthermore, lack of resources for stockpiling comes into play for any but the very low impact models.

Wider society

14. It would be essential for private industries (e.g. transport, food retail, utilities, fuel, finance) to engage in business continuity planning or multi-agency specific planning. The combined efforts of society will be required to reduce human deaths and ill health and minimise short and long term economic damage.

In general, do you find that health authorities have prepared effective plans to deal with a pandemic, and in particular, do the plans deal adequately with the challenges your own professions will face?

15. There are adequate plans in place for the vaccination of, or antiviral provision for vital staff. The alerting mechanisms for incidences of influenza and the methods for cascading of professional advice are also in place.

16. Although the Department of Health is to be applauded for its contingency planning in the event of a pandemic, there are a number of barriers to effective planning. Key challenges lie in service-wide demand management, the maintenance of adequate staffing levels and the lack of NHS surge capacity. Other challenges are:
   — Conflict between regional and county based planning assumptions of the Civil Contingencies Act and the current geography of the NHS;
   — Focus on achieving targets in the NHS distracts attention elsewhere;
   — Lack of specific financial resource and the current financial difficulties of a number of PCTs;
   — Lack of joined up thinking at departmental level—ie assurances to the NHS of the support of other services without commensurate guidance to those services;
   — Lack of effective engagement with all areas of the NHS, especially Primary Care.

17. More preparation is required for:
   — Organisational plans—specific and business continuity, for PCTs and acute hospitals within the NHS and transport, food and fuel related industries in the private sector;
   — Management of demand for non-flu related health care at individual GP and secondary care levels;
   — Provision of resources for mass vaccination, diagnosis and treatment;
   — Provision of public advice by frontline staff;
   — Provision of effective triage systems;
   — Time sensitive flu management algorithms for frontline staff.

What guidance have your members or staff received as to action to be taken in the event of a pandemic?

18. The following are in the professional or public domains but there is no guarantee that staff have accessed or will access these:
   — NHS Influenza Pandemic plan October 2005;
   — Chief Medical Officer cascades and update briefings;
   — Health Protection Agency guidance and algorithms for frontline staff;
   — Recent media reports.

19. Some PCTs and trusts have issued specific advice to staff and GPs but this is the exception rather than the rule. Furthermore, exercises have been taking place at organisational level but these do not address the needs of individual staff and GPs.
What input have you, as individuals or representing bodies, had into the preparation of pandemic flu plans?

20. The BMA has made informal representations to the Chief Medical Officer. Requests have been made for regular meetings including key stakeholders.

Have changes in NHS institutional structures had an impact on preparedness?

21. Institutional structures have had an impact on preparedness in the following ways:

- Mismatch of NHS and Civil Contingencies Act related geographical planning boundaries;
- The focus on targets does not easily recognise emergency requirements;
- Resources diverted to managing NHS reorganisation leading to relative neglect of emergency planning;
- Working relationships between organisations involved in emergency planning require rebuilding after changes;
- Financial difficulties of NHS organisations restricts resources available for planning;
- There is the capacity through the new GP contract to introduce priority service areas and additional funding to back them. For this to happen successfully, the immunisation and contracting sectors of the Department of Health will need to work together.

November 2005

Examination of Witness

Witness: Dr Klaus Stohr, Team Co-ordinator, WHO Global Influenza Programme, examined.

Q199 Chairman: Dr Stohr, thank you very much for coming to talk with us. I think you have been in the room for a while already so I do not need to alert you to the fact that we are being web cast, et cetera, but thank you very much for coming to join us. Let me start the discussion by asking you if you can give us the latest information that you have on human cases of H5N1?

Dr Stohr: You are aware that the first wave of spread of human cases linked with the H5N1 outbreak in birds in Asia started in December 2003. To date there are 121 individual recorded cases: 91 in Vietnam, 19 in Thailand, seven in Indonesia and four in Cambodia. The first wave subsided in around March/April 2004, the small second wave started in August/September last year, and the third wave started in November last year and has since not subsided, so we are in the third wave which has now lasted for a relatively long period of time. This comes as something of a surprise as we had thought that the activity of the disease, the virus, in animals would be linked to the season because the cooler the weather the more the virus can survive in the environment and the more people are going to be exposed. We have noticed a reduction in the number of cases since around November last year. There is another increase now occurring with the beginning of the winter period in Asia already. All these cases have occurred in healthy, mainly young adults. The case fatality rates, the number of those who die of those infected, is in the area of 60 per cent. Well, 63 people have died of the 121, so it is a bit more than 50 per cent. The surveillance in Asia is based on hospitals. Hospital-based surveillance implies that only the severe cases are being detected and considering that normally every infectious disease has a relatively wide spectrum of the disease from mild to very severe, it is very likely that a considerable number of cases with mild disease have gone unnoticed. There are a large number of respiratory disease symptoms which resemble H5N1 in humans so it is not difficult to overlook mild cases. People will not go to the hospital if they think they have normal influenza or any other viral respiratory disease. Human-to-human transmission is something we know an avian influenza virus can cause. We are not surprised to see a limited, we call it dead-end street, unsustained human-to-human transmission of the avian influenza virus. This has happened presumably several times. It is part of the epidemiology of the virus and nothing comes as a surprise. However, it would be a profound change if this virus mutates and acquires the missing capacity to cause a pandemic with easy and fast human-to-human transmissibility. The disease is still an animal virus and it is an animal virus which is very difficult to be transmitted to humans. There may have been tens of thousands exposures of humans to the virus. You have all seen the pictures of the culling of more than 150 million birds in Asia and the way this was done—by people unprotected and people who have not been able to have access to drugs—so there has been huge exposure to this and a relatively small number in comparison of severe cases. The disease is not easy to transmit and the disease will certainly also depend on the infectious dose, and presumably infectious people do not excrete enough to infect another person or there are some other factors which play a role. The human-to-human transmission is
part of the epidemiology of avian virus but it is non-sustained dead-end street and there are normally not more than one or two links in the transmission chain.

Chairman: Thank you. Lord Taverne?

Q200 Lord Taverne: I understand that the recent research shows that the 1918 influenza virus was a pure avian virus rather than a combination of human and avian viruses. What are the implications of that? Does it make the development of transmission from person to person more likely or less likely or are there other implications?

Dr Stohr: The research on the source of the 1918 virus has been going on for several years. There has been the expectation that when it is finished we will have evidence that the 1918 virus is causal or has come directly from animals. Thus the WHO’s recommendations for control have been based on the assumption from two or three years ago that the 1918 virus was a pure avian influenza virus. Therefore, our efforts have always been focusing on trying to eliminate the animal reservoir because without the disease circulating in animals there would be no transmission to humans and there would be no chance for this virus to either—and this is one of the possibilities—to readily mutate and change its transmission characteristics. That is one of the ways an influenza pandemic virus emerges or a reassortment takes place. A reassortment would mean that the genetic information of the avian influenza virus and the human influenza virus would be swapped and the progeny virus would have the transmissibility of the normal influenza virus but, of course, the pathogenicity of these killer strains of the avian virus. The 1918 virus differs. A relatively small number of amino acids (and the influenza virus has more than 4,000 amino acids so in less than 40 of these amino acids) are very peculiar and very specific in the 1918 virus and differ from all of the other H1N1 viruses which were isolated after this. What this tells us is that presumably the small change in the H1N1 virus, which is a pure avian virus, not readily transmissible between humans, could suffice to make it an animal independent virus, jump to humans and be maintained in humans. This is a very important piece of knowledge which corroborates the WHO strategy to focus on the control of the disease in animals in order to reduce profoundly the risk of a reoccurrence of a pandemic. That is certainly one of the key conclusions. Is it going to be more likely that this virus will now change and cause human-to-human transmission? The answer is very difficult to give. The last three pandemics for which we have microbiological evidence of the source of the virus were caused by influenza viruses which were either partially or fully composed of genetic material from pig or avian influenza virus. In other words, all the past pandemic viruses in one way or another were linked to animal influenza virus. Two of the last pandemics were caused by reassortment, the mixing of avian, pig and human influenza viruses. One was caused by a pure avian virus. This is the only knowledge which helps us currently to deduce the likelihood for the next pandemic to be caused by pure avian influenza virus or by reassortment. There is a two to one probability in the future for a pandemic to be caused by pure avian virus (one) as opposed to a pandemic being caused by a reassortment of virus (two). The broad implication of these findings is certainly that we need intensified research and an understanding of how animal influenza viruses can change and which changes in an animal influenza virus will make them more pathogenic and transmissible to humans.

Q201 Lord Taverne: Does what we have learned so far suggest that it is likely to be more deadly and more virulent by being a pure avian virus?

Dr Stohr: Yes, all the evidence suggests currently that pure, non-adapted animal influenza viruses cause more severe disease in humans. The pathogenicity, the way the virus caused disease in humans in 1918 resembles very much what we are seeing H5N1 doing currently in humans. H5N1 elicits an over-exuberant immune response which is then causing damage to several tissues in the body rather than what we are seeing the normal influenza virus doing which replicates in the cells in the lung and through that mechanism causes the disease. Principally, this primary viral pneumonia issue, as we have seen in 1918, is very similar to what we have seen H5N1 doing currently in Asia in humans.

Q202 Lord Soulsby of Swaffham Prior: You mentioned surveillance systems and laboratory facilities being largely based on hospital cases, but I was also taken by your comment that this is an animal virus. In terms of animal viruses there is a report from the World Health Organisation of avian flu H5N1 from cats and we know it goes into pigs and human viruses go into pigs. What surveillance is being done in the Far East of animals other than chickens of the presence of viruses in a sub-clinical way and possibly as carriers of the H5N1 virus?

Dr Stohr: I might not be the best person to answer this question because I am working with the World Health Organisation and I am Head of the Global Influenza Programme in WHO. What I can say certainly is that the surveillance of the disease in animals in most of the countries in Asia tends to be sub-optimal. Just giving you one example, in some countries human disease was first reported before there was knowledge of the presence of the disease in animals in a situation where we know the virus does come from animals. Secondly, what is certainly also ill-understood is what role might pigs play as a
possible carrier for H5N1 virus, or as we call it a mixing vessel, where the human influenza virus and the animal influenza virus mix and this progeny virus can cause a human influenza pandemic. There were isolated events of avian influenza H5N1 found in pigs in China. However, there has been no large-scale serological investigation studies in Asia which would give us a better understanding of whether or not this virus circulates in pigs. If that were the case, the chances of the outbreak of a pandemic would certainly increase profoundly. The number of pigs exceeds by far the number of humans in Asia and there is the proximity of pigs to poultry where the virus is circulated. As far as the human influenza surveillance is concerned, there are profound differences between countries. The sensitivity of the human influenza surveillance depends on very many factors. The first one is primary health care centres, being aware and being alert. The para-medical staff, the nurses, the doctors in the field need to be aware of the clinical science and need to be attentive. Then the patient has to have access to a hospital within proximity. Normally in Asia it takes four to five days before people will come to a hospital. That means they are very sick and then they have to be transported over a very long distance. In the hospital there should also be a good triaging/screening system in the hospitals. Samples should be taken and containers should be available to ship the samples. The country needs to have a laboratory which is capable of doing a good diagnosis. Very often laboratories are not able to propagate virus because this requires higher laboratory standards. At the end of the diagnosis being made the country must be willing to share the information rapidly and completely. All this has to be in place and we see here a difference between countries. For instance, the last cases in Indonesia have been very rapidly investigated, very well detected, and the virus has been shared very quickly with the WHO. There are good examples in Cambodia where the WHO has been invited to conduct field investigations very quickly. Without field investigations surveillance is severely hampered because knowing that there is a sporadic outbreak is one thing, but the key thing to understand is whether this is the only case or are there more cases in the family who have not made it to the hospital, and whether there is somebody else sick in the village or in the vicinity because that would indicate and signal the beginning of the pandemic, possibly by a virus that has increased human-to-human transmissibility.

Dr Stohr: We have a relatively poor understanding, not only in Europe, about the pathways of transmission of avian influenza virus. If somebody were to screen birds one would expect between 10 to 20 per cent of them would have antibodies to a large variety of different influenza viruses. How these viruses are being spread between animals and within regions is relatively ill-understood. The focus for Europe perhaps now should be to have an alert general public, and to have a very well-educated group of ornithologists and hunters, as those who would be the first to detect death in migratory birds. We also need a very alert system in the agricultural sector so that the first cases of H5N1 in domestic poultry would be detected rapidly. Those are certainly the key component of surveillance in Europe.

Lord May of Oxford: Just a very quick observation rather than anything else, and it is a supplementary to what Lord Soulsby was saying. I have a manuscript that is currently under review from somebody who works in conservation biology that has tried to pull together the serological data on a whole set of different animals, mainly in South East Asia and mostly mammals, that show evidence of H5N1 at fairly low levels, but even so it is an interesting thing because the medical aspects of it have intersections with pure conservation biology aspects. You can take a larger view and say there are other reasons why we should not be shuffling these parrots around the world like this.

Q203 Lord Soulsby of Swaffham Prior: Do you think in coming westwards into Europe and in this country that there should be more testing of animals other than the avian host to see what the situation is?

Q204 Baroness Finlay of Llandaff: You were talking about having been invited into Cambodia as the WHO. I wonder whether you were able to do serological testing on contacts in Cambodia and whether you have got any data to give a better indication on the case mortality rates, because you are citing 60 per cent from the cases that are known and that is a long way away from the 3 per cent that is being spoken about.

Dr Stohr: Perhaps I can first try to answer the question about Cambodia. The WHO has country officers and we have one-third of our staff working in countries. The country officers in Cambodia have been working very closely with the ministry of health and immediately after the first suspicion that a H5N1 case had occurred our epidemiologists were invited to go to the field and support the ministry of health, and that was found to be, I hope, very useful on the part of the ministry of health and on the part of WHO, which provided the information necessary for risk assessment not only for this country but also global risk assessment to better understand outside this country what impact these cases might have. So far as case mortality is concerned, as I said, hospital infection control is the foundation, so we will be expecting a much higher case fatality rate, and
perhaps a biased case fatality rate, because the mild cases are not being seen. The models, which are being based on 1957 and 1968, would anticipate that in a mild pandemic between 25 to 35 per cent of the population would be infected. Of those 35 per cent, 46 per cent would be ill but would not need to see a doctor necessarily. A bit more than that, 52 or 53 per cent (we are close to 100 already) would require some type of medical care according to the standards and activities in Europe, North America or Japan. Around about one per cent would be so ill that they would have to be hospitalised and 0.2 or 0.3 per cent would die. These are the figures that are being based on the pandemics in 1957 and 1968, which were very mild pandemics. The total number of deaths would then be two million to 7.8 million deaths and there would be up to 28 million hospitalisations. Those who would be sick and require medical care or health treatment would be in the billions. That needs to be put into perspective. In 1918 the situation was more severe but it was not even near to what you are currently seeing so far as the numbers are concerned, which I believe is because they are biased numbers and they do not consider that there are mild cases and it would not be, from a biological and evolutionary perspective, advantageous for it to kill all its host because there the selective pressure on these viruses would be to find a good balance between killing the host and then finding time to be transmitted to the next one. That is what the evidence currently suggests, that the case fatality rate, as we have seen in 1918, might be at the very upper range of what should be expected.

Q205 Baroness Finlay of Llandaff: I was wondering whether serological testing in the field has been able to support those theories?

Dr Stohr: There have been samples taken in Cambodia from 1,200 people and China has taken samples in 16 provinces from four occupational groups. However, these samples have not been linked with very good epidemiological data to understand what the risk factors are. Fortunately, recently there have been good studies conducted in Southern Vietnam with contacts. These arrived last week at one of our H5N1 reference laboratories in Hong Kong. These samples can give a short answer but, unfortunately, there has been not enough research possible in these countries for various reasons. Ideally, one could look, for instance, into blood donors and one would also have a biased population but that would give a very good indication of what is the background noise between these latest instances.

Q206 Baroness Perry of Southwark: Just a supplementary to your very helpful answer to Lord Soulsby’s question. In the countries most at risk of a pandemic, do you feel that there are political factors which are preventing adequate surveillance? Also, in your own work in the WHO what sort of cooperation are you getting at national level from these countries?

Dr Stohr: Principally, on the part of WHO of course we assist countries and countries assist us also in order to support the larger public health community. The assistance which we would hope to receive affects three areas. One is the very rapid detection and notification of cases. This will be very important to ensure that the rapid response stockpile of antivirals can be used in a timely fashion. It will also be important that the virus is shared with the WHO. That is the assistance we also hope we would receive. That would have implications certainly for the announcement of the pandemic because of course epidemiologically one cannot confirm that a pandemic virus has emerged; one has to do this in a laboratory. Secondly, it is important for WHO virologists to provide up-to-date diagnostic test kits to our member states. Thirdly, of course the virus would be important to turn it into a vaccine prototype 3-D that can be given to the governments. The third area is that currently we would also hope that countries assist in co-ordinating the research effort. Research efforts are particularly important in the area of the epidemiology of the disease. We still have only a limited understanding of the excretion pattern of the virus and the antibody genetics and other factors which could inform policy on hospital infection control and how people are infected. All these areas would require co-ordinated research for which we need more assistance from our member states. The serological studies were mentioned and that is something we would be keenly interested in conducting, but it is very costly and it requires support from countries. Thirdly, what is also important is the prevalence studies of the virus are being initiated in animals. There is a different level of support required from the currently infected countries. I have given already a good example from Indonesia of the rapid sharing of viruses, participation in field investigation, prompt announcement of cases. Cambodia is in a very similar situation. Thailand had a web site from the very beginning on which every day the number of suspect cases was being reported as well as those taken off the list which turned out not to be positive or put on the list those which turned out to be positive. So these are very, very good examples of good collaboration. There are various surveillance systems, particularly in animals. I think the presence of an economically important animal disease may or may not necessarily be in the interests of a given country. If a country announces that it had H5N1 in animals it would have to suffer consequences as far as trade is concerned. Countries like Thailand, for instance, which is where
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27 October 2005
Dr Klaus Stohr

Poultry production is the fourth largest contributor to the gross national product, will be heavily affected from the consequences of this announcement. Sometimes also the control of the disease in animals may not necessarily support the reduction of the risk for the disease in humans. So there are certain areas. What we are seeing in the field generally is there is an increased understanding of the importance of fast investigation, reporting, and that comes certainly at a time where several countries have to realise that the disease is endemic in their territories. The FAO and other agricultural organisations would conclude that this will not disappear on its own and even with co-ordinated efforts it will take several years before H5N1 is going to be eliminated in Asia, so we have to live with the situation currently where we have to be planning long term and as long as the disease does exist in animals we have also to expect that sporadic human cases will occur and there is the risk of a pandemic.

Q207 Baroness Perry of Southwark: Are you confident you will have that level of co-operation in China?
Dr Stohr: I cannot speak for the agricultural sector because that is not my main area of knowledge and influence.

Q208 Baroness Perry of Southwark: I understand that.
Dr Stohr: But what we are seeing in Thailand is that the government has made enormous efforts to control the disease. There have also been announcements that Thailand is seen as an example on how the disease can be controlled in animals. The unfortunate reality now after one and a half years is that certainly five of 72 provinces in Thailand still report the presence of disease in animals. We have to come to grips with the reality which is if we do not devise a strategy which is long term and which takes into consideration the need for international co-ordination that we may have to live with the disease for much longer than anybody anticipated before.

Q209 Baroness Perry of Southwark: I asked about China, do you have confidence that China will cooperate?
Dr Stohr: China has shown after SARS, as you know very well, that these are not only being reported and recorded but also announced internationally. I can give you an example today for instance, there is information on one suspected case of H5N1 in humans in China. This has been reported and very transparent. We have received in the last couple of months viruses very, very regularly from the agricultural sector. The cases in Central China in Inner Mongolia near the south western border have been reported immediately and teams were allowed in. On the other hand, of course we see that China has been using billions of doses of H5N1 influenza vaccine for many years. That may have been the reason. However, as I said, in the disease currently if there are outbreaks or if there are events the WHO is notified very quickly and we are satisfied with the co-operation.

Q210 Lord May of Oxford: A quick supplementary. The best way, if the virus does hop into the human population human-to-human, would be to try and control it at the place where it first appeared. I am sure you are more familiar than I am with the two papers, one from the NIH and the other from here from the Ferguson group, that suggest if you acted very promptly with appropriately geographically targeted antiviral prophylaxis you could, provided this flu is roughly as transmissible as earlier ones, control it. I wonder whether your feeling is that that is a realistic hope, and if it is a realistic hope whether the machinery is being put in place in South East Asia, which is probably the right place, to try and achieve it or is it just that the realities on the ground preclude the possibility of doing that?
Dr Stohr: The reality on the ground would not preclude it. The chances are not huge that it is going to succeed. However, it could not be forgiven if we did not try to do it even though the chances may be relatively small. The models say it can work; the reality would say we have areas in Asia where 80 per cent of the country can only be reached by four-wheeled drive vehicles; where the challenge is to treat in 10 to 15 days 80 per cent of a population with a drug which has to be taken over a certain period of time; where you have to have a very high compliance rate; where you have to practically seal off the territory and make sure nobody gets in or out. It is a huge challenge which has to be accepted and taken into account. We will have by the end of this year, from information from one of the major antiviral, one million treatments and by March next year three million treatments to try it out. Our current challenge is to put into place a system whereby these drugs can be rapidly deployed in the field. We are not there yet, we have to say that. It will also require co-operative companies to try it out to pilot test the system. We know it can be successful. Polio has shown that with the vaccine given to a large amount of people in a very short period of time. The infrastructure is there and the knowledge is there but we have to try it out.
Chairman: Lord Patel?

Q211 Lord Patel: I think Lord May asked the question that I was going to ask. You mentioned just now the one of the industry companies, Roche, had offered three million doses of Tamiflu. I think what I hear you correctly to say is that you have plans to use this to contain the disease if there is an outbreak and
you have the means of proper storage and distribution?

Dr Stohr: The storage, the warehousing, the rotation is taken care of by the company. The WHO is not involved. It is reassured that this has been taken care of by the company. The company will also deliver the product to the destination which the WHO will identify within a very short period of time—24 to 48 hours. This will all be taken care of by the company. Our task will start with a risk assessment triggering the rapid deployment and then, of course, the putting into place the infrastructure so that the drug can be given to those who need it. That is the real challenge now. That is what I am saying where we are not where we would like to be.

Chairman: Let us move on. Lord May had a question.

Q212 Lord May of Oxford: I would like to ask you not to be too polite about this and tell us exactly what you really think. What is your assessment of the UK’s pandemic influenza contingency plan? How do you feel it compares to other countries, both in the OECD and others?

Dr Stohr: The UK has published its contingency plan in, I think, the autumn of last year. If you compare this internationally there are less than 50 countries which have published their national pandemic plans. Sometimes if you count the pages the quality is one page. Others have very comprehensive plans—Canada, UK, US, Australia and also Japan. Very few countries have translated their plans into national law. The quality of the plans, in our view, will not only depend on how comprehensive it is but also how much the plan is translated into policy activity and how much is it underpinned with activity in the field. The UK plan has all the components—communication, co-ordination, surveillance, information-gathering, the public health response, the medical response, the Civil Service response to reduce social disruption, but the WHO has not conducted a very in-depth analysis of this plan. That is not our duty but I must say we would be very happy if we were to be inundated with requests to assess pandemic preparedness plans from developing countries. Unfortunately, this is not the case. We are focusing on trying to find resources and support also from developed countries in helping us to increase the number of countries in the developing world to which have thought through the huge challenges of a pandemic in the absence of antivirals, which is probably the case for most of them.

Q213 Earl of Selborne: Very quickly, following on from that answer, given the risks to the international community and the fact that, as you say, not every country is able to produce the contingency plans you would wish, have you got just one headline message as to what the international community needs to do in the longer term to reduce the risk of influenza pandemics?

Dr Stohr: Influenza pandemics—and I would like to focus on those—have been part of our normal life in the past and they will be coming in the future. However, there is a panacea and there may be a solution not only to the current unsatisfactory use of the influenza vaccine but also to the situation where there will be (and there is no doubt about this) a lack of vaccines and antivirals during the next pandemic. There are no possibilities currently to stock vaccine. We believe that the international research community—and here governments will have a very important role to play—should try to find solutions to develop a vaccine compound. There are indications that it is possible with $500 to $800 million and in 10 years’ time that a vaccine can be developed which can be given to protect not only against influenza but also in the long term to prevent the impact of a pandemic. That is one response. The other response certainly that is required is long term further strengthening of disease intelligence, disease detection, and alert and response mechanisms by countries as well as by the global response and alert capacities to detect the emergence of infectious diseases and control them. I would like to expand a little bit more on this if time would permit because that is very important for the WHO. Our capacity to respond to emergencies like a influenza pandemic will depend on the capacities of the member states to detect and respond and also upon the WHO’s and other international players’ capacity to regionally and locally co-ordinate the response. If the WHO is going to be able to live up to the expectations, the resources which are currently available to do this will not suffice. There is no doubt about this. We would hope there will be in the future a match between the demand to transform the WHO into an operational organisation as well as the support which we receive from the international community.

Q214 Chairman: Could I infer from what you are saying there that your feeling is that overall, let’s say, the leading western nations are not doing all that they could do to help contain this situation?

Dr Stohr: I believe the world as well as each individual country is certainly not entirely prepared for an influenza pandemic. A pandemic is always about damage control. The best preparedness will not avoid people dying or getting sick. 25 per cent of antivirals for a country will mean a reduction in hospitalisation by about 75 per cent but there will still be people who will require hospital care and there will still be people who are going to die. An ideal pandemic preparedness status does not exist. We can only get as close as possible. There are currently ten countries which have antiviral stockpiles for more than 20 per cent of their population. There are 37
countries which have put orders in for antivirals. There are nine countries which will have access to vaccine, and globally there are 250 countries that may. This shows what the gap is. If all the antivirals which exist currently were to be homogeneously globally distributed, it would suffice for two per cent of the world’s population. Seeing this in context I think the argument as to whether or not we are properly prepared will come on its own.

Q215 Chairman: I think in this country we are placing an order for something like 14 million Tamiflu doses. How does that compare with other countries? How does that compare with other European countries like France for example? Dr Stohr: It compares very well. That will suffice, if I understand it correctly, for 25 per cent of the population in the UK—

Q216 Chairman: — It does or it does not compare very well?

Supplementary evidence by Roche Products Ltd relating to comments by Dr Klaus Stohr

INTRODUCTION


Roche has since been asked to provide additional information, further to a public session of the Select Committee at which oral evidence was given by Klaus Stohr, Head of the WHO Global Influenza Programme, relating to the global use of antivirals to slow a pandemic at its source. The requisite information relates directly to the Roche donation of 3 million treatment packs of Tamiflu to the WHO 'Rapid Response Stockpile' and has been requested as follows:

— when will the 3 million treatment courses of Tamiflu donated by Roche be made available to the WHO?
— where the 3 million treatment courses of Tamiflu donated to the WHO by Roche will be stored;
— how the 3 million treatment courses of Tamiflu will be released and distributed in the event of an pandemic outbreak;
— the part the WHO Rapid Response Stockpile has to play in curtailing an initial outbreak of potentially pandemic influenza.

ADDITIONAL INFORMATION

When will the 3 million treatment courses of Tamiflu donated by Roche be made available to the WHO?

There are ten capsules in every treatment course of Tamiflu.

The first 10 million capsules will be available within Roche in bulk form in December, 2005 and then final packs will be available for shipment during February 2006. The remaining 20 million capsules will be available in bulk form during March 2006 and in packaged form during April/May 2006.
This donation has not affected any government pandemic orders that are in the ordering system with. When discussions with the WHO were initiated at the beginning of 2005 an order was placed into the pandemic ordering system which has resulted in the timelines of December 2005 and March 2006.

Where will the 3 million treatment courses of Tamiflu donated to the WHO by Roche be stored?
The “Rapid Response Stockpile” will be stored by Roche or by a designated storage company until such time as WHO requests Roche to ship the material.

How will the 3 million treatment courses of Tamiflu be released and distributed in the event of an pandemic outbreak?
In the event of a pandemic Roche will ship the “Rapid Response Stockpile” to a major international airport nearest to the site of outbreak of the infection. The ownership of the drugs will then immediately transfer to WHO, who will take responsibility for transportation, distribution and local storage.
Apart from the costs associated with local distribution, this will cost WHO nothing, as this is a donation by Roche to help contain an emerging outbreak of a pandemic strain of influenza and to slow or prevent its national and international spread.

The part the WHO Rapid Response Stockpile has to play in curtailing an initial outbreak of potentially pandemic influenza.
The purpose of the “Rapid Response Stockpile” is to contain an emerging outbreak of a pandemic strain of influenza at the epicenter and to slow or prevent its national and international spread. The “Rapid Response Stockpile” is not a replacement for national pandemic preparedness plans and governments should follow the WHO guidance and ensure that local pandemic plans are in place and stockpiles of antivirals are assembled in good time.
Recently 11 Asian countries (Bhutan, Brunei, Burma, Cambodia, China, Thailand, Japan, Laos, Malaysia, the Philippines, Thailand and Vietnam) have agreed to establish a shared stockpile (5 per cent of their supplies) of Tamiflu in preparation for an avian influenza pandemic and to ensure supplies of Tamiflu can immediately be deployed to areas affected by an outbreak of avian influenza.
The WHO Rapid Response Stockpile is not intended to be used for purposes other than addressing a novel and potentially pandemic strain of influenza.

7 November 2005
TUESDAY 1 NOVEMBER 2005

Present: Broers, L (Chairman) Perry of Southwark, B
Finlay of Llandaff, B Selborne, E
Howie of Troon, L Sharp of Guildford, B
Mitchell, L Sutherland of Houndwood, L
Patel, L Winston, L
Paul, L

Memorandum by the Department of Health

INTRODUCTION

1. The Government particularly welcomes the House of Lords Science and Technology Committee’s initiative in conducting an inquiry into the United Kingdom’s preparations for an outbreak of pandemic influenza, which is both timely and topical.

2. In response to the call for evidence, this memorandum outlines the cross-government work the Department of Health (DH) is leading in conjunction with the Cabinet Office Civil Contingencies Secretariat (CCS), Devolved Administrations and other government departments and with support from the Health Protection Agency (HPA), to:
   - improve UK health preparedness and response;
   - strengthen international and national influenza surveillance capacity;
   - improve assessment;
   - commission research and development;
   - provide essential medicines, vaccine and other supplies;
   - produce timely public information and advice;
   - develop arrangements at national, regional and local levels to manage the wider impact and co-ordinate the response to such an event.

This work is being co-ordinated through a cross-government group which includes membership from the key departments involved in planning for an influenza pandemic.

How is the risk of pandemic influenza emerging/spreading assessed, can it be improved?

3. The widely held expert view is that there is a continued risk of pandemic influenza emerging from south east Asia; either arising from re-assortment of the currently circulating avian H5N1 viruses or another new virus subtype emerging. This risk is assessed on the basis of:
   - the extent and geographic spread of the current H5N1 outbreaks in poultry and in migrating aquatic and other birds;
   - the extent, severity and geographic incidence of avian flu in people;
   - the extent of antigenic change in current H5N1 viruses, compared to the viruses which first emerged (in 1997);
   - historic knowledge of the evolution of influenza viruses and of previous influenza pandemics;
   - the demography of the region and opportunities it provides for interchange of genetic material between influenza viruses from different species.

There is a possibility that a pandemic could emerge in another part of the world if the outbreaks of avian flu in poultry spread further than south east Asia. The risk of a pandemic originating in the UK is considered to be remote.

4. The epidemiological and virological information for assessing the risk is collected and interpreted by the World Health Organisation (WHO) and World Organisation for Animal Health (OIE). The European Commission (EC) undertakes assessments on behalf of Member States of the European Union and assessments are also undertaken by HPA and by the Veterinary Laboratories Agency to inform contingency planning by the DH and the Department for Environment Food and Rural Affairs (Defra).
5. UK modellers are amongst the international leaders in using mathematical modelling to assess the risk of the emergence of pandemic influenza and—once confirmed—the time it might take to reach this country. One group has recently published (in Nature) an assessment of the possibility of averting a pandemic spreading from a source in south east Asia following identification of the earliest cases. DH is drawing together the conclusions from UK modellers, including outputs from the HPA, in its preparatory work for a possible pandemic. The results from the modelling work stream are also reviewed by the DH Scientific Advisory Group.

6. Data on the extent to which less severe and sub-clinical infections are occurring in south east Asia—and from ongoing detailed characterisation and phylogenetic analysis of the prevalent viruses to detect antigenic drift or shift—are amongst some of the most crucial evidence. National and international efforts, co-ordinated by WHO, to ensure that appropriate epidemiological (including serological) studies are being performed and that a suitable range of viruses are sent to specialist virology laboratories for analysis, would improve assessment and increase confidence.

**How great are the risks, what confidence can be put on assessments?**

7. As we have never been in such a position before, the risks of a pandemic emerging can only be based on informed expert judgement. Projections of the likely impact of a pandemic are included in the UK Influenza Pandemic Contingency Plan. Those are the best available based on current knowledge, previous experience and mathematical modelling, in which the UK is acknowledged to be one of the world leaders. The Plan therefore provides ranges of potential impact as well as the “most likely” scenario for planning purposes. Those projections would need reviewing and revising in the light of emerging evidence as a pandemic develops. The Office of Science and Technology is leading on the Foresight project on the detection and identification of infectious diseases, sponsored by Lord Bach, with the support of DH, other departments and international organisations such as WHO, FAO and OIE. This international initiative will assess the nature of future risks (10–25 year horizon) and explore how the novel and innovative application of science and technology might feed into the new systems to affect step-changes in capabilities to detect, identify and monitor infectious diseases. The results, due to be published in spring 2006, will aim to inform strategies for the long-term management of the risks of infectious diseases in animals, humans and plants and explore potential synergies between them.

**How is the UK working with international bodies to monitor the development of the virus and reduce the risk of pandemic influenza emerging and spreading?**

8. The UK is active in supporting international efforts to detect, contain and respond to a pandemic. It leads the influenza pandemic work stream of the Global Health Security Action Group jointly with the USA, has hosted a meeting of mathematical modellers and participates fully in WHO and EU work on influenza.

9. The UK hosts one of the four WHO Collaborating Centres for Influenza at the National Institute for Medical Research. The Institute receives viruses for detailed virological analysis and its laboratories—with those of the National Institute for Biological Standards and Control and the national influenza reference laboratory at HPA—work together closely and are all involved in advising WHO.

10. The UK has also given WHO additional funding to improve surveillance in south east Asia and a senior UK epidemiologist—now seconded to the European Centre for Disease Prevention and Control to co-ordinate their influenza work—has assisted in the risk assessments.

11. UK modellers from HPA and Imperial College London are involved in advising WHO on the likely impact of public health measures and on the possibility of early intervention controlling spread. The UK continues to share and exchange experience in pandemic preparedness planning at EU and WHO levels and to contribute to their efforts to support those countries whose plans are less developed.

12. The Department for International Development (DfID) also provides funding to WHO and has encouraged UN agencies to use existing resources to focus on avian flu as a potential precursor for a flu pandemic. It is also urging relevant UN agencies to work with affected countries to develop affordable plans for tackling avian flu and improving wider pandemic preparedness. DfID may devote further resources if additional support is needed. Defra has also provided technical supplies and expertise to WHO, FAO, and to individual countries.

1 available at www.dh.gov.uk/pandemicflu
13. Health Ministers are open to preliminary WHO proposals to establish international stockpiles of counter measures providing it can be shown that they could be deployed effectively and would actually help reduce the risk or delay international spread.

**What is the current assessment of the likely impact of pandemic influenza on the UK in health and wider terms?**

14. Based on current knowledge, analysis of past pandemics, published evidence and mathematical modelling, the likely range of health impacts and various planning assumptions are described in the Influenza Pandemic Contingency Plan. The Plan also describes the most likely scenario for planning purposes. This assumes that around 25 per cent of the UK population will suffer from flu over the course of the pandemic. The modelling also suggests that at least 80,000 people will require hospitalisation and a minimum of 50,000 people may die.

15. Meeting the additional demands of a pandemic would be a major challenge for all health and social care organisations. Higher staff absences, any travel difficulties, possible shortages of essential supplies and disruptions to the wide range of basic supporting services on which modern health services rely are examples of the type of factors likely to add to response pressures.

16. A Ministerial Group on Consequence Management and Resilience oversees UK preparations to respond to a pandemic and to manage its consequences. DH, with CCS support, leads cross-government work to assess the impact, develop plans and to mitigate the wider social and economic consequences of pandemic influenza. That work recognises that:

- an influenza pandemic is potentially a major disruptive threat to every part of the UK;
- robust and resilient inter-agency contingency plans are required to mitigate its effects;
- plans must be inclusive and recognise inter-dependencies;
- clear leadership at all levels will be a critical success factor;
- arrangements for clear public advice and communications are essential;
- effective co-ordination is vital at national, regional and local levels.

17. Cross-government work-streams are also making good progress in addressing non-health issues. They include social interventions, maintaining essential services, dealing with fatalities, business continuity planning in non-health sectors and care of British nationals overseas in conjunction with the Foreign and Commonwealth Office (FCO).

18. A pandemic will have a major international impact on trade, travel and the world economy. It has the potential to increase international tension given likely disparities in its impact and differences in the economic and infrastructure capacity of nations to respond. Securing supplies of essential materials and priority for pharmaceutical products are examples of potentially difficult international issues.

19. The UK economy would be affected by an influenza pandemic. Preliminary estimates of the impact can be made based on the planning assumptions in the UK Health Departments’ Pandemic Influenza Contingency Plan i.e. absenteeism from work (cumulatively 25 per cent of workers off sick over the pandemic period) and a case fatality rate of 0.37 per cent.

20. Undertaking an economic assessment of a hypothetical event like a flu pandemic is inevitably difficult and subject to significant uncertainties. Moreover, the actual economic impact would be conditional on the nature of the pandemic virus and on the prevailing economic circumstances. The overall effects would also depend on how companies and individuals adapt to the onset of a pandemic. The assessment is therefore relatively simplistic and should be regarded as being for illustrative purposes. In particular, it is likely to represent upper bounds of the potential impact of an outbreak. It suggests that illness-related absenteeism from work by 25 per cent of employees could reduce the year’s GDP by £3 billion–£7 billion or 0.3 per cent–0.6 per cent. Premature deaths could reduce the year’s GDP by a further £1 billion–£7 billion depending on whether case fatality rates are low (0.37 per cent) or high (2.5 per cent) and on whether earnings or gross output is used in calculation. In the longer term, the impact of premature death could reduce future lifetime earnings by £21 billion–£26 billion at a low and by £145 billion–£172 billion at a high case fatality rate.

**Are measures described in the Plan adequate, what more could be done?**

21. The UK Influenza Pandemic Contingency Plan, revised in March 2005, reflects the most current information, advice and assumptions at the time of publication. It sets out a range of contingency measures that are proportional to the potential threat and designed to improve health and wider preparedness. It also provides advice and information to support local preparations and the UK’s progress in developing
contingency arrangements has been recognised by a WHO visiting team and others as an example of good national planning. However, planning is ongoing and knowledge developing. In keeping with the intention that it be a living document, a further revision will be available later this year.

22. The scale and nature of the challenge leaves no room for complacency and the Plan recognises that gaps remain. Domestic and international vaccine development and manufacturing capacity, expanding community and acute health provision, increasing laboratory capacity, maintaining essential supplies/services, modelling the potential health benefits of various social measures and exploring whether priority access to treatment or prevention for essential workers could be effective are examples of further work in hand.

23. Self-help measures for the public and private business continuity planning across all sectors will be key to minimising effects of a pandemic. The interdepartmental group has been promoting and encouraging business continuity planning across all sectors in preparation for possible pandemic; building on greater awareness and emphasis on key business activity over recent years.

How well prepared/coordinated are health, emergency and other services?

24. The UK has well established civil contingency mechanisms at national, devolved, regional and local levels to co-ordinate the response to any major disruptive challenge, including influenza. Within that mechanism, DH is the lead department for a pandemic. It has formed a National Influenza Pandemic Committee to provide specialist advice on the health response, supported by a Scientific Advisory Group to provide detailed scientific advice. Strategic Health Authorities (in England) are responsible for overseeing health planning and coordinating the local response.

25. Operational guidance—issued by DH in May—requires health organisations to focus on pandemic influenza as part of their contingency planning with advice, expertise and support from HPA. DH also produced a planning framework for using antiviral medicines in September, national guidance on clinical management, and guidelines on infection control are due to be released shortly and planning advice and information for influenza vaccination is being developed.

26. Regional Resilience Forums have greatly increased the focus on business continuity, maintaining essential services and planning for the wider aspects of pandemic preparedness. Health organisations participate in those forums and Regional Directors of Public Health help ensure that plans are harmonised and coordinated. International, national, regional and local exercises have been organised with HPA support to test various aspects of the arrangements and an on-going exercise programme arranged.

27. This is underpinned by the statutory duty in part one of the Civil Contingencies Act, which comes into effect in November 2005 and requires all category one responders to plan for emergencies and to have effective business continuity planning arrangements in place.

What is being done to increase public knowledge and awareness?

28. An effective communications strategy is a major component of the Government’s pandemic preparations. Research commissioned by DH earlier this year suggested that the general level of awareness and understanding of influenza amongst health professionals and the public is currently very limited. Timely advice and information will help prepare the population for the potential impact of a pandemic and be critical to its management.

29. The DH communication strategy is based on increasing understanding of seasonal and pandemic influenza before any pandemic vaccination and preparing materials and systems to:

— convey accurate, timely and consistent advice to the public and health professionals if alert levels increase;
— promote awareness and understanding amongst the general population;
— explain how the NHS, DH and government as a whole intend to minimise the impact of a pandemic as far as possible and some of the constraints;
— give advice on self help and preventative measures.

30. The FCO provides routine advice to travellers. Further work underway, led by DH, includes communicating with “hard to reach” groups, building a portfolio of stand-by broadcast/print materials, developing an advertising brief, producing leaflets on antiviral use and vaccination, research and material pre-testing and training materials for frontline health staff.

31. In addition to material to increase awareness of seasonal influenza the DH website has pandemic material available including:

— The UK Health Departments Influenza Pandemic Contingency Plan;

www.dh.gov.uk/pandemicflu
— Operational Guidance for NHS planners;
— The Chief Medical Officer’s guide “Explaining pandemic flu”;
— A Pandemic flu key fact sheet;
— Frequently asked questions;
— An information leaflet “Pandemic flu, important information for you and your family”—also available in health clinics and surgeries.

32. The Government’s News Co-ordination Centre is set up to manage the communications aspects of a crisis, emergency or other disruptive challenge and supports DH as the lead government department by providing co-ordinated media and public communications.

Is the UK’s stockpile of antivirals adequate, how will it be distributed, what steps to ensure access to antiviral treatment and vaccine in a pandemic?

33. Until an effective vaccine is available—or as an adjunct to vaccination—antiviral medicines may lessen the severity and duration of illness, reduce the need for antibiotics and lower demand for hospital care. Antiviral medicines are used to treat seasonal influenza but normal stock levels would be inadequate in a pandemic, international demand is already high and rapid post-event supply would be unlikely. UK Health Departments are therefore building stockpiles of 14.6 million treatment courses of oseltamivir phosphate (Tamiflu) which will be complete by December 2006.

34. The UK is securing one of the largest stockpile of antivirals as a proportion of population, which will allow for treating all influenza patients at a cumulative clinical attack rate of 25 per cent or less. It is impossible to predict the attack rate, but 25 per cent is generally considered prudent for planning purposes and is recommended by WHO as the basis of national plans. Should the actual attack rate prove higher—or until the stockpiles are fully established—priority for treatment will be given to those frontline health staff at higher risk than the general population and patients considered at most clinical risk of complications.

35. A planning framework describing arrangements for the storage and distribution of antiviral medicines, their use and the local planning needed to make them rapidly available to patients was issued to health planners by DH in September and is available on the website.

What is the role of vaccine development, manufacture, distribution?

36. Although it remains the most effective countermeasure, a strain specific vaccine is unlikely to be available at the start of a pandemic. To produce an influenza vaccine, manufacturers need a suitable reference strain of influenza from which to derive seed stocks. This has to be produced from the wild-type strain causing disease by re-assortment or reverse genetics and must be safety tested before use. Developing the seed stocks normally takes around two months. It would take about six months in total before production can start in earnest, but that is dependent on manufacturers changing use of their facilities from routine to pandemic vaccine production.

37. It may be possible to shorten the time to develop a vaccine to two months by having already prepared and tested a library of reference strains, which is constantly updated as new strains emerge. This depends on the existing strain being reasonably close to the pandemic strain and providing cross-protection. A small amount of additional time could be saved if seed stocks for manufacture were prepared in advance and by undertaking tests on candidate material for vaccine production in parallel rather than in sequence could also assist.

38. Once developed, demand would far exceed international vaccine manufacturing capacity, which is currently based on seasonal influenza vaccine demand and globally sufficient for only about 5 per cent of the world population. Supplies could be limited to those countries that have negotiated the advance purchase of manufacturing capacity in the first instance. In conjunction with the NHS Purchasing and Supply Agency (PaSA), HPA and vaccine manufacturers, DH is actively exploring a range of preparatory steps to improve the prospects of early delivery of pandemic influenza vaccines. This work—much of which is commercially sensitive—includes:
— developing “mock up” or prototype vaccine;
— the production of vaccine “seed stock”;
— encouraging manufacturers to submit dossiers on prototype vaccine for regulatory approval;
— exploring the possibility of reducing the time needed to determine the pathogenicity of reference strain;
— investigating novel methods of manufacture;
— discussing options for priority supply;
— purchasing a supply of H5N1 vaccine to protect health and other front line workers required to respond to an influenza pandemic arising from the strain currently circulating in south east Asia (currently being finalised).

39. Whilst research to accelerate pandemic flu vaccine development may benefit from international co-operation, sharing inadequate supplies may be counter productive. DH officials have met representatives of all appropriate vaccine manufacturers to discuss vaccine development and capacity issues.

40. DH officials have also met with a company that is developing DNA influenza vaccine—which might be a longer-term possibility—and have commissioned and received a consultant’s report on antigen sparing methods such as intradermal inoculation and other ways to extend supplies of vaccine. DH has also commissioned an external independent expert review of what possible role national institutions such as HPA Porton could play in accelerating protection against emerging infectious diseases such as pandemic influenza.

What is the long term strategy for reducing the pandemic threat?

41. The influenza virus has already shown its adaptability and resilience. Eradicating the threat is unlikely to be achievable in the immediate future. A range of veterinary and social strategies—particularly improved animal husbandry, veterinary control and education—in potential source countries would help reduce the risk of antigenic shift and improving understanding, research, mathematical modelling and surveillance will assist in developing more effective counter measures.

42. Advances in pharmaceuticals and other health care improvements can reduce the transmission and severity of influenza illness: thus reducing morbidity and mortality and slowing or limiting a pandemic’s spread. DH is also working with Research Councils UK to take forward issues relating to the UK’s national preparedness and response strategy.

CONCLUSION

43. The UK has made good progress in preparing for the health and wider effect of an influenza pandemic and raising awareness of its potential. Its high-probability, high-impact nature leaves no room for complacency and demands on-going attention to ensure the progress made is maintained and improved. The Government is committed to maintaining that momentum.

September 2005

Examination of Witnesses

Witnesses: Ms Rosie Winterton, MP, Minister of State for Health Services, Dr David Harper, Chief Scientist, and Dr David Salisbury, Head of Immunisation, Department of Health, examined.

Q218 Chairman: Minister, welcome. Thank you very much for coming to give evidence to us today. As you will be aware, this is our fourth hearing into pandemics, and it is very important at this stage that we have a chance to hear from you. You need no introduction, but perhaps for the record you would introduce yourself and your colleagues, please.

Ms Winterton: Yes. I am Rosie Winterton, Minister of State for Health Services. I have with me Dr David Harper, who is the Chief Scientist from the Department of Health, and Dr David Salisbury, who is Head of Immunisation at the Department of Health.

Q219 Chairman: You will be aware that we are being webcast today and that webcast may be taken by some of the broadcasting companies. May I open the questioning by asking you what is your assessment of the likelihood of a pandemic occurring and of its likely timing?

Ms Winterton: It is highly likely that at some time in the future, as the Chief Medical Officer has made clear, a pandemic will develop, but it is quite impossible to say with any certainty when that will happen. All I can do really is to reassure the Committee that we have experts in this country, and we are in contact with international experts, who give us the best evidence that they have as the situation develops.

Q220 Chairman: What is your assessment of the recent media coverage of avian flu and the possibility of a pandemic?

Ms Winterton: I think the recent media coverage has shown how important it is for us to perhaps redouble our efforts to make sure that the media are aware of the true situation, that they
understand the difference between avian flu, seasonal flu and a pandemic and the fact that at the moment there is no evidence of a pandemic, but obviously, there have been occurrences of avian flu being caught by humans. But the fact remains the same, that this avian virus is not something which is easily passed between humans. I think it is very important that we are quite clear about the distinction between that, because otherwise we do get rumour and misinformation which gets in the way of communicating a clear message to the public and also to other professionals.

Q221 Earl of Selborne: Minister, I wanted to ask about costs and projected costs, first of all of the Government’s contingency planning for pandemic influenza, how this might compare with the possible cost of pandemic, and perhaps to what extent the Government investment in contingency planning has been subjected to any cost benefit analysis.

Ms Winterton: There are some very clear figures that we can give in terms of costs. For example, £200 million that we are spending on antivirals, and some slightly broader figures that we can give in terms of the H5N1 vaccine that we are purchasing. If you were to take the same cost as that would be for seasonal flu vaccine, that would be in the region of £30 million. In terms of communications plans, we would be able to put a figure in the region of £25 million, but I should emphasize that that is for a full escalation as well of a communications plan, in a sense, the worst case scenario. We have obviously said that we will put in orders for something like 120 million doses of vaccine if and when that becomes possible. Those are some straight figures, along with something like £0.5 million to the World Health Organisation to improve surveillance in south east Asia. Those are some figures that we can be firm about. Other figures—it is not quite so easy to separate that out from general resilience planning, which has taken place across government for all sorts of emergencies, for general emergency preparedness. That happens across government, but it is quite difficult to put an actual figure on that, except to say that there has been an increase in general planning for emergencies since, obviously, 11 September 2001. There are some very firm figures, there are wider figures for cross-government planning and it is quite difficult to separate out a pandemic cost in that, and in terms of the wider figures, we have submitted some figures to the Committee which talk about possible costs to the economy itself, but again, some of those depend, of course, on the severity or otherwise of a pandemic.

Q222 Earl of Selborne: I wonder, Minister, if you could relate that to the possibility of a cost benefit analysis. Has that been practical or possible or has that not been attempted?

Ms Winterton: In a sense, what we have to do is look very clearly through all the advice we have as to what we need in terms of combating any pandemic, and I suppose if we were to talk about cost benefit analysis, would it be appropriate to use the example perhaps of purchase of antivirals, where we have said that we believe that this should be used for treatment and not used prophylactically? I do not know whether that would have been subject to a cost benefit analysis. Perhaps I could ask David Salisbury to come in on that.

Dr Salisbury: In principle, vaccines are by and large cost-eficacious compared with many other medical interventions. When we routinely do cost benefit analysis, we find that for the greater part vaccines are favourable. Certainly, in this instance, we would anticipate that, given the potential burden for a pandemic, both in direct and indirect costs, and what we know of vaccine costs and what we know of antiviral costs, we would expect, again, that this would be a good investment in everything that we can do to either prevent or mitigate the consequences. Since we do not have prices for a vaccine that does not yet exist, of course, the best we can come up with is indicative guides, but were we to undertake the sort of routine cost benefit analysis that we would do under other infectious disease circumstances, we would find that this would be a good use of resources.

Q223 Lord Mitchell: I want to ask whether new money is being made available from the Treasury with respect to this whole pandemic issue. We are going to be asking several questions today. We have talked about vaccines, we have talked about antivirals, and we are going to be talking about manufacturing capability and many of the other things. I just wanted to know whether, since the heightened awareness of this pandemic issue over the last six months or so, new money has been put into the equation, or is it just shuffling around within the Department to make it available?

Ms Winterton: As I understand it, there is a mixture of the two. Some of the planning that is done has involved using existing resources, but certainly in some of the more far-reaching expenditure, we have obviously had to seek Treasury approval. Perhaps I could give the example of the purchase of vaccines, where in a sense we would undertake a contract which would mean that we have to put some money down to say that if necessary, we will purchase 120 million doses of a vaccine. That obviously requires getting approval for a figure in the future but that
Q224 Lord Mitchell: If we were speaking to Roche or some of these companies, would they see it that way as well? Would the manufacturers of the vaccines see that that is the case?

Ms Winterton: The discussions are ongoing with manufacturers at the moment, and my colleagues here will be undertaking those, obviously with all due commercial considerations taken into account. To what extent they will be entering into discussions that they may or may not have had with the Treasury with manufacturers, I would not like to speculate.

Q225 Lord Sutherland of Houndwood: Minister, you suggested money would be payable “as and when”. Does that include “if” it is necessary? In other words, is it possible that the money would not be payable? I think this is part of the point that Lord Mitchell was pressing.

Ms Winterton: If it was impossible to actually manufacture a vaccine to deal with the virus, which I suspect is highly unlikely. Once we know what we are up against, the work can take place to put the manufacture of it into practice, but the idea of the contracts that we have secured is that the final payment is made on delivery of the vaccines that we have ordered. If for any reason they could not make it because they could not identify the virus, then obviously, that would not happen, or if they could not manufacture the appropriate vaccine that dealt with it, but I think that is highly unlikely, is it not?

Dr Salisbury: Clearly, the best circumstances were that we did not have a pandemic.

Q226 Lord Sutherland of Houndwood: Precisely. What happens then?

Dr Salisbury: We are not planning to pay for something that is not even manufactured. The purpose of the sleeping contract arrangement is to guarantee that once production takes place, you are well positioned to get a product. There are some things that no doubt industry would see the sleeping contract as funding, for instance, their mock-up dossiers that they would require, so the advance payment is certainly taking forward industry’s preparedness, but you are not paying for something that you do not have, and hopefully it would be a very long time before we had to.

Q227 Lord Sutherland of Houndwood: How long does the contract run? One year? Two years? Three years?

Dr Salisbury: These are currently under negotiation.

Q228 Baroness Sharp of Guildford: So in effect, you are dividing efforts really. At the moment there is the issue of preventing a pandemic from appearing and the sleeping contract means, should a pandemic emerge, you have plans to tackle that, and to some extent the costs could be divided between those two?

Ms Winterton: Yes, because essentially, you cannot manufacture a vaccine until you know the virus that needs to be combated.

Baroness Sharp of Guildford: Yes, I understand that.

Q229 Lord Patel: Minister, this might be a question for Dr Salisbury but I will ask you. You may have seen the evidence that the vaccine manufacturers gave to us last week. Their concern was that they need to enter into negotiations with you now to increase their capacity in the event that vaccine production has to be geared up to the level that you require, 120 million doses. If they increase this capacity, they need to have a guarantee that the British Government would increase its requirement for flu vaccination in between pandemics, otherwise the cost will be considerable. Hitherto, they have not had this negotiation or any contracts. These are virtually their words.

Ms Winterton: I will ask Dr Salisbury to take up some of the individual points about discussions that have been held between the Government and the manufacturers, but I actually think it is worth reminding the Committee that we constantly look at the number of people for whom seasonal flu vaccine is available and we have doubled the number of people who are eligible and who receive seasonal flu vaccine over the last five years. It used to be over 65s. It is now people with asthma and diabetes. We constantly keep that under review. We have a very good track record in terms of achieving the targets we have set, which was something like 70 per cent of people over 65, or 60; I cannot remember which. There is a bigger issue that is in a sense about what we do to increase worldwide capacity. That is something that was discussed in Ottawa last week at a meeting of about 30 countries to discuss the whole issue of pandemic flu. Many of the points that were made there I think would be of interest to the Committee, because really, we were talking with other countries about how they needed to increase their purchase of seasonal flu vaccine. This is an issue which is worldwide, and if there really is to be a dramatic increase in the amount of manufacturing capacity available, that does need to be something that we work on through international contacts as well. There are some countries that are not up to the level that we are in terms of seasonal flu vaccination and manufacturing thereof. Another point that was made in Ottawa was that the WHO would go away
and look at what was generally available in terms of the ability to manufacture vaccines worldwide and look at the various options there might be for expanding that. Dr Salisbury might like to talk a little bit about the individual points made by the companies at the Committee.

Dr Salisbury: The first thing is that, with colleagues both from my team and others, we have had a series of meetings going all the way back through this year with individual vaccine companies. All of the companies who could possibly provide flu vaccine came into the Department. They explained to us issues to do with their capacity. They explained issues to do with their research and where they saw their new influenza pandemic products going. So we have already had a complete round of these and we have come close to completing our second round of these meetings with all the manufacturers. I was also surprised when I read the comments, but I think the comments made to this Committee were made by UVIG, which is the United Kingdom Vaccine Industry Group, rather than the individual companies. It is the case that we have met with all of the companies and we have discussed with all of them their capacity and their products that are in development. Where seasonal flu is concerned, the Minister has exactly given you the information that we are one of the higher-achieving countries in our ability to reach our seasonal flu coverage targets, both for those over 65 and now, increasingly, pushing for higher coverage of those with risk factors. There are many countries with far lower utilisation of influenza vaccine. If one really wanted to push at the places where improvement needs to be made for the greatest, it would be those countries with lower utilisation of influenza seasonal vaccine. Nevertheless, we do need industry to be able to increase capacity so that it can both respond to demands for seasonal vaccine and respond to requirements for a pandemic vaccine, and that is a problem that is not just for the industrialised countries; that is a problem that is going to be global, and there are many countries that have no utilisation of seasonal flu vaccine and will be in an extremely difficult position when they have to try to deal with accessing pandemic vaccines. This is a real issue and we take it very seriously, not just whether capacity needs to increase, but industry—and quite rightly, they are already doing this—needs to look at ways of making the current vaccines even more effective so that you could use smaller doses and thereby maximise capacity.

Dr Salisbury: That is the reason for the sleeping contracts, so that we can ensure that once industry starts making pandemic vaccine, we will be well placed to receive product as quickly as possible.

Q231 Lord Paul: Minister, we are talking of advance payment for the sleeping contracts. What kind of money will we have to pay for that?

Ms Winterton: Discussions are ongoing at the moment and it is rather difficult to give figures, frankly, just at this point in time. Dr Salisbury is engaged as we speak in discussing with manufacturers some of the issues around that.

Q232 Lord Paul: Cynics say that because of the advance payment questions, the whole problem is being exaggerated to a scare level.

Ms Winterton: I would hope that people would not take that view. I think it is our job in Government to take advice from the experts, to evaluate it as best we can and then take the action that we think is most appropriate. The evidence that we have been given, as I said earlier, has been put together by national and international experts. We take that advice very seriously and that is why we are entering into the contracts.

Q233 Chairman: I would just like to ask one question, Minister, before we leave these demands for seasonal vaccine and respond to requirements for a pandemic vaccine, and that is a problem that is not just for the industrialised countries; that is a problem that is going to be global, and there are many countries that have no utilisation of seasonal flu vaccine and will be in an extremely difficult position when they have to try to deal with accessing pandemic vaccines. This is a real issue and we take it very seriously, not just whether capacity needs to increase, but industry—and quite rightly, they are already doing this—needs to look at ways of making the current vaccines even more effective so that you could use smaller doses and thereby maximise capacity.

Q230 Lord Patel: In the event that appropriate vaccine is available or can be manufactured, the citizens of the United Kingdom will be able to get that vaccine?

Q234 Chairman: So this is just a supplementary payment, is it?
Dr Harper: It is a supplementary, extra-budgetary sum of money for a designated need that was identified 12 months ago.

Q235 Baroness Sharp of Guildford: To some extent, the question I want to ask you picks up the same issues of co-ordination of international efforts, and in particular, given the difficulty of gaining access to China and the somewhat chaotic situation in both Vietnam and Indonesia, how are we keeping tabs on the situation and linking up with other developed countries, the WHO and UN agencies and for that matter the EU and G7 countries? What is happening at the international level?

Ms Winterton: Most of the international effort is obviously being coordinated through the WHO, but the European Union also plays a part. We had an informal meeting on 20-21 October of health ministers within the EU where we discussed the issue of pandemic flu. In addition, as I said, there are a number of meetings that take place both at political and official level. I thought the Committee might be interested in some of the deliberations at these types of meetings, so I have the communiqué which came out of the Ottawa meeting. I thought you might be interested to look at the areas that that covered, which were to do with further assistance in terms of surveillance, greater cooperation on research, looking at issues around containment, looking at how we can increase the number of vaccines available or the vaccine manufacturing capacity available worldwide. If you feel that that would be useful, we could circulate that to the Committee later. At the same time, there are other meetings. There will be meetings between UN agencies and the World Bank next week to look at the pandemic flu issues. The UK also co-chairs the Pandemic Flu Working Group of the Global Health Security Action Group, which brings together the G7 nations and Mexico. There is a lot of co-ordination going on at international level and, as I have said, through the European Union as well.

Q236 Lord Mitchell: If we can continue on the international theme, clearly, the monitoring of avian flu and in particular the spread and mutation is very important. I just wondered what steps the Government are taking to actually support the efforts of the United Nations and other international bodies in monitoring any developments in south east Asia.

Ms Winterton: As I say, this is something which there have been ongoing discussions about. To a certain, extent, it was taken even further at the meeting in Ottawa. Not only are we pressing through the World Health Organisation for increased cooperation, but we are also taking some quite specific steps. For example, representatives from the Medical Research Council have been out to south east Asia to see whether there is more that we can do in terms of technical assistance. The Health Protection Agency also offers its technical expertise to other countries. Using our research facilities and evidence we have and making that available to international partners and working with them is an important part of the overall strategy we have. I do not know whether Dr Harper wants to say anything in particular about the situation in south east Asia that may have developed recently.

Dr Harper: One of the issues that was recognised a little while ago was the urgent need for the animal experts to work very closely with the human health experts, and there have been a number of meetings that the Minister has referred to, not least the meeting in Washington a few weeks ago, where the international partnership on pandemic influenza was launched. This brought together at a high level officials from the various countries, the countries most affected, but also experts within the animal health area and the human health area. The issues that are being identified will be picked up in various ways, not least at the meeting in Geneva next week, where the World Health Organisation, with its sister organisations, the FAO, the World Animal Health Organisation and the World Bank, will be looking specifically at surveillance and infrastructure issues in south east Asia and in those countries that are currently affected by the avian flu problems. The samples that are being taken, sampling the virus itself in those areas, are being sent to laboratories around the world where the expertise exists to do the sort of molecular sequencing that I think you are referring to, to keep a very close eye on the changes in the virus itself, in the bird population. So our laboratories are very much involved in the molecular typing and the molecular sequencing of the viruses to keep an eye on how this virus is changing as it goes from country to country and as time passes.

Q237 Lord Mitchell: You mentioned the FAO. We hear that they face a serious shortfall in their funding. I just wondered first, is this true and, if so, on an international basis, how is this being addressed?

Ms Winterton: This was certainly not something that was raised at the meeting in Ottawa. As we have set out, at the Ottawa meeting we emphasized the need for greater international cooperation, and in terms of the work that will come from that meeting, if that was an issue that was raised, it would be something we would give consideration to, but it is not something that was drawn to our attention, as far as I am aware.
Q238 Chairman: While we are still on this matter, we also gather that the HPA is not funded to take part in international activities, unlike many of its international equivalents, for example, in Canada, and has to fund such activities out of its own current budget. Furthermore, it appears that it cannot be funded directly through DfID but that DfID funds have to go through a supported country. Do you plan any changes in these arrangements?

Ms Winterton: In terms of DfID funding, I know that DfID has adopted quite strict criteria as to how it makes funds available. A lot of it is to do with making sure that it is going through the most appropriate channels within each country. I cannot say I am aware of whether it is stipulated in terms of anything to do with the Health Protection Agency. If the Committee would allow me to take that away, I will certainly look at the points that are raised, but I am not aware of that. However, I understand that the HPA is involved in some of the work that is being undertaken, and certainly is not prevented from doing it.

Dr Harper: The remit of the Health Protection Agency is to protect the health of the population, as you might expect. International work is very much a core part of the work that the Health Protection Agency does. It needs to be aware of what is going on internationally, in particular, if you like, with communicable diseases that do not recognise international barriers. They need to be working scientifically and administratively at an international level, and that is exactly what they do, and they contribute a great deal to the Department of Health’s activities in that international sense, but also they are working very closely with other departments, so they are playing a major role with Defra at the moment in terms of the avian flu side of the whole influenza preparedness situation.

Q239 Chairman: You are saying that its activities are funded by a “business as usual” budget, as it were?

Dr Harper: There is a core budget that is provided by the Department of Health. There are lots of other sources of income that are open to and used by the Health Protection Agency, but as part of the core funding there is an expectation that international business, where it is necessary and appropriate, is a part of that core funding.

Ms Winterton: Perhaps I could just add that the HPA is also leading in terms of European Union exercises on pandemic flu, so it is working at that level as well.

Q240 Lord Sutherland of Houndwood: Minister, we understand that the Government has recently ordered over 2 million doses of H5N1 vaccine, and I wonder if we could talk a little bit about this. Firstly, could you explain to us a little bit of the reasoning which led to this decision, and secondly perhaps could you tell us what the vaccine will cost. Is that where the figure of £200 million came from or is it a different number? Finally, how will the vaccine be allocated?

Ms Winterton: It is true that we are ordering something like 2.5 million doses of the vaccine, and that is a vaccine which can be used against the H5N1 avian influenza strain. In terms of costs, if we based it on what would happen in terms of seasonal flu, that is usually between £5 and £10 per vaccine, so I think it adds up to something like £30 million. That is in the region of, we have to stress in all these matters that if you were to take it from one to the other, that is the cost you would be looking at. But we are obviously in discussions about that. The reason why we have ordered that is so that we know that we can actually protect front-line health workers and perhaps others who might be directly involved in the culling of poultry if that became necessary, if there were an avian flu outbreak. It is also possible that we can use some of the vaccine for research purposes as well. One of the things that we are obviously trying to do is to minimise the amount of time, so that if a virus did develop that could be transmitted from human to human, to make the time that you could develop a vaccine as quickly as possible. So we would be able to use some of it for research purposes as well. As members of the Committee will, I am sure, know, it may be possible that if another virus developed, the H5N1 vaccine might offer some protection, but we just would not know.

Q241 Lord Sutherland of Houndwood: I find this reassuring, particularly to look at the needs of those working in the front line with the contaminated or sick birds.

Dr Salisbury: I think the Minister has made most of the points. Clearly, this is an insurance policy, that it seems good to be prepared, and since the assessment of risk is that H5N1 does not look good at the moment, it is timely that we at least have a reserve stock. That will allow us to get some research done. It is particularly important because the mock-up dosiers that may be being used for licensing purposes are quite limited in that they do not include children and they do not include the elderly as being needed for the preparation of a mock-up dossier. So if you already have a candidate vaccine and you have a research infrastructure available, you can at least get some of these policy-related questions answered that may not be necessary in fact for the licence in due course. So we would see this as useful for research. We would also see it as a possible first line if H5N1 emerged, because health workers would be at significant risk.
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and we would want to do our best to minimise those risks. So we see many uses. It also encourages industry, I think, as part of the issue of capacity and helps industry get experience of making some of these vaccines.

Q242 Baroness Finlay of Llandaff: Can I just ask you to expand a little bit on this group of front-line people you were referring to. Are you including in there people working in the funeral industry and people who are in teaching who may be exposed to large numbers of young people, and people who are involved in food distribution, or are you restricting it to clinical health care staff in your definition of front-line people?

Ms Winterton: At the moment we have been talking about front-line health workers, for obvious reasons. Also, people who would be involved, as I have said, either in the direct culling of poultry or people who had to be involved in other control measures at that time, but mainly we are talking about health care workers.

Chairman: We spoke a lot about what the Government is doing to increase the quantity of vaccine should we need it, but I think Lord Winston has a question about regulation.

Q243 Lord Winston: In the event of a pandemic, what steps might the Government take to speed up the regulatory process to produce vaccines? One of the issues is that some companies feel that vaccines are hardly worth being involved in these days. Is there a process whereby the regulatory framework could be speeded up?

Ms Winterton: Obviously, many of these issues are dealt with on a Europe-wide level. We obviously have our input into that. I hope the Committee understand that it goes without saying that we would do everything to make sure that safety was not compromised. There is a lot of work that can go on in a sense prior to the development which Dr Salisbury has just set out, and particularly if we are able to use the H5N1 vaccine to do some of that testing. The European Medicines Evaluation Agency (EMEA) has also set out some guidelines for manufacturers involved in manufacture of a virus for a pandemic which should actually help to accelerate the licensing of any vaccine as well. So it is something that happens at European level. There are measures that we can take to help along the process of safety. Obviously, we would not want to compromise safety, but it is important that we work with other international partners on that.

Dr Salisbury: The EMEA has been extremely forward-looking in preparing so that the process of regulatory business is done as much as possible before there is a pandemic, and that is the purpose of the mock-up dossiers, so the manufacturers already have a whole lot of the package that they would need for a licence already done and approved, and they do that on a mock-up vaccine that they have prepared in advance. When the pandemic emerges and the virus is known and the ultimate vaccine is prepared, it is simply a matter of making a variation to the mock-up package, and that can take two days. So the regulators, I think, should be applauded for what they have already done on a Europe-wide basis to really try to get as far ahead of this issue so that there are not blockages that are simply bureaucratic in getting a licence. One of the important pieces of intervention where I do think we can influence, and I think the Minister was alluding to it, is the piece of time between the identification of a virus that could be causing human to human transmission and then a pandemic, and manufacturers being given material on which they can then base the production processes. That period of time is critical. That is when we know there is a virus and we cannot yet start manufacturing. The National Institute of Biological Standards and Control is looking extremely carefully at how the various regulatory processes that are necessary in that period of time can be brought together and made to run concurrently rather than sequentially so that the interval between having a pandemic virus and having the seed material for production is brought down to the absolute minimum. That would make a huge difference.

Q244 Lord Winston: I can understand the Minister’s reluctance to compromise safety, and that must be right, of course, but if you are dealing with a really deadly virus which is human to human, and you do decide to try and move things forward quickly, are there any steps by which the Government would consider indemnifying manufacturers against adverse consequences of any vaccines produced by a manufacturer?

Ms Winterton: There are obviously issues around that. I am not sure how feasible some of that would eventually turn out to be. I know that Dr Salisbury has had some discussions around these issues.

Dr Salisbury: This is something that is certainly being discussed on both sides of the Atlantic, in Europe and, of course, North America, because the manufacturers feel very vulnerable on the issue of preparing a vaccine that is not going through all of the usual steps, although it may go through many of them. Nevertheless, we will have to find a way that is both acceptable to the purchaser and acceptable to the provider so that there is indemnity, and that is currently being discussed and it is part of this bigger package of taking the sleeping contracts through to eventual production. We know that indemnity will have to be resolved one way or
another between the industry and those that are buying vaccines.

**Q245 Lord Mitchell:** It seems to me these are political decisions that have to be taken. I have a sense from reading through the evidence and in particular the written evidence from some of the manufacturers that they feel that all that should be done has not been done. I just pick up a different degree of urgency from them than I am picking up from the evidence we are receiving today. I just make that observation.

**Ms Winterton:** I would hope from the reports that I get back from those who are engaged in the discussions that they are moving things forward. These are issues that are being addressed. It may well be that there are those in industry who wish things to move more quickly and wish for clarity immediately, but it is important that we work through this properly. As Dr Salisbury has said, there are discussions that are taking place on both sides of the Atlantic. I can understand people’s anxiety perhaps to be able to have this sorted out. We are not unaware of the problem, but it will take time to resolve. It also needs to be put in the context of some of the other developments that are taking place as well, as we are able to use some of the work that Dr Salisbury has talked about in terms of how we can test certain dossiers, which all have an impact on that.

**Chairman:** Shall we move on to antivirals?

**Q246 Lord Patel:** My questions relate to antivirals, and particularly inhibitor drugs such as Tamiflu. Based on a fairly conservative model, the UK Government has decided to stockpile 14.5 million doses of Tamiflu, and we understand from previous evidence submitted to us that we will have this stockpile by September of next year. I said based on a fairly conservative model because other countries, such as France, the United States and others, are stockpiling millions more doses. France, we are told, is stockpiling 50 million. You shake your head, so maybe you will tell us the right figure and we will check it. The question is, if that modelling is wrong—and we are told that this drug will be effective in reducing serious complications and deaths if given at a certain time in the early phase of the development of the disease, the first 48 hours—then clearly, it will not be available to everybody who develops early-stage influenza-like illness, in which case there would have to be some form of—and I use the crude word—rationing. Will there have to be some rationing, firstly? If there has to be, how will we manage that? Can we be confident that this drug will be available to all of our citizens who may develop this illness?

**Ms Winterton:** I will ask Dr Harper to talk about the modelling, which may be able to give you some reassurance, but first of all, we are certainly almost world leaders in terms of the stocks that we have of Tamiflu. France does have stocks of antivirals but they tend to be Relenza, which comes in powder form. They have some stocks of that as well as some of Tamiflu, but they can be quite difficult to distribute. They are also more difficult for old people and people with asthma to take because they have to be inhaled. In terms of the World Health Organisation recommendations, we are certainly at the top end in terms of the 25 per cent, and that is because the 25 per cent is geared towards the estimate in terms of the modelling of the number of people who might actually suffer during a pandemic. This is for treatment; it is not for prophylactic use of the whole population.

**Q247 Lord Patel:** It is a treatment for early phase though.

**Ms Winterton:** Yes. It is for treatment, and the estimates in the modelling are that 25 per cent is likely to be the amount of people who would have that. There are those who say why not get it for the entire population and treat people beforehand to prevent it happening? There are a whole range of issues around that, not least to do with the fact that you have to be very careful, if you are talking about prophylactic treatment, how long that would mean somebody taking it for. There can be issues of building up resistance to the drug itself. The best evidence we have—and I do want to emphasize that in terms of the World Health Organisation assessment of what we have done, we really are doing incredibly well to have reached that level of 25 per cent. If you look at many of our European partners, you will find it is nowhere near that, and I think the Americans are something like 1 per cent. We are 25 per cent, and that really is, as I say, very good planning, if I may say so.

**Q248 Lord Patel:** I agree that it is for treatment of early phase disease. The question—and I think you answered in the affirmative—is that the amount of drug that we are stockpiling will be enough to meet the demand of every citizen that develops early symptoms of avian flu.

**Ms Winterton:** David, can I ask you to say something about the modelling itself?

**Q249 Lord Patel:** No, the question . . .

**Ms Winterton:** What I am saying is, yes, 25 per cent is based on estimates which have said the numbers in a population which may get influenza . . .

**Dr Harper:** There cannot be a guarantee that every person who needs Tamiflu, if Tamiflu indeed is the effective antiviral, would get that, because we have
to prepare on the basis of a whole lot of uncertainty and assumptions. The best information that we have at the moment is to work on a 25 per cent clinical attack rate. It could be that, once the virus emerges, there is a much lower clinical attack rate. It could conceivably be a higher clinical attack rate, but the international consensus at the moment is that 25 per cent is a reasonable target figure to have, and that is the basis for our stockpile. But there cannot be a guarantee until the virus actually emerges as to the efficacy of Tamiflu and how many people would actually require it. These are the assumptions that have gone into the preparedness. What I would say is that we are keeping this under review all the time. So we have made our order. This is a limited shelf life product, after all, with a five-year shelf life. We are taking scientific advice also on issues such as the need or otherwise for Relenza, which the Minister mentioned, zanamivir, the drug itself. There is no evidence of any resistance at all associated with zanamivir. The original decision to go for Tamiflu was largely on the basis of ease of administration in a pandemic situation. So we are keeping a very close eye on any emergence of antiviral resistance to oseltamivir, and that alone would mean that we might need to reconsider our antiviral strategy as there are developments and as the science changes.

Q250 Chairman: There has in fact been one case, has there not?
Dr Harper: There has been one isolate from a patient in Vietnam of a virus that is resistant to Tamiflu. That is of dubious public health significance but is of great interest and significance scientifically.

Q251 Lord Patel: We should qualify that that particular case also may not have had full, adequate doses of treatment, which increases the risk of developing a resistance.
Dr Harper: Absolutely right.

Q252 Lord Winston: One issue which you raised in answering the question is that, as you mention, a number of our European partners are much less well provided with these antivirals. What will be the policy in the event of one of our European partners faced with a major pandemic, with us untouched, and what will we do about supplying them with drugs that we might or might not need in the future?
Ms Winterton: The WHO is acquiring a stockpile of 3 million courses of Tamiflu, and at the moment we are obviously working through the WHO on how that might be used in those circumstances, but of course, what we are doing is encouraging countries throughout the world to look very closely at the recommendations of the WHO in terms of the courses of Tamiflu or Relenza that they may be ordering.

Q253 Chairman: A final question, Minister. Given the fact that this drug has a five-year life, are we committed to maintaining a stockpile of 14.6 million? It is not a one-off purchase?
Ms Winterton: No, that is exactly the point that Dr Harper was making, that we do keep under review this whole issue, depending on latest information that we have from experts at national and international level. The way that the ordering has been done is obviously very effective because it does mean that you have a continual fresher stock.
Chairman: Let us move on to issues of NHS reform.

Q254 Baroness Finlay of Llandaff: You may have seen in this week’s BMJ there was a leader on bird flu and pandemic flu. Its final paragraph says, “Delivering health care would be a considerable challenge, not least because illness among NHS and other essential staff would diminish the work force.” During a 15-week pandemic in the UK there would be an estimated additional 1.5 million consultations in Primary Care, 0.75 million visits to accident and emergency departments, and more than 82,000 admissions to hospital, which is a pretty phenomenal load on the system. The NHS itself is going through a period of radical reform. Concerns have been expressed that in the event of a major emergency such as a flu pandemic, initiatives such as the reconfiguring of Primary Care Trusts or the merging of Strategic Health Authorities could undermine the ability to respond effectively. I wonder what steps you are taking to allay these concerns and to make sure that reorganisation does not damage the ability of the clinical service to respond.
Ms Winterton: I think there are various points to make here, and the first is I think to look at the work of the Chief Medical Officer and the structures that have been set up to ensure that the NHS is provided with these antivirals. What will be the di—cultiesthatmaybefacedbytheNHS.Ialso think that in terms of the overall planning that has gone on, particularly since 2000–01, we are in a good position to ensure a response. When we talk about NHS front-line workers, that is exactly why we have taken some of the steps that I have just talked about both in terms of vaccine procurement and also Tamiflu antivirals. It is difficult—and you as much as anyone will know this, I know—in terms of planning because so much depends on the severity or otherwise of what occurs. What we have tried to do is to ensure that we are able to
communicate with health professionals about what needs to happen, that we have very practical steps that health professionals, PCTs and Strategic Health Authorities should take. I would say when it comes to things like PCT reorganisation, what we want to see, obviously, in any NHS reorganisation is to make sure that the service itself is performing as efficiently as possible. As we have said already, one has very little idea as to, if a pandemic did strike, when exactly it would be, in how many years’ time it might be. It would be a slightly curious proposition to say that we could never do anything to the NHS in case this upset planning and took people’s minds off the job. I happen to think that is not what will happen and we are keeping a very careful check. As I have said, we have given PCTs and health professionals very specific advice about what we are doing and most recently have sent out a document. I have brought copies of that for the Committee because I thought it would be useful for you to see exactly what we have sent out to all GPs for example and what we are doing with PCTs. They are conducting their own analysis, it is managed through the SHA, so I am confident that any reconfiguration will not get in the way of that, particularly as what we will be looking for from a reorganisation is the ability to offer services even more efficiently than we do at the moment.

Q255 Baroness Finlay of Llandaff: One of the difficulties with reorganisation is that the relationships that people have worked with, which are personal relationships, can be broken and they find they are relating to a different set of people. What we were wanting to be reassured of was that the framework of central command and control, if you like, is in place which transfers across and which allows for very high sickness rates in some parts of the service which may destabilise the normal pattern, so the service can still respond and shift resources across when perhaps a large tranche of it is knocked out. In some areas that may happen if one general practitioner is unable to function.

Ms Winterton: Those are absolutely the kind of considerations that we are looking at, and incidentally quite a few of those scenarios are set in terms of when we look at contingency plans in other areas as well for general emergency preparedness. Obviously we are all too well aware of recent incidents where it has been put into practice with exactly the kind of cross-referencing you are talking about. We have some specific groups set up, for example, to look at requirements in terms of intensive care and so on. What we are very clear about as well is that as one would move through the different phases of the WHO’s assessment alert state that is when you would as well disseminate further information to health professionals based on what was actually happening at the time. That is the important thing. We can look at the different scenarios but the practicality is that we have to look at the situation as it develops.

Q256 Lord Patel: Part of this we have already discussed but it relates to the responsibility of the Health Protection Agency, because the responsibility has been changed, as we understand it, and the funding has been affected on the basis they do not have any further responsibility for frontline management, but now if they are going to be responsible for emergency strategy relating to the pandemic flu we have been told this will create problems for them—

Ms Winterton: For the HPA?

Q257 Lord Patel: Yes, the Health Protection Agency.

Ms Winterton: The HPA at the moment provides a lot of frontline services to the NHS, to local authorities and to others, and it will be very much involved in any efforts to deal with the pandemic. For example, consultants in communicable disease control at the moment with the HPA would continue to be there, and particularly as well the laboratory services for testing. If you wanted to send us any information that you were particularly told that they would not be able to do, please do so. That is certainly not what we are feeling at all, we see this very much as part of not only service delivery at the moment but also in the future.

Q258 Lord Patel: Exactly, Minister. I think they recognise that, particularly with the situation of pandemic flu developing, they will have a role in emergency planning.

Ms Winterton: Yes.

Q259 Lord Patel: The question which came up in the evidence was whether the current funding, which apparently was cut because of the reorganisation, would be able to meet that requirement.

Ms Winterton: What is happening following on from the Arm’s Length Body review is that they are being merged with the National Institute of Biological Standards and Control. In all those mergers obviously we believe there may well be room for certainly efficiency savings in terms of things like backroom staff or whatever, but the idea of that is to put more resources at the frontline, not to cut funding to organisations.

Chairman: We will move on now to guidance to GPs.

Q260 Baroness Sharp of Guildford: This brings us back to the question of PCTs and GPs and the role they will be playing. You have assured us that PCTs
and health professionals will get very specific advice but can we raise some specific questions to reassure us as to how you see these things playing themselves through? Will the PCTs and GP targets on patient access be suspended in the case of a pandemic? What steps are you taking to expand the critical care facilities in the event of a pandemic? How far will patients gain rapid access to antiviral drugs in the event of a pandemic? What information would someone, for example, ringing up NHS Direct with flu-like symptoms be given in those circumstances? I wonder if you could give us a little bit of advice on these things.

**Ms Winterton:** Again, I hope the Committee might find the information we are going to pass round helpful. In fact we can pass that round now. *(Documents circulated)* It is quite important to remember that in terms of information dissemination what we really need to do is make sure we disseminate the appropriate information at the appropriate time, and I think there have been some people who say, “We want the answer to XYZ now”, and quite frankly we might get very confused messages if we started to do that. What we have done at the moment through the information and through the websites is at the moment send out to GPs what they need to do now and essentially that is about understanding pandemic influenza in the first place. I am sure it would be highly unlikely, if not impossible, a GP would be confused about that, but obviously we want to be absolutely clear everybody is able to explain the difference between bird flu, seasonal flu and a pandemic. We want them to ensure they are keeping a very close eye out obviously because as frontline professionals they are able to assist, if you like, the surveillance and reporting. We want them to liaise with Primary Care Trusts about their plans so that the two of them they are aware. What is important is that at the moment we establish the relationships between GPs and those they would be working most closely with in the event of a pandemic, so that it is quite clear what would happen and who is doing what. I can understand that some people would say, “We want to know everything now”, but quite honestly we have to give out the information depending on the circumstances of the moment. I can assure the Committee that we do have advisory groups, and Lady Sharp has mentioned particularly the issue of intensive care and we have an intensive care working group with Professor Menon who has joined that and is able to give us advice on those various issues. So we are trying to pull together the relevant professionals, stakeholders and others to make sure we can effectively communicate, quite rightly, the issues people want to know about.

**Q261 Chairman:** Would you consider suspending the targets that PCTs and GPs normally have if there is a pandemic?

**Ms Winterton:** We have to respond to the circumstances of the moment. There is no doubt we do have to look at what would be the effect perhaps on elective surgery if there were a very, very severe outbreak. It would be ridiculous to say we would not look at that. Again, I would say those are decisions which are not only being looked at in terms of the implications of all sorts of areas, in terms of how hospitals, PCTs, GPs operate, of course we look at that, but the message we have to get over very clearly is that there is not a one-stop answer because it absolutely depends in a sense on first of all the severity of any virus but also on the age group which might be affected. We know that the 1918 flu affected people of working age more than older people, so again there may also be issues there in that if somebody had lived through those outbreaks certain age groups might be more resistant, so we have to look at all those implications and make sure what we are not trying to do is set in stone something which will need to be flexible depending on the circumstances of the time.

**Q262 Chairman:** Do you think we could get into a situation where people would have to diagnose themselves? If that was the case, how would we cope with the distribution, for example, of antivirals? It could get to be a very large problem.

**Ms Winterton:** What we are being very clear about is that PCTs and others have mechanisms in place for distribution. In terms of self-diagnosis, part of our obvious communications strategy would be for people to look out for symptoms in themselves and their families, certainly that is what we would hope but obviously we would want health professionals being involved in (a) confirming that and (b) distributing any antivirals or treatment as was appropriate.

**Dr Harper:** We are looking at a whole range of scenarios and if it developed into a situation where it was necessary for people to confine themselves at home, we would look at Primary Care Trust level to have in place arrangements to get the antiviral to the people who needed them. That is the sort of consideration we are looking at right now.

**Q263 Baroness Finlay of Llandaff:** I think we understand that when you are dealing with an unknown you cannot give hard and fast answers for X number of people who are going to be affected, but it sounds as if a lot of this planning is going from the centre out in terms of distributing whatever stock of Tamiflu there is or having algorithms to decide at which point people trigger their ability to have the drug. My concern is, in a changing situation how are you going to get the information back into the centre from the ground to know over 24 hours how rapidly stocks are being raided and
therefore how much is left and whether the threshold has to alter so the information going back out to the periphery is altered. Whilst you can have information going out there is the feed-back loop coming back into the centre and I am not clear from the way people have been talking how that really grassroots information is going to go rapidly back to the centre to alter policy. There may come a time when we have to say to GPs, “Forget your targets, just treat that, don’t worry, you will be paid, your staff will be paid” and it will be important to do that to maintain the morale of people who are still working. Similarly, you may have to say, “We suspend all NHS targets” and have a decision taken rapidly, and you can only do that if you have information coming into the centre.

**Ms Winterton:** We have the experience for example of what we have done during severe winters, and we have set out what I think are very good information reporting systems. Over the last few years we have been able to get very quick advice on what was happening, for example in accident and emergency services or ambulance services. We do have very good systems of reporting now, including on winter flu as well. So I think we have those structures in place but, through the communications programmes we are distributing at the moment, we are making it very clear we want the connections to be made between different health professionals. If you have a look at the letter we sent out to GPs, it is saying, “Make sure you are in contact with your PCTs in terms of distribution and so on, that we work through Strategic Health Authorities.” We do have quite clear ways of being able to set this up. I take absolutely your point that that needs to be a two-way system but I think in terms of what we have set up not only have we built-up expertise over a number of years in terms of communicating with the service through those structures, which I think have been very effective, but also in emergencies as well. I know that we can at the centre get information very quickly about what is happening in individual service areas.

**Dr Salisbury:** You make a very important point about the need for information to be coming back both in terms of burden of disease and on issues such as how many people have been given Tamiflu, how many people are going to hospital and what their outcomes are. We have already been working to raise the sensitivity of all our existing flu surveillance systems so that the Royal College of General Practitioners’ central surveillance system is increased in its scope and sensitivity so it reports more often and we get better coverage across the country. So some of this is being done. We are also putting in place a means of bringing together a whole lot of the surveillance work including real time data from general practitioners on the number of people they are seeing daily, the number of people they are treating daily, what they are treating them with, and all of this will come into a gateway which can be accessed by the Health Protection Agency so that they can be doing the epidemiological surveillance, and the modellers can be taking data and making projections on the pattern of the pandemic which will then allow informed policy decision-making and we can look also across the whole country.

**Q264 Baroness Finlay of Llandaff:** Does that work across the four countries? I say that living in Wales. If it starts with us, is it going to work across all the borders?

**Dr Salisbury:** All I can tell you is that the meetings I have been chairing have all four countries represented and they are working together on surveillance.

**Q265 Lord Patel:** Is this not an important point because in the evidence that we heard from the General Practice Research Unit, their anxiety is their ability to do this surveillance. I agree that the surveillance we have through the general practitioners in Primary Care is very efficient but we have to maintain that, particularly in a situation where a pandemic is about to start or has started when we need it. The evidence we have had from the General Practice Research Unit suggested their contract runs out with the Department I believe in April and there are no current plans to renegotiate this contract. Is that right or wrong?

**Dr Salisbury:** I have to say that is probably wrong in that we have already been having discussions with the RCGP about their central surveillance scheme, including expanding the scheme to take in parts of the country which were not previously covered. One of the considerations which has been paramount in this whole concept of expanding surveillance has been resilience. Whatever we put in place has to work at a time when Primary Care could be extremely busy.

**Lord Patel:** I am pleased Scotland is included.

**Q266 Lord Howie of Troon:** Chairman, I would like to apologise for my late arrival, I thought the Minister was arriving at 3.30 and I apologise for my discourtesy. I have a somewhat naive question arising from something you said, my Lord Chairman, about self-diagnosis. If it has been answered in my absence, just tell me to go away and read the transcript. Suppose you are taken ill and you think you might have something, is there some kind of general public guidance which says, “You have got...” whatever it is? What I have in mind is a year or two ago I had a flu injection and I became ill a couple of days later and I had
pneumonia. Can I distinguish between pneumonia and this thing? Is there guidance to help me so I do not burden GPs unnecessarily?

Ms Winterton: I suppose we have to be quite clear as to what we might be talking about at this stage.

Q267 Lord Howie of Troon: Which I am not.

Ms Winterton: Obviously if you were talking about avian flu which you might have caught from a bird—

Q268 Lord Howie of Troon: No, from a person, that is what I am thinking of really.

Ms Winterton: Okay, I think there are two things because to a certain extent there may well be, and I will have to ask my colleagues to help me out here, particular symptoms we would be very clear about.

Q269 Lord Howie of Troon: I would like to know what these are.

Ms Winterton: I will ask them to explain them. Obviously there are symptoms of seasonal flu that will differ from that and in a pandemic if the virus had mutated into something which was passing very quickly between humans I suppose it might be different again. There might be some similarities but I think one would be, in the latter situation, having to issue, if one could issue, much more detailed guidance at the time when it was known what the real symptoms were so as not to worry people about other symptoms which may not be related.

Dr Salisbury: The public information material which we have prepared has been done so each stage of our preparation matches the WHO levels of building towards a pandemic. So we have got in preparation public communication materials as we get towards and have a pandemic. Included in those materials, which we have already market-tested with the public, are descriptions of signs of symptoms, so the public will be receiving information that not only tells them what sort of things to look out for in terms of flu-like symptoms but tells them what to do about it and also tells them where they can get more advice. Much harder is telling them about everything else which is not influenza. During the times when you do not have a pandemic, clearly you are going to have to take great note of people who think they have got pandemic flu to see what they have got. At the time of the pandemic, most people with flu-like symptoms will have influenza, and the routes through which they can get advice will be made clear to them and we will have advice which is made to them through NHS Direct. All of this work is well advanced in terms of communication materials.

Q270 Lord Howie of Troon: What I have in mind is this: when many years ago you got the Black Death, you had a fair idea you had something pretty serious. Are there clear guidelines so you can be sure that what you have not got is a broken ankle?

Dr Salisbury: Again most people in the course of a pandemic who have got flu-like symptoms will have influenza.

Q271 Lord Howie of Troon: Ordinary flu?

Dr Salisbury: No, the pandemic flu.

Q272 Lord Howie of Troon: They will be much worse then.

Dr Salisbury: They may be much worse but we do not know how the virus will manifest itself. We do not know until it starts. We can have general ideas of the signs and symptoms based on seasonal flu but what we cannot tell is whether there will be different presentations affecting different age groups differently. For that we have to wait and see. We know in 1918 the signs and symptoms and the age groups affected were quite different from ordinary seasonal flu. We just do not know. The population distribution in 1918 was very different from now when the number of people over 65 was of the order of 1 per cent at that time, and now of course it is very much higher.

Q273 Lord Howie of Troon: Happily.

Dr Salisbury: Absolutely. So there are many differences which we will have to wait and see before we can get advice on some of those narrow specific points.

Q274 Lord Howie of Troon: So you are very unlikely to know if you have really got it unless you panic?

Dr Salisbury: I think most people will know what they have.

Q275 Lord Howie of Troon: Will they?

Dr Salisbury: Yes, they will, and the advice we are preparing will help them both look after themselves and know where to go to seek further advice.

Lord Howie of Troon: Thank you, Chairman.

Q276 Lord Mitchell: I wanted to take Lady Finlay’s question a little further, and that is the issue of communicating data from the ground level up to the central point. It is not an unfair comment to say that despite the spending of huge amounts of money in the NHS, information systems have not quite become a beacon of best practice. I know an awful lot is still cooking and due to happen but I am an information technology person and anything to do with the NHS just fills me with horror, and I have a degree of scepticism when I hear in the case of a
pandemic suddenly there will be this magical information flowing to you in Whitehall. I would like to be reassured if I could.

Ms Winterton: I can only reiterate what I have said about the experiences we can build on in terms of recent passing of information when it has come from our winter plans. During the winter we look very closely at the information that goes from the frontline back to the centre; we have had a lot of experience building that up and I think that is effective. We need to expand that, that is what part of this is all about, because it is in a sense making sure we can cascade that further down to GP and frontline health professional level. That is why we are using the PCTs and the Strategic Health Authorities to help manage that. I certainly am clear that that kind of exchange of information can happen effectively and, as I say, certainly through the winter planning it is almost built into the NHS that it is possible during times when we know there will be extra pressure on accident and emergency services and others and we are very clear when that is going to happen and we can set in place mechanisms to ensure the centre is aware of where there are particular pressures. This will happen and it is necessary to happen very much for example in terms of accident and emergency departments and ambulance trusts, when there will be times when if there is severe pressure on an accident and emergency department it will divert ambulances to other areas to deal with that. There is some very good joint working which happens already because we understand the problems there have been in the past when, during times of heavy use such as winters in the past, the NHS have found it very difficult to cope. What we have done is set in place communication mechanisms now so when those pressures are there the NHS is able to respond very quickly. That is why in a sense during last winter at a time when there was heavy pressure, it was possible for the NHS to achieve for example the four hours’ maximum wait for people in accident and emergency. It is quite a feat to do that in the middle of the winter when there are all those extra pressures on the service. So we must build on that and that is exactly what we are doing, but we do have a mechanism we can use very effectively I believe.

Q277 Lord Paul: Has any assessment been done as to when one has the symptoms how quickly one needs help before things really deteriorate?

Ms Winterton: What I do know is in terms of Tamiflu if the symptoms develop, it is important to get the treatment there within 48 hours.

Dr Harper: That is the answer. The quicker, the better between the on-set of symptoms and Tamiflu. It is 24 to 48 hours. The current evidence is that within that 24 hours the quicker you receive Tamiflu the better it is.

Q278 Lord Paul: So it is very essential to make sure you know that.

Ms Winterton: It is the ASAP scenario.

Q279 Earl of Selborne: I was going to ask about guidance on contingency planning. The Government’s own revised contingency plan says that, “local authorities, education establishments and businesses will wish to consider the likely effects of a pandemic on their organisations.” One would rather hope they would do more than that and produce co-ordinated contingency plans, and I wondered to what extent the Department can get guidance and indeed encourage such co-ordinated contingency planning?

Ms Winterton: We are doing that not only through cross-government meetings of top officials to ensure that all departments are aware and are making proper emergency preparedness plans, but also through the ministerial committee DOPIT, rather curiously named, which does look at public services resilience so we can make sure at political and official level—

Q280 Earl of Selborne: Will that get through to local authorities?

Ms Winterton: Yes, the local authorities are certainly consulted as part of those groups. They are a very, very important part of the contingency planning in that area and will increasingly be so. It is important obviously that they are in close liaison with Primary Care Trusts as well. Again that relationship, at local level, is very, very important because that is where the real work, if you like, is going to take place. So we can build on structures which have already been developed. I think I am right in saying, and I will come back if this is not correct, by November 2005 there is through the Civil Contingencies Act a duty—is there not—to produce plans?

Dr Harper: Yes.

Q281 Lord Sutherland of Houndwood: A very quick follow-up to that. If, or as some say when, a pandemic comes, what is the Government process for looking at civil contingencies, implementing measures relating to that? For example, banning large meetings or indeed looking at the question of travel. Hanging on to the issue of schools, will that be a local decision or will that be a national decision, whether schools close and the consequent impact on the workforce?

Ms Winterton: I do not know whether you have had time to go through this document?
Q282 Lord Sutherland of Houndwood: I have not had time to read it because I have been listening to you.

Ms Winterton: This is actually the plan which was issued by the Chief Medical Officer and it sets out how within that there will be liaison at national level across the departments. This will obviously again, I have to stress, relate to the assessment of who is being affected, how it is being passed, if you like, and all the implications of whether closing schools or shutting down businesses or banning public meetings will actually have the desired effect. Again, it is very important to say that we would be, through the ministerial and top level officials group, looking at those issues as the situation develops, and, of course, working with international partners as well as to actions which were being taken in other countries. But it would then be for guidance obviously to be issued at local level.

Q283 Lord Sutherland of Houndwood: Would it be a matter at the discretion of a head teacher or a school board whether a school closes, or could they do that before guidance comes down the line?

Ms Winterton: There might be different decisions in different areas but obviously there would be very clear guidance from national level because, quite frankly, there would have to be an exchange of expertise and information. So it would be very much a local and national working-together but it may well be, and again my advisers will be able to give you further information, in the particular UK situation possible to contain things and have one thing happening in one area and another thing happening in another. That would depend on how any virus was developing.

Dr Harper: Infectious disease experts and our modellers and our public health epidemiologists are currently working on exactly those issues in the sense of school closures, cancelling large public gatherings and so on. The models are being revised as we speak, and they will continue to be revised in the light of new information, new scientific considerations. So it will be when the virus and the characteristics of the virus are clearer as to the attack rate, the susceptibility of the population and so on, that those will be fed directly into the models which will be there for real time use, where we can base the policy decisions and ministers can base the policy decisions on the best available information at the time that the virus emerges.

Q284 Lord Sutherland of Houndwood: It sounds a fairly frenetic process as the gap begins to narrow.

Dr Harper: That is why a lot of the preparatory work and the models are being done now, and the scientific press will be looking at that over the next few months. There will continue to be publications around, for example, international travel, school closures and some of these big issues, where we can use peer review work, which is very important, internationally and nationally, but we have those modellers who are helping us in our policy development right now.

Chairman: I think we want to move on now to the question of the funding of research.

Q285 Lord Paul: According to the evidence we received from the Medical Research Council, the annual budget for research was about £1.6 million which was spent and this covers key areas such as assessment of the risk posed by avian viruses, analysis of the development of the H5N1 virus and of its effects upon humans, and research into innovative methods of vaccine development. Is this really enough?

Ms Winterton: We can assure the Committee that we are very committed to improving research in this area and to work closely with the Medical Research Council, Defra and others, to ensure we have got a good research strategy here in the UK but also to make sure we are aligning what we are doing at EU and also at international level. That is a very key point, particularly in terms of what came out of the Ottawa meeting. That was certainly defined and there was a real sense at that meeting that there was research taking place in different parts of the world and that there was a very key co-ordinating role which needs to be filled. So I would say the issue is not only about direct research which we can undertake but also research one can feed into and help to co-ordinate in other parts of the world. We do want to look at what else can be done in terms of specific research on pandemic flu vaccines. Already we have £750,000 committed to flu vaccine research, and as you have said the MRC’s current investment is something like £1.6 million. I think it might also be worth Dr Salisbury saying something about the work which is going on by vaccine manufacturers as well, because I do think that is quite an important part of the equation for us to consider. It is obviously being in a sense stimulated by the fact that we are making it quite clear this is an area we are interested in.

Q286 Lord Paul: My question was that you have done a tremendous amount of preparation about what can happen but £1.6 million looks so small.

Dr Harper: The £1.6 million is MRC funding. If we take into account as well all of the work we have been alluding to this afternoon which has been done, for example on diagnostic development, near-patient testing both for national use and possibly for developing country use, and there is work going on in academia but also our Arm’s Length Body, the Health Protection Agency, has done a great deal of
work through what we might describe as core funding. The HPA have also successfully competed for European Union funding from the Framework Programmes. So in a broader sense, and if we look at the running of exercises and scenario development, the Health Protection Agency has won contracts for two very large exercises on a European scale which are being funded by the European Commission. We also have a lot of work going on in the National Institute for Biological Standards and Control on elements such as reverse genetics and developing those technologies so they can be applied to vaccine development and the development of standards. So we have to be slightly careful when figures are taken and earmarked as if they are the totality of research and development funding because, apart from those specific figures, there is an enormous amount of activity which is going on through these agencies and academia and other channels.

Q287 Lord Winston: Is it not a fact that in Britain generally we have run-down academic microbiology and that this is a problem for research in this area, and the fact we have not filled chairs in this area, and we are now very vulnerable?

Dr Harper: I think there is a real issue there in clinical microbiology and other specialisms as well—clinical toxicology is another very good example. There are some gaps in academia, but my point is that there is still a substantial amount of work which is going on throughout academia but also through the Arm’s Length Bodies we sponsor.

Q288 Lord Patel: Currently, as we know, there is a high level visit from MRC to China and Vietnam to understand the spread, organisation and epidemiology and, hopefully, that will identify areas where research could be targeted; basic science research particularly the kind you have mentioned the NIBSC is doing. If they come back and suggest there are areas where targeting research would be profitable, would we be able to find more money?

Ms Winterton: We obviously look at any proposals in this area. As I have said, one of the very important results of the Ottawa meeting and other meetings which are going on is we need to look jointly with international partners at research proposals and particularly in the area you have spoken about there.

Q289 Baroness Finlay of Llandaff: Could I follow up on research proposals? One of the problems for anyone putting together a research proposal is the lag period from when they get the research proposal together and then getting ethics approval, whether it is ELREC or MREC or however, and of course time is not going to be on people’s side in this. The other difficulty though is going to relate to consent over data and information. Clinical research in this area is going to be absolutely key and will be a one-off opportunity and we will need to know whether we dramatically alter survival by for example giving antivirals within 24 hours versus 48 hours, whether when people become pulmonary compromised they should have steroids first-line or bronchodilators first-line, but they will probably be too ill to give consent. They will also probably be too ill, and the people working in the frontline will be so busy they will not have time anyway, to go through the complex consent procedures over access to specimens and access to data, and using that data. If we are taking sputum samples, they will have cells in them and bits of DNA in them inevitably because they will have bronchial cells in them, but if we do not have a system in place to collect those samples and systematically to deal with them and analyse the data at a national level, we will miss a golden opportunity which may result, if we get it right, in being able to alter the course of the disease by saving many people’s lives. So we are not just talking about it being interesting and a small number, it is possible that if we can get the data in very fast in week one and begin to analyse it, we will begin to alter what we do in week three or week four, and certainly by the time we get into the tail of the pandemic. I wonder if you have given any consideration to special measures that would allow people to by-pass some of the bits of regulation which are currently in place which effectively mean they would not be able to collect those sorts of samples or undertake that type of research with the current framework around research?

Ms Winterton: As I said earlier, the Chief Medical Officer and others are looking at a lot of the points to do with not only the issues that we talked about earlier in terms of safety regulation and so on but a lot of the points you have made which are extremely relevant to the discussions which should be going on. I cannot give you a definitive answer now to say this is what would happen in this or other situation with regard to consent, and this is always a very sensitive issue as I know through the Human Tissue Bill and Act and we have had discussions at other times.

Q290 Baroness Finlay of Llandaff: Absolutely.

Ms Winterton: What I can say is, if there is any progress which has been made so far which I think it would be helpful for the Committee to have, I would be happy to take away those points and write to you if you think that would be helpful, because they are all areas which are extremely important, particularly in terms of management of and identification of virus spread.

Chairman: Thank you.
1 November 2005  Ms Rosie Winterton MP, Dr David Harper and Dr David Salisbury

Q291 Baroness Finlay of Llandaff: I think our concern as a Committee is if such issues are not addressed and opportunities are missed, then we will all feel to blame. We have time at the beginning to begin to work them through and get some of the protocols in place and think through some of the issues in the cold light of day. Once people start to be ill, no one will have any intellectual energy to look at that because they will be far too busy coping with the pandemic.

Ms Winterton: That is absolutely right and these are all issues which are being looked at very closely at the moment. Both Dr Harper and Dr Salisbury touched on that earlier but what I am saying is if there are any specifics which have been addressed in terms of the points you have raised already, I can write and let you know.

Q292 Baroness Perry of Southwark: Dr Harper, you mentioned near-patient testing and diagnosis, which obviously in the very early stages of a pandemic, particularly reaching here, would be vitally important, so that we do not have to wait for samples to be sent away to some distant laboratory and wait days for the results to come back. I know there is some work going on in Cambridge in Dr Helen Lee’s unit on this. Is the Government putting money into that, because it does seem to me to be one of the key links in the speeding up of controlling the pandemic?

Dr Harper: Dr Lee is working at least in part very closely with the Health Protection Agency, which is the agency we sponsor, so they are looking at the molecular virology with one of the leading scientists at the Health Protection Agency, who is working directly and closely with Helen Lee at Cambridge.

Q293 Baroness Perry of Southwark: And that is Government money?

Dr Harper: The Health Protection Agency is funded by the Department of Health.

Q294 Baroness Perry of Southwark: Is the Health Protection Agency funding her? I thought it was Wellcome money which was funding her.

Dr Harper: Maybe there is some confusion here. I am not talking about the funding for Helen Lee, I am talking about the Health Protection Agency side of the collaboration at the moment. That is Government funding.

Lord Winston: A very brief observation. The committee where I work has taken seven months with a very low grade research proposal and still it has not been agreed to give us ethical approval, for something which does not affect patients in any way adversely. I think you have to recognise that the ethical approval system is creaking at the seams already and it is going to get worse.

Q295 Chairman: Minister?

Ms Winterton: I am sorry, I thought you said that was an observation.

Q296 Lord Winston: I was backing up what Lady Finlay was observing and I think it is going to become an increasing issue.

Ms Winterton: Okay.

Q297 Chairman: Minister, we have gone on for quite a long time and we have run out of time now. Let me thank you very much, and Dr Harper and Dr Salisbury also for being very helpful and answering our questions. If we may ask you to keep to what you have just offered to do, to let us know anything else you think would be useful to us, and perhaps we can come back to you if we have further questions. But I would like to thank you very much for being so helpful.

Ms Winterton: Thank you and I hope these various documents are helpful.

Q298 Chairman: Thank you for those.

Ms Winterton: We can circulate the Ottawa communiqué if it would be helpful.

Chairman: Thank you.

Letter from Rosie Winterton MP, Minister of State, Department of Health

During the House of Lords Science and Technology Committee session on 1 November, I promised to write to you with further information regarding the issue of whether the Department for International Development (DFID) is able to fund work carried out by the Health Protection Agency (HPA). I also agreed to write with further information regarding the collection of clinical evidence during a pandemic.

With regard to the first issue, and on further investigation, it appears that DFID chooses not to fund work at the HPA directly, rather than being unable to do so. DFID is very unlikely to fund HPA directly and separately, as it works on the basis of responding to specific demands from developing countries, not offers to supply technical assistance from agencies in the UK, or other developed countries. DFID would, however, consider funding work at the HPA through WHO or other multilateral organisations, as part of a co-ordinated response to the needs of third countries.
On information collection, we need to make a clear distinction between the collection and analysis of data for public health and health protection surveillance purposes and setting up research projects. Surveillance of infectious diseases is not research and does not require the formal approval of a Research Ethics Committee. As part of medical practice it is governed by the general ethical requirements of medical work — albeit with a population as well as an individual focus — so it still has an ethical framework, but not one monitored by research ethics committees.

We are setting up a working group to examine these issues with the aim of ensuring that we have the protocols agreed and in place before a pandemic arrives. The Health Protection Agency has already produced a report in a similar issue for CJD, which will form a useful start for this work.

22 November 2005

Examination of Witnesses

Witnesses: Dr David Nabarro, Senior UN System Co-ordinator for Avian and Human Influenza, and Louise Fresco, Assistant Director-General of the FAO, examined.

Q299 Chairman: Good afternoon, Dr Nabarro. Can you hear me?
Dr Nabarro: Yes, very clearly, thank you, and we can also see the group. Thank you for waiting.

Q300 Chairman: Thank you very much and we very much appreciate your being willing to speak to us. As I think you gather, we are the Science and Technology Committee of the House of Lords. We are in the middle of this inquiry, what we call a short inquiry, into pandemic flu, so it is very relevant that we be able to speak to you. May I open the discussion perhaps with our having learned that the President has just made an announcement about the United States’ position on pandemics. Perhaps you could fill us in on what he said, especially the prospects for international, particularly the US support for, UN efforts, please.
Dr Nabarro: Can I just start by thanking you for giving me this opportunity and I would like to make one, possibly surprising, aside to you. I am sitting in the offices of FAO here in Washington and one of my most senior FAO colleagues, Louise Fresco, is here also because we have done some other testifying work that was necessary over here. If at any point there are issues for which you would want to get the latest update on FAO thinking, she has indicated to me that she is very prepared to be brought in. I have just come from an event at the National Institute of Health where the President of the US talked for about 20 minutes in detail about the US national strategy for pandemic influenza. He started by acknowledging the presence of both J W Lee, the Director-General of WHO, and myself and then making the point that, as far as he was concerned, preparedness and response in the United States was things that involved an international effort as well as strong national action. He made it very clear that anything which the US was doing was with a view to supporting international capacity-building and action. He spelt out, in particular, his concerns for there to be greater openness and transparency amongst countries with regard to influenza issues that they face. He talked about the importance of the international partnership on avian and pandemic influenza that the United States set up in October and described a little bit about what that had done. He mentioned that the US strategy is in three parts: detecting and attacking outbreaks in animals and humans; stockpiling necessary medicines, vaccines and other requisites to enable a response to a pandemic to take place; and then the actual undertaking of that response. Most of his conversation from then onwards was pretty domestic in focus. He was very clear on the need for bio-surveillance globally and then for having a national bio-surveillance initiative that would stop or slow the spread of any pandemic inside the United States, having spent some time stressing the difference between pandemic influenza and avian influenza. On stockpiling he talked a little bit about the importance of medicines, referring to both Tamiflu and Relenza, and said that there would be some investment in the purchase of antiviral drugs, a billion dollars, in order to help equip first responders and frontline personnel, but he was very clear that this is not a very satisfactory mainstay of pandemic preparedness. The most important thing, as far as he was concerned, was to get vaccine development improved. He mentioned that current vaccine production required waiting for the virus, which is going to cause the pandemic, to appear and using 1950s slow technology, as he put it, would take a long time to develop. He is launching a crash programme to develop new-style vaccines using cell-culture techniques, very much working initially on H5N1-derived vaccines. The ones that have already been produced are in clinical trials from NIH and NIAID. He wants to have enough for the vaccination of a large number of US citizens and so is putting $2.8 billion into this vaccine programme. Also he wants to protect vaccine manufacturers from litigation. Moving on to the third strand, the response side, he was very clear he is investing very significant money, half a billion dollars, in pandemic preparedness at local and state level; setting up a whole stack of...
mechanisms to make sure local and state are in line with their preparations with medical personnel and equipment, some stockpiling of equipment and medical goods; rosters for people, who participate in search activities and the preparedness of facilities for possible pandemic; plus a huge public information campaign and a new website. Then he went back, having talked about this, for which there is quite a significant price tag that I mentioned earlier, to state how important it is what the US does locally is reflected in the US’s global involvement in prevention and preparedness work, and how important it is that the US co-ordinates with other countries, so there is no duplication, and gives international assistance. He did not mention a figure, but I understand that there is not an insignificant amount of money for the USAID and CDC, which from the USAID side will be routed through FAO and WHO; that was in private discussion with Andrew Natsios, the head of USAID. He stressed that all of this is going to have four spin-offs for the US. One of them is the development of a much stronger national public health infrastructure here which is too weak. Second is the development of cell-based technology for vaccine production. Third was the real step-up for the domestic vaccine industry, which he feels is not doing too well. Fourth is an emergency planning capability being put in place which will enable either dangers to be addressed, for example bio-terrorism, or other major convergences, but he did not refer back to some of the recent difficulties they have had, though that was the implication. That was a quick summary of what I heard and I must say that it was pretty impressive both to hear and read it, but, as I often feel when we have discussions on influenza, although he started with a long description of the bird flu problem, I felt he did not refer enough to what that means for the world. It would have been nice to have a few more paragraphs, perhaps talking about the US’s role on helping countries to address influenza in animals. Thank you.

Q301 Chairman: Thank you for that very concise and informative report. That is very useful. Perhaps now we could turn, though, to your personal view. You were appointed Senior UN System Co-ordinator for Influenza only in September, I think. We are particularly interested to understand what your priorities are and how effective you feel the UN can be on this issue.

Dr Nabarro: The appointment was a month ago and the priorities were pretty clearly set up right from the beginning of my appointment by a senior steering group, set up by the deputy secretary general, membership of which includes either principals or one under the principals from each of the major agencies. It has been recognised by all in the UN that FAO and WHO, as the specialised agencies with particular expertise in animal health and human health, are at the vanguard of the response both to avian influenza and possible human pandemic influenza. The thinking from the deputy secretary-general was that there is a lot more to the UN system that can be made available to support the work that is being done by these technical agencies. She particularly picked on the resident co-ordinator system at country level and then the regional directors and other agencies which can provide support. An example is UNICEF which has a huge reach into communities, enormous experience of vaccine liaison and procurement work and then its role in communications. She then stressed the role of the World Food Programme in contingency planning and response work and then gradually, as we took forward the thinking and planning in September and into October, we were able to recognise that many of the other parts of the UN system are active. It goes beyond that though, because by bringing the UN system together we provide a core of capacity that is available to countries which then adds to the meaning that exists in other parts of the international system. For this purpose the World Bank is quite happy to be seen as part of the UN system and it is key to liaising and supporting countries on the fiscal and institutional side of action in the vet sector and human sector. In addition, we can bring in regional development banks, we can form a satisfactory relationship with a large number of international non-governmental groups, such as the Red Cross movement and the big NGOs: Save The Children Fund, Care, and the international medical corps, Médecins Sans Frontières, for example. So a co-ordinated UN provides a maypole around which the different organisations can dance and be more effective. It also provides us with an opportunity to fold the UN around some of the political initiatives that have come up recently, particularly the US international partnership, the Canadian initiative, the Australians’ work, and emerging initiatives that we do not yet know what they are going to look like which the European Union seems to be putting together. Taking them together, therefore, the co-ordination function is not simply having UN agencies sit in meetings talking to each other. It is about making the UN a vibrant entity, supporting the specialised agencies, being able to link sideways with other similar international bodies and moulding itself around the political partnerships. Therefore, my top priority is to have a very slim co-ordination office. It is not going to be an agency. It will have six or seven staff whose main job is going to be to track what happens at country level and global level in these partnerships in regard to communications and also the kind of response planning that needs to be done, but then to work through the different agencies
to make sure that they are able to take up the work rather than to second-guess it. It will be very different in style and concept from UNAIDS.

Chairman: Thank you very much. Let me ask Lord Selborne to follow up on that a little bit.

Q302 Earl of Selborne: Thank you very much, Dr Nabarro. From what you have told us already, it is clear there is a number of international partnerships, all of which have to be co-ordinated, and indeed you have described your own role as co-ordinating the roles of the different United Nation agencies and the World Bank. There is clearly now going to be a new initiative to the American-led international partnership. Where do you see the opportunities for synergy and, for that matter, where do you see the risk of duplication and confusion?

Dr Nabarro: My Lord, there are three dimensions to what we are trying to do at the moment on this. The first is what I call the technical dimension which is the business of trying to enable governments to have the correct responses to an avian flu outbreak or human flu pandemic. We cover that pretty well with the WHO, the FAO and their associated agencies, the international and national communicable disease centres, the animal health groups and the OIE around the world. The second dimension is the institutional dimension which is about getting governments to be able to be sufficiently well organised, financed and managed to deliver essential services to people. The institutional dimension of veterinary services in many countries is not strong, but I am afraid public health services are also pretty weak. Go to Vietnam and see that on both sides the situation is far from satisfactory. There is the third dimension to our work which is the political dimension, the kind of thing we saw today which is quite courageous from the US President, where a senior figure steps out and gives additional political cover to the ministers of health or the ministers of finance so they can do unusual things or have access to extra resources, even though their current workbooks are very full. For me, the partnerships of providing that political impetus, which you have to have when dealing with uncertainty that requires bureaucrats to do special things, will only be effective if they do lead to real action to improve institutional capacity in the main sectors with which they are concerned. I am particularly keen to see these international partnerships leading to a lot more action to improve the functioning of veterinary services so they can detect and respond to outbreaks of disease and also, where necessary, vaccination and bio-security can be introduced. That will only happen if the minister of agriculture and his or her team feel that the deputy prime minister or prime minister of a country is really taking an interest. That high level political interest will only be there through things like these international partnerships. The first US meeting I thought was pretty well done. A lot of trouble was taken by some very good officials. The US government joined itself up. Paula Dobriansky, the Under Secretary of State, is accomplished and Mike Leavitt, the Secretary of Health here, is a pretty exceptional person as well. We were not so sure whether the Canadian meeting, which focused more on health, was going to be so good, but they managed to get both Jacques Diouf, J W Lee plus Mrs Sardie, the Vice-President of the World Bank, along, senior people from other agencies and also ministers from a lot of different countries. They worked very hard with good chairing to get these ministers of health to realise that they have got to be intersectoral in their thinking, that they have got to not knee-jerk on Tamiflu stockpiles, that they have to get much more organised on surveillance, and they produced a good communiqué. So I think that looked pretty exciting. I am not sure about some of the other political initiatives around the place at the moment. I do not know enough about what happened yesterday and is happening today in Brisbane, but I am pretty clear in my mind that these political initiatives are vital if we are going to be able to increase in energy. So much now hangs on the skill with which FAO, WHO, OIE and the World Bank are able to use the meeting next week in Geneva, which is designed to take forward the technical and institutional work in which we are all involved, within the environment of the political partnerships so that countries are going to get the backing they need to work effectively. There is an awful lot of behind-the-scenes work to try to make sure these three days with over 600 participants, with quite a lot of hype in the media, understandably, give us what everybody is expecting of them. Plus we know that there are going to be countries coming along which are wondering what sort of resources they are likely eventually to be able to get for their own work or whether they are going to get Tamiflu. The handling of that, which is, in my view, quite an important junction within the political partnerships and then action, is going to be tricky. The danger of all this politicisation is threefold. One: the possibility that we just raise the heat of the issues to such an extent that room for manoeuvre of ministers in developing countries becomes limited because they feel they are under too much media scrutiny. At the moment I do not think that has happened but it could. Number two: we raise the political temperature so that we end up having disagreements globally between different blocs. This has not happened yet; this seems to be pretty much internationally non-partisan, but I worry a little bit that we get ourselves into a tangle on intellectual property issues not because they are necessarily important but because people see these as ways to make positions for themselves that play well back
home. The third and the most important risk is that each partnership will spawn its own mechanism for bringing resources to countries, and that we are all very frightened of. We are hoping to use the meeting next week and activities subsequently to try to make sure that does not happen. Louise Fresco is with me and I know that she would be able to add to this if an additional view would be necessary but I do not know what time is like and I do not know what your rules are, so she will not come in unless asked.

Q303 Chairman: Our time is quite tight but if Louise Fresco has specific points she would like to make, I am sure, we would like to hear them. Ms Fresco: I quite agree, my Lord, with the statements made by Dr Nabarro so far. I just want to emphasise that the real key issue will be the speed with which we can deal with the avian side, the animal side of it. It is very clear increased exposure of humans to animals which are infected is increasing the risk of reassortment or genetic drift or whatever risks we have on the human side, so to control the animal side is absolutely key. We have to recognise that not all countries are at the same level of being able to control and deal with this. So while it is important to have a worldwide and global approach, it is also very clear we must identify the countries which are most in need of a specific approach, specific strengthening. There are countries which are quite overwhelmed by what is happening, a case in point being Indonesia where we have probably 1 billion backyard chickens, and that is an enormous task. So I would just make a plea for understanding, on the one hand, the diversity of the situation and, on the other hand, the great importance of dealing with the animal side before we spend too much time in meetings and trying to generate resources and concentrate ourselves on co-ordination. The real work has to be done in the backyards in Indonesia, in the waterways of the Mekong Valley, in very, very concrete ways. Chairman: That sounds very logical. Perhaps we could move on now to a question which Lord Mitchell has about funding.

Q304 Lord Mitchell: Dr Nabarro, I wanted to ask you a very specific question about the FAO which may well have been overtaken by events. We have heard that the FAO was under-funded and was unable to function as it should do, and I wanted to know if this is the case. If it is the case, what should be done, particularly by our country in the UK? Dr Nabarro: I am going to speak as though Louise is not here because I know this question is to me in my co-ordination role. Louise has actually made the point which I would have said in the beginning in response to your question. Really it is absolutely vital to get countries better able to deal with the avian flu outbreak at source and we are not winning this battle in several of the severely affected countries. The only organisation we have globally which has the potential penetration to do this is the Food and Agricultural Organisation of the UN. They are under-funded. In the animal health area I sense they might have been under-funded for quite a long time. They do need more resources but also they need encouragement from governments to help them build up their capacity very quickly so they can act, so it is not just money, it may also be people. I have been very impressed by the Dutch government’s approach. I talked a lot to the chief vet of the Dutch government when I was in Beijing recently and what they are doing is not just offering cash, they are offering people and they are offering to use their own bilateral links to link up the people they offer with a number of key vet institutions with their training institutions, reference laboratories or specific programme elements in order to drive this up. You cannot expect FAO to move from the present situation to having two or three times the field capacity, which is what I believe it needs, just using funding alone; it needs other inputs. I have been in discussion with the UK Government a little on this. I was rung by the influenza point person while I was in Beijing, who had been in discussions with Hilary Benn about this explicit issue, and I said FAO needs cash, it needs support to build up its institutional capacity to back up vet services at country level, and it needs it yesterday. So I do hope that this is seen to be a priority by all governments but particularly those governments who see themselves naturally as supporting the multilateral system and being prepared to provide bilateral assistance alongside. Chairman: Thank you. Baroness Finlay would like to talk a little about China and Vietnam.

Q305 Baroness Finlay of Llandaff: Thank you. Perhaps the question goes to you both. We have heard about some of the serious difficulties faced in monitoring development of avian flu in China and Vietnam and particularly some of the diplomatic challenges that that poses as much as scientific challenges. I wondered if you could tell us about the steps which are being taken through the FAO and the UN to improve access of international agencies and experts to the region and to get information from the region. It may be that you have some examples from the Dutch model you have just referred to. Ms Fresco: Indeed there has been a problem with degrees of transparency in the Chinese situation. The Vietnam situation is not entirely identical. Vietnam was more overwhelmed than China. The Chinese government however has been in touch with us at a very intensive level lately and I am pretty confident the situation is improving. They have indicated to us,
for example, that they are willing to exchange bio-
sequence data and bio-isolates possibly, and that
augers quite well. Nevertheless, I think we can only
put pressure on these countries in the international
context. I think the awareness is growing that they
stand to benefit from part of the international trans-
boundary effort. The main reason is that there are so
many biological links between what happens in
China and what happens in the rest of the world
through migratory pathways and the fact that this
particular area, south west China and north east
Vietnam, is a concentration of so many of these
diseases and potential problems that I think the
awareness is growing in China. We have found them
certainly opening up more than some time ago. As
David said, one of the key problems is the lack of co-
ordination at national level between the veterinary
and the public health services and also down the
levels to the districts. This is a major problem also in
Vietnam where the central control does not always
reach out to village level.

Dr Nabarro: With regard to China, when I visited just
over a week ago I did note with my Chinese
interlocutors that there still seemed to be some
serious concerns from many outside groups that
things are not as open and transparent as they should
be. The reaction was quite strong. I was told very
clearly that if others feel this, that is not the because
the Chinese are not trying, they have a number of
internal difficulties they have to deal with themselves
with regard to centre and province relationships, and
also there are a number of other challenges such as
the vastness of the country. But the willingness to be
open, particularly on avian flu issues was stressed to
me again and again. They have also decided to put
control of the whole influenza issue up to Vice-
Premier and Premier level above the individual health
and agriculture level, and they have indicated to me
in public and in private that they want to become a
global player on influenza issues, and they realise that
if they do not demonstrate transparency in a way that
satisfies the outside community they are not going to
be taken seriously in the international arena. The
same kind of thinking happened when I was in
Vietnam. It was nothing to do with the fact I was
visiting but at the time they were also putting the
issue up to Vice-Premier level in Vietnam, and they
were increasing the extent to which the whole
political machine was getting engaged, so that the
chairs from 64 different provinces were brought into
Hanoi and the Premier and then the relevant Vice-
Premier spoke to them very clearly, saying “You have
to sort this out. I do not want any more nonsense
between health and agriculture at provincial level and
information does have to reach us.” They have a bit
of a problem in Vietnam in that there is a true
disincentive for information to go up because if a
provincial person reported they had a problem at
provincial level they got charged for the cost of
dealing with it, even bringing in the central capacity.
So, in sum, it is only the national governments which
can really sort out this problem of openness and we
are seeing signs in the two countries you have
mentioned there has been some shift. Then because
we really only have a relatively small number of UN
staff—even if you take the whole UN family together
our penetration is quite slight—I do not think we will
ever be in a situation where we can keep a supervisory
role in place, we have to instead work by building
trust and by building the general pressure on
governments to believe they will only be taken
seriously by the rest of the world if there is pretty
good evidence of transparency. I am sorry that is not
direct answer to the question but I think you can see
from that the way I am trying to go about this.

Baroness Finlay of Llandaff: Thank you.

Chairman: This is somewhat encouraging,
particularly in respect of fast action should
something break out. I think Lord Patel has a
question on this.

Q306 Lord Patel: Thank you very much, Lord
Chairman. Nice to see you, David, even if it is on the
video screen.

Dr Nabarro: Hello.

Q307 Lord Patel: My question relates to how to stop
the pandemic in its tracks. Modelling suggests that
the pandemic could be stopped by early and decisive
intervention at source. Given the source is likely to be
south east Asia, what steps are you taking to make
such intervention practicable? What will you do with
the 3 million doses of Tamiflu? What else can we do to build capacity
in south east Asia?

Dr Nabarro: I am quite interested in the way you
posed the question, so this is a good head-scratcher.

Q308 Lord Patel: You should be used to that!

Dr Nabarro: I am certainly used to it from you! Let us
start at the top. I must say I am very impressed by the
modelling which has been done, particularly by Neil
Ferguson and colleagues from the UK, and I was
interacting with Gordon Conway, who as you know
is acting as scientific adviser to DFID on these issues.
It is interesting just how taken Gordon and others are
with the results of the modelling which has been
done. I am sure you have all studied this, and perhaps
you have even taken evidence from that group. It
really looks as though we only have a window of
about three weeks to get moving if we are going to
significantly delay the pandemic at source. That is the
reason why we are putting number one emphasis on
surveillance and early-warning systems. I am not
convinced that we can do that just by simply
business-as-usual working through normal channels
of trying to drive up surveillance capacity. We need to be engaging with governments on what additional mechanisms they might be able to put in place through district authorities, through military, through even retail channels, because often retailers have got excellent logistic systems—we all know about how Coca Cola penetrates the places that others cannot reach—and we may need therefore in conjunction with some governments to say, “Use all channels to collect information”, particularly early rumour information which can then be put into not just the Ministry of Health but Ministry of Agriculture and which is then subject to very rapid verification and intervention. We have seen some of this for example in a recent case in Vietnam where, as you remember, from news reports over the weekend there were reports of deaths and of bodies being buried before they had been properly checked out and very quickly the information got back and action has been taken. So, number one, a surveillance capacity and an early warning capacity which goes beyond what normally exists inside the Ministry of Health. Number two is preparedness planning that means it will be possible to move frontline personnel to the first site of infection and to reduce social mobility and to restrict movement in and out of these areas. That is more difficult and we can only do that through preparedness planning but it is starting in some of the countries I have mentioned, particularly Vietnam, and I think we will see it also in the not too distant future in Laos and in Cambodia. It is already underway in Thailand and Malaysia and we have a bit of a way to go in Indonesia. The third and most difficult problem you allude to is what about the precious WHO stockpile which is building up, it is not already there yet, of 3 million treatments of oseltamivir, where is that going to be located, how is it going to be got to the sites where it might be needed quickly, what will be the rules about distribution, who will get access to it. That is still work in progress. WHO have been asked to do something on this in time for the meeting next week in Geneva. I am not sure that is going to be done in time and it is something I have got right at the top of my list of what I call global issues which need urgent action, addressing the question of where the stockpiles should be and what arrangements need to be put in place for moving them so that the frontline personnel can have them. Just a last point on this, I believe it will be necessary to have dialogue with military capability. I know all this has to go on the public record but I think it is reasonable I should say this. Given we are going to have very limited time to move stuff to where it is needed and we do not know where that is going to be, and given that there may well be difficulty with civilian air transport once the first rumours of pandemic appear, we need to have some extra back-up present. There are just the beginnings also, and they are going to have to move very fast, of dialogue to see whether or not we can get some stop-gap arrangements with the military. I was actually discussing that this morning with the relevant person here.

Q309 Lord Patel: Thank you very much, David, and sincere good luck.

Dr Nabarro: Thank you, Sir.

Chairman: Lord Winston would like to ask a question about international preparedness.

Q310 Lord Winston: Dr Nabarro, we are finding your answers really very cogent. Could you give us your assessment of the level of international preparedness for a possible pandemic, and particularly would you address what countries you think are furthest advanced and where we stand in the UK? You have been on record as saying that every country should have a Cabinet-level minister with responsibility for pandemic preparedness. Do you think there might be a risk with such a headline-grabbing proposal that you might undermine the prospects for effective action? Could you also give us some brief assessment of what action is likely to provide the best return on investment, for example, in surveillance and rapid intervention in south east Asia, the development of new vaccines, vaccine production, contingency planning and so on? That is a pretty broad question but we would be very grateful for your observations.

Dr Nabarro: My Lord Chairman, I did not fully hear the second-to-last comment about the quotation that was put in the Times a couple of couple of weeks ago when I said there should be a high-level minister with responsibility for flu. What was the downside of that which you wanted me to dwell on?

Q311 Lord Winston: We wondered in this room whether a headline-grabbing proposal like that might undermine the prospect for effective action.

Dr Nabarro: First of all, I do not think the world would do very well if the reassortment or mutation occurred within the next few months and we were to start to see pandemic influenza start. I think we would in fact be in a pretty bad way. Although a number of countries have started to think about preparedness planning and have started to get different government departments together, joining up perhaps sometimes, as in the France case, eight departments working together, and I know there is a similar cross-governmental approach in the UK, with the necessary work of different department officials thinking through what might actually happen under circumstances of a pandemic emerging not necessarily inside their own shores but some way away, I am finding there is still quite a gap between the planning process being put into place and people
actually beginning to articulate with each other the reality of what might actually happen in terms of being able to mobilise people, being able to mobilise stocks, being able to move people, being able to move stocks and being able to communicate with countries in a reasonably productive way. There is still I think a lack of perception among those who have started to do this work that there are likely to be a number of countries which are going to really close the door, and which are not going to be prepared for their own professionals to be moving around outside, they will want them to stay inside, they are going to be very nervous about their own diplomats being at large and who will be extremely concerned if they have military contingents abroad to get them back. If that is the case, if we are going to see a fairly quick wish of countries to contract, of pilots not wanting to fly, logistics organisations finding they have to cut off branches, the impact of how we as a world community respond will be really very dramatic. I have seen very few groups really focus on this. The only ones I have been impressed with doing this are large multinational companies who have started to do their own risk assessments and risk planning, business continuity scenarios, and I am finding them very, very scary. They are closing down, retrenching, lock-down of personnel, staying in their homes, one or two months’ survival rations, their own Tamiflu stocks in some cases and other medications. That kind of reaction will make the necessary joined-up early response work very, very difficult. One of the tasks that the participants in the first US international partnership on avian and pandemic influenza gave to my office was to think about what steps we can take to try to prevent there being a sort of general lock-down the moment the thing starts. I mentioned that I thought there was a necessity to take the responsibility for preparedness planning above the level of the Minister of Health versus the Minister of Agriculture versus the Minister of Interior versus the Defence Minister and to have an over-arching ministerial responsibility, because all the evidence I have had over the last few months before I took this job and since I have taken this job on any emergency work is that it is very hard to get different government departments and ministers to work together in a joined-up way on contingencies unless they are encouraged to do so by the highest authority in the country. That was the basis behind what I said. The thing was given perhaps, as I am learning more and more each time I deal with the media on this issue, more prominence than you sometimes want, but I stick by it and I have not actually noticed any backlash, in fact I think the reverse, that governments have been at pains to tell me that they have taken this suggestion quite seriously and I have seen some good results. Certainly the well-prepared countries, and I do put the US as reasonably well prepared though Bruce Gelman, the first point person here, says he is still very nervous. I think the UK Government is moving forward quite nicely, but again the Minister told me, and she might have told you in her evidence just now, that there are still quite a lot of difficulties, so generally I think a lot more has to be done. My assessment of international preparedness is nowhere near good enough and I think we have least six months’ leeway—perhaps a year, perhaps longer—to get ourselves planned, and that is why I am using every invocation I can to request the mutation does not occur for another year or so. I have not dealt with all the parts of your question but you will see I am sufficiently worried about this that I think I have some way to go to deal particularly with your last point.

**Lord Winston:** Thank you very much for the clear view.

**Chairman:** Thank you very much for that. I am going to turn to Lord Mitchell now to talk a little about international relations.

**Q312 Lord Mitchell:** I wanted to ask the question about the prospect the pandemic is having on international relations. There are a number of issues. First of all, the whole issue of international patent laws and whether companies will be side-stepping these. Secondly, whether the pandemic when it comes, if it comes, could lead to a serious break-down in international relations. I think you have touched on these points but it would help if you could elaborate a little further.

**Dr Nabarro:** Again I am going to see whether Louise wants to come in, because I think this is the most difficult question in a sense. Here goes: I think the current avian influenza epidemic is potentially quite bad for international relations, because we have seen it before. Louise and I worked in my previous job on a whole stack of issues to do with food safety, and we have found issues between countries on food trade can have very bad consequences, especially when they are located within health concerns, and it is really very important when countries make decision about the import or non-import of particular kinds of food from particular countries those decisions are based as far as possible on good evidence rather than on other possible concerns. So I still am not happy about what the avian flu epidemic is doing for trade relations in particular. I am very pleased that the FAO has come out quite strongly on this following Turkey—was it?—who came out on it. Secondly, I think the threat of a pandemic is having a relatively positive impact at the moment on international relations. So far I have seen no evidence of anything other than countries putting their heads together and being really very focused. I am a bit nervous about whether that dream environment will stay for the
next few weeks and months, especially as there becomes some prospect of competition over money, and we will see more and more concerns from African and Middle Eastern nations, but they need as much help as the Asian ones do or possibly more. I think that the patent laws issue maybe, maybe, a bit of a red herring. My reason is as follows: I have talked and others have talked to Roche and I am starting to get involved, but not directly myself, with GlaxoSmithKlein, and the suggestion that the way to deal with lack of access certainly to oseltamivir or Tamiflu is to encourage the production of the compound by generic manufacturers, perhaps in some way disregarding intellectual property provisions, is not really relevant I do not think. Certainly from what I have been told in this situation, Roche, which is a licensee of the manufacturing process, has indicated that it is very happy to discuss and then to conclude sub-licensing arrangements with anybody who can make oseltamivir effectively because they are aware that their manufacturing capacity, even with the projected increase over the next year, is far, far too little. The difficulty however is that the production process, as you may have heard in other evidence you have received, is really quite complicated—there are three difficult stages and secondly the raw material is not available in abundance—so unless some new synthetic process becomes available the production of antivirals is going to be limited more by capability, and particularly at the production side, rather than anything to do with intellectual property. When the Secretary-General says he does not want intellectual property to stand in the way, he is merely exhorting preferential pricing by the major producer so that poor countries can access the stuff cheaply, and Roche are certainly practising that. Secondly, he is exhorting the companies to do deals with generic manufacturers who can do it and they are trying to do it. So I am hoping that we are not going to see spats over this, though I did hear one or two remarks in one of the recent meetings that suggested that not everybody shares my view on this, and I have to watch it, and we may need to do some careful communication work. But the most serious point to your question is what might be done to international diplomatic relationships once the pandemic starts, whether it is access to viral material, antigen production in order to produce a vaccine, or access to information, or closure of borders and the stigmatising of people who come from particular parts of the world. This happened on a small-scale with SARS which was a relatively minor thing compared to the pandemic and I believe we will need to get groups, for example Chatham House, to start looking at this quite seriously and to see what can be done to anticipate potential snap decisions, knee-jerk decisions, being made which might have really long-term adverse effects on diplomatic relations.

Certainly I would like to encourage countries to approach the pandemic from the point of view that if you do not find a way to support the country which is facing the pandemic in its first stages, where they are facing it, with all the resources you can sensibly put to bear on it, it will come back and hit you later when the pandemic gets out of control and starts going across the world in a phase-like way. So to deal with the problems, for example, that might be faced in the long-term by the UK requires urgent action at the site. Secretary Leavitt’s quote which I like to use is that it is like fire, “A forest fire starts with a little spark and you can easily stamp it out with a foot, but if you wait for hours or perhaps days then it gets out of control and you have lost hectares of land due to the fire and have a huge amount of damage and you regret you did not put that spark out in the first place.” So diplomacy at the early stages must be one of international solidarity.

Ms Fresco: The discussion on access to patents and so on is also very relevant for the animal vaccines, which is the subject which is somewhat an orphan of this discussion. You may be aware of the fact we feel very strongly we should find alternative ways of administering the vaccine to animals because of the problems involved in actually injecting it. That requires more research and although international efforts are going on, it is very clear that we need to be absolutely sure that the investments in research—and the UK is very much involved in this—really be shared as soon as possible with all the countries concerned. With an increasing crisis, as David indicates, the sharing of research results may become more difficult. The second issue is that I am less worried perhaps about snap decisions being made by governments than I am about the lack of understanding by the public and the knee-jerk reaction of the public, as we see for example already in Italy where chicken consumption has gone down by 40 per cent, which is not based on any significant data or facts, to the contrary there is not even avian influenza in wild birds in Italy let alone in domestic birds. These kind of reactions have major potential impacts on trade relations, on international relations, and they can only be dealt with if we put in place parallel to all we have mentioned a massive effort on risk communication for the public. We have some experience of this for example in an area like biotechnology but it requires us all giving the same kind of message to the public, whether to the private sector, government, local government, internationally. This is something I would really like to make a plea for, and David and I will discuss it with our colleagues, that the issue of risk communication on which there is some good evidence and good experience from before really needs to be tackled, because it is how the public reacts, how individuals react, to people for example.
coming from Vietnam or Laos. That is going to be hugely important for international stability I believe.

Q313 Chairman: Thank you very much for those remarks. I am afraid we have come to the end of our time here but we have covered a lot of territory and I think we are, all of us, very impressed with your answers. Dr Nabarro, and with yours, Louise Fresco, perhaps a more realistic and down-to-earth viewpoint than we have heard from almost anyone.

Although it does not necessarily fill one with calm, at least it is reassuring to know you are there and appreciate the seriousness and difficulties which would be ahead of us as we face a pandemic. Let me thank you very much indeed for spending this time with us. We very much appreciate it, it will be very valuable to us and your input will appear in our report which will be published before Christmas. Thank you very much indeed.

Dr Nabarro: Thank you for the opportunity.

Ms Fresco: Thank you.
THURSDAY 3 NOVEMBER 2005

Present

Broers, L (Chairman)
Finlay of Llandaff, B
Howie of Troon, L
Mitchell, L
May of Oxford, L

Paul, L
Sharp of Guildford, B
Taverne, L
Soulsby of Swaffham Prior, L

Examination of Witnesses

Witnesses: Deputy Chief Constable Alan Goodwin, Chair, ACPO Emergency Procedures Committee, Mr Philip Selwood, Chair, Civil Emergencies Committee, Ambulance Services Association, Professor Sue Atkinson, Regional Director of Public Health for London, and Mr Zyg Kowalczyk, Director, London Resilience Team, examined.

Q314 Chairman: Let me welcome you and thank you very much for coming to talk to us today; we very much appreciate your time and your willingness to answer questions. We are aware that Professor Sue Atkinson and Mr Zyg Kowalczyk only really want to talk about London issues and not national issues. That is fine with us. Perhaps we could start by asking our witnesses to introduce themselves.

Mr Kowalczyk: I am Zyg Kowalczyk; I am Director of the London Resilience Team which is based at the Government Office for London. It is a multi-agency team which supports the London Regional Resilience Forum which supervises emergency planning across the capital.

Professor Atkinson: I am Sue Atkinson; I am Regional Director of Public Health for London, part of the Department of Health—part of CMO’s team in that respect—and I am also Health Adviser to the Mayor and the GLA.

Mr Selwood: I am Philip Selwood, Chief Executive of the Gloucestershire and Wiltshire Ambulance Trusts but I am here in this capacity the Chair of the Civil Emergencies Committee of the Ambulance Services Association.

Deputy Chief Constable Goodwin: I am Alan Goodwin, Deputy Chief Constable from the Derbyshire Constabulary. In today’s capacity I am here as the Chair of the Emergency Procedures Committee, Association of Chief Police Officers.

Q315 Chairman: My first question is to what extent are emergency and local services ready for an influenza pandemic? What do you expect to be the major challenges you will face?

Deputy Chief Constable Goodwin: In terms of readiness the national flu pandemic plan has been shared with all the responding communities and, in my particular case, with the police service. I have been involved in a debate nationally in terms of the formulation of that plan and now it is in place it is forming the base of discussions, plans and exercises at the local and the regional level in terms of the preparedness for a pandemic situation. In terms of challenges for the police service I think the biggest challenge that we will have will be the same as any other public or even private sector organisation. It will be in terms of business continuity because clearly from the point of view of the police service there is the potential—in the same way as any other organisation—to be without 25 to 40 per cent of the workforce at any one time. The biggest challenge for the police service will be to maintain a core service to the public and that will no doubt have to involve a degree of prioritisation of tasks if we do not have the workforce available and at the same time contribute to the local, regional and national responses to the pandemic situation itself. That may include issues around the protection of vaccine stocks, the protection of vaccination centres and potentially increased duties to assist the coroner in relation to an increased mortality rate.

Q316 Chairman: Do you have a back-up plan for the policing of the country? Would you bring in the military, do you think?

Deputy Chief Constable Goodwin: That is an option. There is certainly the potential for military assistance if that is required. If it were a sporadic outbreak in terms of geographical location there are the facilities to be able to call upon police resources from other parts of the country that perhaps have not been affected in that way. We have a well tried and tested way of actually accessing resources through the Police National Information and Coordination Centre based here in London which actually keeps an overview of any situation, usually for things like the G8 event in Scotland or the Tsunami response last Christmas. We have a well tried way of being able to access resources and allocate them across the country to assist colleagues where they are perhaps having difficulties.
Pandemic Influenza: Evidence

3 November 2005
Deputy Chief Constable Alan Goodwin, Mr Philip Selwood, Professor Sue Atkinson and Mr Zyg Kowalczyk

Q317 Chairman: Is there good collaboration between the various parties?
Deputy Chief Constable Goodwin: Yes.

Q318 Lord Paul: They played a video in the City Hall today about the 999 services called on 7 July—most of you must have seen that by this time—is there something we have learned from that?
Professor Atkinson: There are obviously always lessons to be learned from every event that happens and that certainly happened after the 7 July events and others. I think the crucial thing that is different about that sort of event—which was a one-off terrorist attack—is that pandemic flu would be a slow rise and would go on for a much longer period. In terms of the emergency planning for pandemic flu what we have been doing in London is to encourage all the local organisations to look at their own emergency plans in the light of the particular scenario about pandemic flu. We have produced for them a prompt document which takes them through the various alert levels of pandemic flu and highlights for them, at those different levels, what might be the things that as organisations they need to think about in terms of aspects of business continuity. It is that business continuity which is important to them, over a long period of time while there may be somewhere between 10 per cent and 25 per cent of their staff out at any one time, depending on the scenario. That is what we have been doing. There are always lessons to be learned from those sorts of events or from exercises but the pandemic flu one is slightly different from the short, sharp shock.

Q319 Lord Paul: While you may all be very prepared, how far do you think businesses and the ordinary people are aware of the consequences of this?
Professor Atkinson: In the Resilience Forum in London we do have business representatives, voluntary sector, utilities—everybody is represented there—and we have been working with some of the business sector on developing those approaches. We have had one workshop which was for all organisations at the beginning of October in which some people were more developed than others and we have another workshop specifically for the business sector, coming up which will be particularly to work with businesses.
Mr Selwood: I have a very similar answer to my colleague. In exactly the same way ambulance trusts do work in collaboration. I represent ambulance trusts on the Chief Medical Officers Committee that are preparing for a flu pandemic. That then translates to the committee that I chair, the Civil Emergencies Committee, which is set up on a regional basis. Locally ambulance trusts, in accordance with the Act, are part of the local resilience forums in the way that Sue has described. That means that we have good collaboration locally. From my perspective the dialogue is going on at those three important tiers.

Q320 Chairman: It is a detail, but what about 999 calls?
Mr Selwood: If we take 7 July as an example we went on television broadcast immediately to ask if members of the public could avoid using the 999 system until the full consequences were understood and we had a good public response. Returning to the point that Alan Goodwin made about prioritisation, there will be some activities that we will have to stop doing which are more routine work in order to generate a capacity to respond to a flu pandemic.
Mr Kowalczyk: Could I just make the point that there is a structured approach to emergency planning in London and in the rest of the country as well, headed in each region by a regional resilience forum. Following the 7 July events the London Regional Resilience Forum met and commissioned a detailed debrief process on those events and on the response. We have had that debrief process and a particularly important element of that was the telecommunications aspect and we have a detailed report on that, et cetera. The Forum met again on 12 October to consider the lessons from the debrief and now we are taking forward the actions to deal with that. Similarly on flu pandemic planning at the Forum meeting in June the prompt paper was agreed—which is the self-assessment/self-analysis which Sue referred to—and will go out to all the public agencies in London. They have had that; they are testing themselves against it; we have had the workshop. We are monitoring their response and we ask them to send back their modified business continuity planning against the flu pandemic. We will look at that again at the January meeting of the Forum and see what progress has been made, where the gaps are, et cetera. At the same time, with our business sub-committee of the Forum we are modifying that on paper to make it appropriate for business and London First and the other key business organisations; they are then going to take it forward in business themselves. So there is a structured way of looking at things, making sure the lessons are being learned and the plans are being taken forward accordingly.

Q321 Lord Soulsby of Swaffham Prior: In an emergency situation the public wonder who they can talk to and they call the police. Are you certain that you have enough information to spread right throughout the chain from the senior persons right down to the “bobby on the beat” sort of idea so they can answer the queries in an informed way?
public at times get very concerned about this and when we had the foot and mouth disease problem many people were concerned when they went to the local police they did not know how to answer the questions. Are you confident that your people can do that?

Deputy Chief Constable Goodwin: From the point of view of any situation such as a flu pandemic we would put in place very quickly a strategic co-ordinating group which is a group of all the local responders who are planning in peace time and when things happen we get together to direct the response to that particular situation. A key element of that work is the formulation of an appropriate communication and media strategy to be able to provide information to the public not only in terms of what is happening but also in terms of what they can do to assist by way of their own health and welfare. In a situation of this nature the likelihood of it is that that would be directed from central government in terms of the important messages and public information. We would then put in place at the regional tier and the local tier the right strategies to get that information to the public in the most appropriate format. I think a very important point is that we also need to make sure that our own staff are fully aware of what the issues are. For me a key element of that communication strategy would be: do our staff, do our 999 call takers, do our call centre call takers actually have the information to hand to give the people who are ringing in—possibly in a distressed or panicked state—to be able to satisfy their query and at the same time make sure that that information is available at the local point of contact—the police officer on the street or whatever—to be able to give that reassurance and that message? That sort of communication plan is not without difficulties, but it is an essential part of the response to a situation such as this.

Mr Selwood: This of course would be a health event and the Department of Health through its various tentacles has quite a sophisticated mechanism in my observation to get those sorts of messages out because it is obviously not just the first responders; it would extend to GPs, it would extend to nurses, to NHS Direct, the whole raft of people who have public contact and I think working in collaboration with colleagues we feel quite confident we will get it right. A lot of it is about prevention and reassurance and getting those types of messages out to both practitioners and public.

Q322 Lord Howie of Troon: Should the pandemic actually occur and should it turn out in the worst scenario it will be catastrophic. As you said yourself large numbers of personnel who would be expected to deal with it would themselves be out of it. In that circumstance would you be seeking international aid from some flu-free area should there be any?

Deputy Chief Constable Goodwin: Certainly from the police perspective we would be looking to make whatever use we could of the resources that we had available to us that were fit and able to provide policing services. If it was a widespread outbreak and affecting most of the UK and therefore some of our services—even with a series of prioritisation—were a little bit at risk, then the first port of call in my view would be that we would look to try to get some assistance from the military for some of the issues. There are well-defined protocols in terms of getting military aid to the civil authorities in terms of assistance from the military whether that be for law and order enforcement purposes or whether it is assistance for the actual impact of the event that we are dealing with. From the point of view of the resilience of the police service I think the first port of call would be to look for whatever the military could do.

Q323 Lord Howie of Troon: What about a second port of call?

Deputy Chief Constable Goodwin: That is an area we need to look at. If we need additional policing capability we need to look at where that could come from. It may well be that some form of international assistance may be an issue that we would have to look at.

Q324 Lord Howie of Troon: Has any thought been given to this?

Deputy Chief Constable Goodwin: Not that I am aware of in specific detail, no. There may well have been some work looking at what could be provided elsewhere. The issues for us would be the different policing styles, different policing jurisdictions elsewhere. There may well be an issue in terms of bringing an international police contingent into the UK within the legal framework we operate.

Mr Kowalczyk: From a different perspective our planning is based on the fact that all of the country and all the surrounding countries are likely to be equally effected so we have to stand on our own two feet. In terms of business continuity planning it is a question, as my colleague said, of identifying what are the critical services and what do we need to keep those services going and prioritising so that we would stop doing some other things in order to keep those core critical services going.

Q325 Chairman: Are we in a good position with respect to the capacity of the mortuaries?

Mr Kowalczyk: We have a group working on that and we are planning to be in that position. We have a mass mortality plan for London; there are similar
plans being developed for the rest of the country. It worked well for both the Tsunami and 7 July. We are looking at a different scale with a flu pandemic and we are working to make sure that we do have that capacity.

**Q326 Lord Mitchell:** Can you describe the process whereby the contingency plans of local and emergency services will be implemented during a pandemic, and what will trigger various alert states? I think these are equal questions to the country and to London specifically.

*Deputy Chief Constable Goodwin:* We have a well-established series of local and regional committees that would come into being to deal with any major incident. We have activated it many times in the past to deal with things like industrial action in certain other parts of the public sector, with foot and mouth and those sorts of issues. At the local level a strategic co-ordinating group would actually be formed. The trigger in this particular scenario with the pandemic flu would be from our colleagues in the health services because quite clearly from the police perspective very often we activate these strategic co-ordinating groups in response to a specific incident—be it a terrorist incident or some naturally occurring disaster—and we would need to be alerted to it by our health colleagues. We would then put the strategic co-ordinating group in place. Ordinarily it would be chaired by myself or another chief police officer in the various regions, but on this occasion there would be a good case for health colleagues to actually chair that group. If it were a localised issue—for example, in my county of Derbyshire—it would be dealt with within the county. If quite clearly the impact of the particular situation—or the flu pandemic outbreak in this case—was wider than one county—which it would be in this scenario—the regional tier would then put together the regional co-ordinating committee; if it were a national issue then clearly the government mechanism would be put into place. Those arrangements have been utilised many times both in genuine situations and in exercises and from our point of view the police service would be a very keen player within that whole structure of the various different levels, but the initial trigger I would say in this case would come from health colleagues.

*Mr Selwood:* We very much see this as something led by health, looking to other partners to assist, which is a reversal of the way things would normally go on in a terrorist situation where we take a subordinate role to the police co-ordinators. If I can just give you an example of a local planning going on, in Avon, Gloucestershire and Wiltshire—which is the strategic health authority area where I work—we have a specific tabletop exercise in December part of which is contingency planning for flu pandemic to test how do you co-ordinate and control the health economy with the assistance of other partners in such circumstances.

**Q327 Lord Paul:** So far as the emergency services contingency plans at local, national and regional levels, what kind of contact have you had with the Government and what is their input?

*Mr Selwood:* As I said earlier, I am representing ambulances services on the Chief Medical Officer’s group which is looking at flu pandemics. Within the capacity of the Civil Emergencies Committee of the Ambulance Service Association I can confirm that colleagues around the country are all part of the regional resilience forums and the local resilience forums, all of whom have on their agenda—I feel confident, given the exposure just recently—the issue of response to a flu pandemic. Ambulance services are very much engaged; they are part of the health service, the emergency arm of health and also the third blue light service so they look in two directions. In these particular circumstances they would be an integral part of the health response as I stated earlier.

*Deputy Chief Constable Goodwin:* From a police perspective there is exactly the same representation. I have represented the Association of Chief Police Officers within the TIDO committee structure and I obviously had some input with the Civil Contingency Secretariat on the plan itself. Again, just to echo Philip’s comments, I am confident that within every regional and local resilience forum there have been very detailed discussions around the national pandemic flu plan and also some very large scale exercises at the local level to test the plan as well.

**Q328 Lord Paul:** In your contacts with each other have you had quite a bit to learn from each other?

*Deputy Chief Constable Goodwin:* Absolutely. The beauty of the Civil Contingencies Act is the way in which now all the responders are around the table planning and exercising for the same issues. We understand each other’s roles far better now and we are also able to identify the inter-dependencies so that we, the police service, may be planning on the basis or on the assumption that the ambulance service, for example, could perform a certain function and the ability to plan and train together will either reinforce that awareness or make us change the assumption. So there is very close liaison at all levels.

**Q329 Lord Soulsby of Swaffham Prior:** To what extent will the emergency response in the event of a pandemic be devolved to local or regional bodies? I presume there has to be co-ordination between these various bodies, but how will it work? Will it be driven from the centre?
Mr Selwood: There will be a framework through the national committees that we have all signed up to. To try to control local solution from the centre in my experience does not work; equally it is not a “one size fits all response”. Depending on the level of exposure round the country one would want to use one part of the country as aid to another, but it has to be co-ordinated at a regional level, depending on the scale of the pandemic that we are talking about.

Mr Kowalczyk: Essentially what would happen is that the Department of Health would lead nationally on the health response. The Civil Contingencies Committee at the Cabinet Office at COBRA would lead on the wider response to the pandemic. They would activate regional civil contingencies committees in each of the regions, including London, which would deal regionally with the response to the pandemic. Within that the regional health organisations would be dealing regionally with the health aspects but also feeding into the regional civil contingencies committee. If I give the example of London, we would have the Regional Civil Contingencies Committee chaired by the Minister with the Mayor as deputy, all the key organisations around the table with health professionals—such as my colleague Sue—feeding in the health situation in London and then the rest of the colleagues deciding first of all what they need to do to support that and secondly what the impact is on the core services be they transport, emergencies, local authorities, whatever.

Mr Selwood: Sitting outside of that group would be a dedicated group of health professionals at whichever level we are talking about—depending the exposure—actually thinking through the co-ordination of the health response which then feeds in directly to the resilience forums.

Deputy Chief Constable Goodwin: In terms of the role of the regional tier, it is very clear that the regional tiers are co-ordinating tiers and they operate on a principle of subsidiarity whereby the actual decisions for the doing are taken at the lowest most appropriate level. Within the local resilience forums or the co-ordinating groups, those decisions are taken at the lowest level and then the co-ordination comes at the regional level and the securing of wider resources and then the next level up to the centre.

Q330 Lord Soulsby of Swaffham Prior: Will this be put on the web so that the general public can see what is happening? As happened with foot and mouth disease, will you tell us what is happening in different parts of the country? Will this be the same with a flu pandemic?
Deputy Chief Constable Goodwin: Certainly in terms of the principle of the way we described how that the various tiers of the response operate. Much of that information is already available on various websites, not least the Cabinet Office and the Civil Contingencies Secretariat. Part and parcel of the communication and media planning would be to see how much of the information specific to that particular emergency we could get out to the general public in whatever means. The general information is there now about how we would operate in response to any situation. If we got into the response phase on a pandemic situation we could tailor that to the more specific circumstances.

Q331 Baroness Sharp of Guildford: As I understand it this structure was part of the Civil Contingencies Act 2004 and from what you have been saying it is in the process of being set up. How far has this been carried through across the country or does it vary from region to region?
Deputy Chief Constable Goodwin: I have to say that the Civil Contingencies Act, certainly from the police service’s point of view, was very much welcomed because it put onto a statutory footing what had been in place in many areas for a good number of years and brought some of the more peripheral responding community to the same table and gave us the holistic view of what we are trying to achieve. The Act itself was very welcome in terms of providing that statutory basis, but I think it is fair to say that a lot of the co-operative working and the inter-relationships between the various agencies has been in place across the country. There will be some variations but I think across the country a real core of good activity has been there for quite some time. Although the Act itself does not come into force until later this month, there is certainly a lot of work that has been done ever since the Bill was published and we knew where we were going to have to be by November in terms of community risk registers, in terms of joint training and planning, looking at the business continuity plans and how they inter-act and inter-depend with each other. Although we probably will not be perfect on day one later this month when the Act comes into force, we will be a long, long way down the road in terms of building and formalising on what has been there for many years.
Mr Kowalczyk: The regional resilience forums were set up in April 2003 with regional resilience teams to support them in anticipation of the Act. In London, of course, it was going on for two years before that.

Q332 Baroness Sharp of Guildford: Mr Selwood, would you agree with this as well?
Mr Selwood: Absolutely. I can speak with experience in London up until April where ambulance services were part of the resilience forum for London and, having now moved down to Avon, Gloucestershire and Wiltshire they are represented on those regional
resilience forums. It is true to say that London had a two year start. The point was made about learning from experience, and that has been very true about resilience forums and the good work that the London Resilience Forum did led by Zyg has been transmitted round the country so that we do not have to keep re-inventing the same solution.

Q333 Baroness Sharp of Guildford: So in planning terms we are quite well prepared on these things.
Mr Selwood: I support Alan Goodwin. It is something we have all wanted for a number of years and in the run up to the Civil Contingencies Act these forums are now doing the work we all wanted to see in place for some years as professionals in this field.

Q334 Lord May of Oxford: It seems to me that the scheme brings to mind the expression think globally and act locally and you are the “act locally” bit of that expression, but in respect of the larger co-ordination what exactly is the role of the London Regional Resilience Forum when and if there is a pandemic?
Mr Kowalczyk: The role of the forum is to prepare but once we are in an active situation then it becomes changed into a London Regional Civil Contingencies Committee. It is a change of name and a change of function but most of the personnel around the table will be the same. The role of the London Regional Civil Contingencies Committee will be to take the overall view and coordination of London’s response. It would be linked closely to the national Civil Contingencies Committee. The Cabinet Office will sit on the London RCCC; the Minister will direct and co-ordinate and my team and the Government Office of London will provide the support. Essentially it will be the table around which all London’s key agencies and the business community and voluntary organisations are represented and around which London’s responses are co-ordinated.

Q335 Lord May of Oxford: If I could elaborate on that a little bit, these local resilience forums were born of 11 September in a sense and they responded well last summer, but here we are talking about something which is maybe going to go on month after month and the metaphor embodied in resilience is pulling a piece of elastic and letting it snap back. What if it is going to wrap it around the bundle that it is going to be stretched for six months? How do you see that going?
Mr Selwood: I think it is more complex around the country than it is London; London is, in a sense, a neat solution in terms of co-ordination of effort, but a personal observation would be that one would have to assess how you co-ordinate it depending on the scale. As it becomes more global in terms of the UK one would need to think very seriously about how one co-ordinates that effort. We have seen experience over the years—as Alan Goodwin referred to—in sustained industrial action where a national co-ordination group has sat but the solutions are then delivered locally according to experience and knowledge that has been gleaned. One would see a similar sort of infrastructure put in place, but I think it is very difficult to describe it without knowing the specific circumstances that we are faced with.

Q336 Lord Howie of Troon: Going back to London, is the main driver of the forum the Government Office of London or is it the GLA? Is that a difficulty?
Mr Kowalczyk: There is no difficulty; it is a place for some years as professionals in this field.

Q337 Lord Taverne: You have already dealt with the role of the armed services, but are there any other organisations that would assist the ambulance service?
Mr Selwood: As part of the contingency planning we have had dialogue with private ambulance services, for instance, and local transport organisations came to the aid of London on 7 July. That is a not untypical response. As Professor Atkinson has said, we will have lead time to this and we would have agreements in principle locally but one would bring those into play as and when the need arises. Within health and social care there is quite a considerable transport infrastructure so again, through the regional resilience forums and local resilience forums, it is about coordinating that effort and if you link that to prioritisation—stopping doing some of the work that we are doing—we would be able to call on additional transport capacity. The issue of course is one of medical care; it is no good having the transport if you do not have medical care to go with it. We would have to think that through carefully as well.

Q338 Chairman: You will have to communicate with these other organisations fairly rapidly, particularly if we lose 25 per cent of our capability. Have you established some sort of routine for communicating with those people?
Mr Selwood: The system that we have used in the past as a design framework was to have a point to which people would go to be communicated with, so you
pre-plan assembly points then get the briefing out and ask for the response that is required and deal with it in that way. Clearly radio and telephone could be compromised in these circumstances so one has to get back to some fairly basic methods of communication.

Q339 Baroness Finlay of Llandaff: In the event of the geographical distribution of a pandemic being uneven and with more serious outbreaks occurring in particular cities or regions, I wondered how the emergency services would then respond if it were very skewed across the country? Linked to that is whether different police or health authorities would share out available resources and how a trigger to do that would be determined. I realise it goes beyond the scope of the London Resilience Forum but I wondered what the arrangements are to the devolved administrations of Wales and Scotland as well and whether resilience forums have been set up in Wales and Scotland that would link in and respond.

Mr Selwood: The issue is one of mutual aid and if one again takes the events of 7 July ambulance resources were moved from Gloucestershire and Wiltshire into Royal Berkshire whilst Royal Berkshire came into London to assist in a fairly conventional system but one which was put in place as a direct result of 11 September and it worked at all four points round London very well. We would manage the co-ordination of that centrally through the Department of Health, but again the control goes back to local control arrangements. Zyg may be in a better position to answer the question about the dissolved administrations but I am aware that within association there are Welsh representatives and also for the Channel Isles. They have similar plans but I do not know about the legal positions of those.

Mr Kowalczyk: There are similar resilience arrangements in Wales, Scotland and Northern Ireland. They have different names. I think there is a Welsh National Resilience Forum, for example; in Scotland the arrangements are slightly different. The principles are all the same, all the key agencies and the devolved administration around the table taking forward emergency planning. Resilience teams from Wales and Northern Ireland have been to look at some of the planning that we have done.

Deputy Chief Constable Goodwin: From a police perspective I mentioned earlier the Police National Information Coordinating Centre—PNICC—is based here in London and that is activated at the request of the president of ACPO—the chief police officers’ association—in response to something which has clearly got national implications, an incident such as the Tsunami where it was activated then to be able to get resources from all the UK police forces to help with the deployment overseas in terms of the Tsunami issues. More recently it was utilised to be able to co-ordinate the response and support that was given from English and Welsh forces to colleagues in Scotland for the G8 event. During the course of the planning of that event at Gleneagles there was a similar structure in Scotland which mirrored exactly what was happening in England and Wales and there was very, very close liaison between the two. There is a well-established mechanism of being able to move resources around and in the original question in terms of an uneven distribution of the flu pandemic we would look to put that in place very early to be able to say that we have, say, a gap in the north west and the rest of the country is not as badly affected, what can we do to support policing services in that area?

Q340 Lord Taverne: Was the Tsunami experience relevant? It was clearly a very different issue with some people going overseas.

Deputy Chief Constable Goodwin: It certainly had lessons in terms of the sharing of resources. From the police perspective within each of the 43 police forces we have a lot of specialist resources in terms of victim identification, body recovery and those very specialist skills. What it allowed us to do was rather than putting the onus upon one particular police service to give support to colleagues overseas we were able to tap into the specialist resources from across the country and to provide a continuous service to colleagues out in Thailand and Sri Lanka particularly. There was a lot of relevance in terms of the willingness and the contribution that individual police forces could make to the wider effort.

Mr Selwood: The ambulance service response centred around the airports in Greater Manchester, London and Gatwick and the triage of returning patients or public was carried out by the ambulance service and then they co-ordinated efforts so that no one hospital became overloaded. We were able to move patients around—a major issue is that people are suffering routinely cardiac arrests or other life-threatening illnesses, so if we overload one part of the system then people will suffer as a consequence from natural causes as opposed to the particular issue that we are dealing with.

Q341 Lord Howie of Troon: Where a pandemic occurred there would be a period possibly of some weeks before it exploded, as it were, into something really serious. During that period some of the afflicted would need help but the general public would require information and reassurance. Have the local emergency services made any plans for that?

Mr Selwood: I think through the resilience forums one of the workstreams is communication and how to use the media to best effect.
Q342 Lord Howie of Troon: The media will be important; they will be stirring the pot.
Mr Selwood: Absolutely, and the lessons that we have learned over the years both in this country and elsewhere is to harness the assistance of the media at a very early stage to get the messages out by whatever medium is available to us to the public. Often that is a better way. We have also seen poor examples of that where it has not been done and it has left a vacuum.

Q343 Lord Howie of Troon: Are you confident you will get help from the media?
Deputy Chief Constable Goodwin: As part of the regional response within the regional resilience teams—certainly across the UK and Zyg can speak better than I for London—one of the bodies that is established within the regional structure is a media emergency forum whereby in peacetime planning, if you like, we actually get very influential members of the media (my example in the East Midlands is to get all the broadcasters and the key people in there) and keep them informed about what it is we are doing, what we are planning for, what the potential risks and threats may be, to give them an understanding of what the issues are so that if we did find ourselves for example in a flu pandemic situation we can gather those people and say, “This is the situation we are now dealing with; these are the key messages that we need to get out to the public, please help us do what we need to do”. The establishment of those relationships at an early stage is very useful.

Q344 Lord Howie of Troon: I must say that as a life member of the National Union of Journalists I wish you luck.
Mr Kowalczyk: Putting a London gloss on that, obviously the key messages will be delivered nationally but within London the same arrangements apply. We have a public information protocol which involves all the key agencies and the Cabinet Office and all the key government departments which we have used successfully in the past to co-ordinate the message to London citizens from the key agencies. We also have the Mayor, the voice of London in any crisis. The focus in London for getting the key message across would be the Mayor leading the key relevant agency.

Q345 Chairman: He has set up his own forum so he gets the correct information I assume.
Mr Kowalczyk: He is Deputy Chair of the London Regional Resilience Forum so we feed all our information to him. He has advisers such as Professor Atkinson. He also has his own plan in terms of the distribution of antivirals to key members of staff across the capital.
Professor Atkinson: Clearly the communications staff on those teams work closely together on a routine basis so during this sort of time they would know each other and be used to working with each other.
Mr Selwood: Our experience with the media is that providing we work with them at a very early stage and give them good information they are very, very happy to work with us in a positive sense.
Chairman: Thank you. Do members of the Committee have anything else they would like to ask? Well, let me thank you for your answers which have been very useful to us, very straightforward. You have clearly done a lot of planning already and we very much appreciate you coming and telling us these things. Thank you very much indeed.

Letter from Professor Jim Norton, Institute of Directors

Health Warning

Perhaps I should start by saying that I have no specialist knowledge of avian flu. However, I do have strong interests in the resilience of various areas of our national infrastructure to withstand disruptions such as that which might well result from a major flu pandemic.

Provenance

I am a Chartered Director of the Institute of Directors—Senior Policy Adviser covering ICT issues. The IOD represents in particular, the interests of our more than 50,000 members in small and medium sized companies in the UK. These companies are perhaps more at risk of lasting harm from infrastructure disruption than are larger enterprises that have the scale to take more elaborate precautions.

Several of the points that I wish to make are also endorsed by the Institution of Electrical Engineers—where I am also a Chartered Engineer and serve on the IEE’s IT Sector Panel.
My points draw on my past experience as Chief Executive of the DTI Radiocommunications Agency from 1993 to 1998—the UK’s then radio spectrum regulator and now the largest component of Ofcom. I also draw on my time, during 1998–99, as Director of the very first project team in the then Cabinet Office Performance & Innovation Unit—now the Prime Minister’s Strategy Unit.

I am particularly worried about cascades of failure, where loss of one key utility such as power leads rapidly to consequential failures in others such as communications.

**An Apparent Paradox**

I have spent many years working to improve the effectiveness and efficiency of UK organisations through the application of Information and Communications Technologies, expressed through new business processes and skills development. To that end I have endorsed much activity that removed unproductive slack, such as just-in-time manufacturing and the tight integration of supply chains. It is an inevitable corollary though that removing such “slack” makes organisations ever more dependant on the smooth running of our basic national infrastructure, power, communications, water supply, transport, and so on. I regret to tell your Lordships that, in my personal opinion, many aspects of our infrastructure have steadily weakened over the past 20 years—just at the time our dependence on them has steadily increased.

**What is Being Done?**

I would pay tribute to the work of the Cabinet Office Civil Contingency Secretariat (CCS) to reverse this trend. I think that they are doing excellent work, but I do not believe they command the support across Whitehall, and particularly in the Treasury, to drive through the major programmes (and substantial associated expenditure) required. Sadly, I doubt that there is much political capital to be made in building defences against threats whose timing is unpredictable. Whilst good “systems thinking” exists in organisations such as the CCS, addressing areas such as cascades of failure, I’m unconvinced that the necessary steps are being taken in implementing adequate protection across Whitehall and more widely.

**Key Areas**

I would like to highlight two areas that I believe are worthy of this Committee’s detailed attention:

First—Mobile communications.

The UK’s mobile communications networks were not designed for high resilience against major disruption, yet increasingly, citizens, other utilities, businesses and government services assume that they are. In particular:

- Loss of power causes immediate loss or at least major degradation of service. Most microcell sites have no backup power. Backup power at larger cell sites is highly variable and often limited to perhaps 45 minutes.
- Even where the power stays on, the process of shedding civilian traffic to give priority to essential services needs significant attention—many key users do not have the correct access to priority handsets. We saw some of the effects of this on 7 July.
- The UK power distribution network companies are in the process of abandoning their wide area private mobile radio systems (which had long-term backup power) in favour of the (much cheaper) use of cell phones. Yet if we lose power across a particular geography the cell phones rapidly follow. Having just a very few satellite phones as well may not be enough to co-ordinate service repair and restoration.
- Airwave, the integrated emergency services radio network covering, in particular, police, fire and ambulance services may also have insufficient duration of backup power at key sites to sustain itself during a major power outage.

Second—infrastructure telemetry systems.

The so called SCADA systems, which are radio based, are used extensively in areas such as water supply and sewerage. They are often quite old. They date from an era with a different perception of threats:

- In some cases they don’t use authentication or encryption technologies and are thus open to radio based hijacking or jamming.
- They are increasing connected to the Internet for linkage back to control centres opening all the familiar possibilities of Internet based hacking.
We do not need malign action by terrorists or even avian flu to precipitate a cascade of failure. One occurred in Italy a couple of years ago when a falling tree took out a key power inter-connector from Switzerland to Italy. The Italian power grid underwent rapid and progressive collapse. Restoration was severely hampered by lack of communications, when the cellular networks were also lost. In Los Angeles a couple of months ago a major area of the City was blacked out for hours, simply by maintenance engineers cutting a series of cables in the wrong sequence. Such events will happen.

3 November 2005

Examination of Witnesses

Witnesses: Professor Jim Norton, Institute of Directors, Mr Kevin Hawkins, Director General, British Retail Consortium, and Mr Alan Lacey, Regulatory Affairs Manager, J Sainsbury plc, examined.

Q346 Chairman: Good afternoon, gentlemen. Thank you very much for joining us. Perhaps you could introduce yourselves before we start with questions.

Mr Hawkins: Kevin Hawkins, Director General of the British Retail Consortium. We have 80 retail companies as members, many of the larger and middle sized ones in the UK, both food and non-food. We also have 18 trade associations as members who represent smaller or specialist retailers. We have, as the BRC, co-ordinated the response of our food retail members on a number of food scares over the last few years, namely the Sudan I most recently, foot and mouth and BSE. Before I joined the BRC in my present post I had nine years as a director of Safeways—now demised—so I have some experience of dealing particularly with the media on food scares. Professor Norton: I am Jim Norton. I am here this afternoon as a Chartered Director and on behalf of the Institute of Directors where I am a senior policy adviser covering information and communications technology issues. The IOD represents in particular the interests of more than 50,000 small and medium sized companies in the UK. Those companies are perhaps more at risk from lasting harm from infrastructure disruption than larger enterprises which perhaps have the scale to take more elaborate precautions. A number of points I am going to make are also endorsed by the Institute of Electrical Engineers where I am also a chartered engineer and I serve on the IT Sector Panel.

Mr Lacey: I am Alan Lacey, Regulatory Affairs Manager for J Sainsbury plc. As you know we have several hundred supermarkets throughout Great Britain and Northern Ireland. My background before I joined Sainsbury was in public health dealing with food safety and I have dealt with various food safety crises on behalf of Sainsbury in the past.

Q347 Chairman: Let me open with a rather general question. What impact is the current spread of avian flu and associated media coverage having on business in the UK?

Professor Norton: I think it is raising business’s awareness of resilience issues, and I think probably not before time. I can share some data with the Committee. We carried out two surveys in the last year. One is a year old; it was carried out with a balanced sample of IOD members roughly in June 2004. We found then that 50 per cent of our members’ companies had actually got formal plans in place against major disruption such as terrorism; 50 per cent had not. Furthermore there was an imbalance by size of company. Only 38 per cent of companies employing one to 25 staff had contingency plans whereas 77 per cent of companies with more than 200 staff had such plans. There was also quite a significant sector skew so 71 per cent of our members in the financial services sector had such plans; only 38 per cent in manufacturing. If we come to a more recent point, a survey of ourselves with Cable and Wireless, of mid-size companies of 30 to 500 employees we found that two thirds of those firms had no provision for staff to work from home (for example using Broadband communications) if there was perhaps disruption which made access to their office unavailable even perhaps through quarantine arrangements. Furthermore, 65 per cent of those companies felt they would be very seriously affected if they lost access to their site for more than one day. Just to rub this in a little more, four out of ten of those companies either did not bother backing up critical data or backed it up on site where it would not be available to them in the event of a quarantine. Whilst the IOD is actually very worried that there might be spurious concern over the immediacy of avian flu, it welcomes the general raising of awareness of contingency business continuity resilience issues.

Mr Hawkins: I will deal with the factors as we see it on the customers—the consumers—who frequent supermarkets. Most consumers find out about these things from the mass media—the tabloids and the broadcast media—and initially I think there was quite a lot of confusion for ordinary people between avian flu and pandemic flu. The consequence of that was a fairly sharp drop in sales of poultry (chickens, of course) of between 5 and 10 per cent in volume terms across a broad spread of food retailers. That has since largely recovered but that may be slightly misleading because it probably will only need a major development in the disease to be suitably communicated through the tabloids in their usual balanced and non-emotional way which will again provoke a reaction in terms of sales. I have to say the
initial government response in terms of reassuring the public that there was no danger from avian flu to people was unco-ordinated and rather hesitant which did not help.

**Q348 Chairman:** Has the experience gained in the foot and mouth crisis been carried forward to this situation? Is it relevant?

**Mr Hawkins:** I would like to say that all the lessons learned have been carried forward. All I can say—and it may be very early days yet and this may be an unfair judgment—is that so far I have not been unduly reassured by what I have seen and the dealings I have had with various government departments.

**Mr Lacey:** My comments are essentially the same as Mr Hawkins’. We are always aware of the need to communicate with our customers and that is something which is done on a day by day basis in this sort of event. From a business point of view the foot and mouth outbreak taught us some lessons and enabled us to enhance our crisis management procedures and certainly that is already useful and will become more so if this develops.

**Q349 Lord Mitchell:** I would just like to pursue what you have said about government departments not being that great. It is an important point; can you expand on it?

**Mr Hawkins:** Just to backtrack a few weeks, when the issue was first raised in the media the Chief Medical Officer did one or two television interviews—you may have seen him on breakfast television—but they were not entirely reassuring. I think the problem that officials—experts if you like—like the Chief Medical Officer and others have is that they tend to talk in media terms and not in terms that ordinary people understand. I think there was a certain ambiguity about some of the things that he said. The Food Standards Agency simply put out a statement saying that chicken was perfectly safe to eat on its website. Frankly the great majority of consumers do not consult the FSA website; they need something which is a lot more proactive, especially in the context of tabloid headlines which are giving the consumers a very different and rather alarmist message. What we learned during foot and mouth—and indeed from BSE—is that there needs to be one simple message communicated by all the relevant government departments and it needs to be repeated and repeated and repeated for as long as the evidence supports it.

**Q350 Lord Mitchell:** We have heard it said that there have been recommendations that there should be a minister responsible for this; other countries are thinking about it. To me that would co-ordinate the points you are making.

**Mr Hawkins:** What has become clear to date—and other witnesses may have comments—is that there does not seem to be a great deal of co-ordination between government departments, particularly the Department of Health and Defra and, of course, the FSA as well. We saw this again during foot and mouth and it seems to be the case now that the Government does not really get its act together and speak with one voice at the same time.

**Q351 Lord Mayor of Oxford:** It seems to me, however, that there is a difficulty because I am sure you are not suggesting that the Government should simply be co-ordinating, telling everybody that there is absolutely nothing to worry about in handling or eating chickens unless they are dead parrots, as it were. It is slightly more complicated. People who are working with poultry at some low level ought to be a bit worried at the moment because we do have migratory birds that come in. That fits into an area which many of the civil servant people still have not quite learned, that is the skill of communicating what you should not worry about without taking the extra step of saying that there is nothing whatsoever to worry about and in the aftermath of BSE puts up a warning sign in Scotland.

**Mr Hawkins:** I am not advocating for one moment you have said about government departments not that the Government should oversimplify or make claims that cannot be justified. I will give you an example drawn from the Sudan 1 a when the Foods Standards Agency put out a statement saying there was a “small risk to humans’ health”. Then in the statement they said, “By the way, please return all products containing this substance; do not eat them, return them to the retailer”. That, I think, set up a lot of this ambiguity. By all means if there is a qualification to be made to a general message that something is safe, then make it but be precise.

**Q352 Baroness Finlay of Llandaff:** What is your estimate of the likely effect of an influenza pandemic on business in general, and on your sectors in particular. That would be taking into account things like high absenteeism rates, perhaps closure of schools and working parents then feeling obliged to stay at home with their children, difficulties with transport, infrastructure around the country. People would perhaps be reluctant anyway to come out to places where other people are and would stockpile at the beginning, raiding shelves—the situation that one has seen quite a few times already—and in the worse case scenario some of the young, fit workforce are the ones who are most severely affected and may not survive.

**Professor Norton:** I think the thing that most worries us at the IOD is the prospect of cascades of failure. Let us assume—and it might even be that this is aggravated by avian flu—that we have a serious
power outage in central London. There is a touching faith amongst the public, business and other utilities—and indeed government—in the resilience of the mobile phone network. They were never built to be resilient; they do not in general have power back up, for example; they go down very quickly once you have a major power outage. We see in the Civil Contingencies Secretariat—to whom I will pay some tribute—a good deal of system thinking, saying, “What will be the consequences of this?” What I have not seen I regret is that reaching out across government to the actions that would be required to contain and block those cascades of failure.

**Mr Hawkins:** I think our main challenge would be to keep the food supply chain going in the event that on the DoH’s figures of 25 per cent of the population being infected over a period of 17 weeks. Clearly they will have justified that estimate; it could be more, it could be less. The main points of vulnerability in the food supply chain would be heavy goods vehicle drivers; they are the people who get the product from the manufacturer to the retail distribution centres operated by supermarkets and of course the connection between the farms and the food processors and manufacturers. The heavy goods vehicle drivers are not particularly numerous as a group but they are vital to the extent that there is a shortage of qualified heavy goods vehicle drivers in this country. Therefore if 10, 12, 25 per cent of them fall sick for any period of time the chances of replacing them with qualified vehicle drivers are very remote. The second issue arising from that, even if that part of the distribution chain was relatively unaffected, is that if the predominantly female staff in supermarkets—mainly part-timers—were affected then we would not have enough people in stores to ensure that products got from the stock room to the shelves. The other problem, of course, would be panic buying. When people believe that by going out of doors and going into food stores they are increasing the risk of them catching some disease, then they would tend to panic buy to hoard and to keep indoors for as long as the crisis lasted. We would have to move very quickly to ensure that there was no panic buying.

**Mr Lacey:** Just to endorse that, we do have an occupational health team who have looked at the various possibilities based largely on the Department of Health’s predictions. We have taken each layer of the business one at a time, looked at the risks, looked at the particular jobs that are business critical and looked for ways of multi-skilling so that we could keep the business running. We have also had to look at the issues of our internal staff policies on absenteeism recognising that there would be situations where our colleagues in store might need to stay home to look after family members and so on. There has been a lot of work done on that so far.

**Professor Norton:** Over the last 10 years, for very good economic reasons and very good business reasons, we have taken much of the slack out of our systems in many sectors, whether it is retail or any other. I have personally driven campaigns on just-in-time manufacturing, removing stock and so on. I have observed that through that action—which made perfect economic sense—we do rely on the smooth running of our infrastructure far more than we did 10 years ago. The consequences of failure cascade much more quickly.

**Q353 Lord May of Oxford:** You say you share the awareness of the drive for increasing efficiency having also increased the fragility, so in what sense it makes economic sense must be a rather limited sense in my view. If you go back 50 years to the last war, this was a less urban society and there were many more people directly connected to the land, but here you have very large numbers of people who depend for food on being able to get it and you have just said there could be power problems, there certainly could be delivery problems and so on. What are your thoughts about how you will address this, in particular food supplies, if some of the problems you have just sketched so well are upon us? How are you going to react?

**Mr Hawkins:** As Professor Norton has said, the level of stock within a supply chain generally is much lower than it used to be. That said, I think there will be more pressure on fresh foods than on packaged dry groceries. I think frankly should there be problems of this nature and the food supply chain becomes seriously impaired, then I think manufacturers and retailers together would have to decide on a priority list of foods, those that could be brought into supermarkets that people really could not do without. Some of the other stuff would have to stay where it was or not be produced at all. We would not be caught flat-footed by that; we would certainly be able to put together very quickly a list of what we consider essential foods. That would not suit everybody and again we would have to ensure that that was not destroyed by panic buying.

**Q354 Lord May of Oxford:** Is there any futuristic sort of scenario where you begin to think: if it looks like this is developing you do actually produce things that are, as it were, military-like food kits that you can store and if people do want to start stock piling well in advance they could do that.

**Mr Hawkins:** That would certainly be a possibility. What we have noticed before—particularly with the fuel crisis in October 2002 when in fact the food supply chain came within a few days of collapse—is that people were buying rather irrationally in some respects. I think sales of toilet roles exploded, which is paradoxical if people expected to be eating less. There were also other things which you would not
think was a particularly rational choice for a crisis period. What you are suggesting, Lord May, would be in a way a parallel course to rationing because we would in fact be producing ready made packs for survival.

Q355 Lord May of Oxford: I was also suggesting in some way you take the advice you were offering the Civil Service, to think a bit more laterally about co-ordinating things and are there not things that you can do to help the public in general respond more rationally given that it is going to respond? Professor Norton: I am at one with you on your economic point, and I think we should be ploughing back — this Committee might want to consider that in its recommendations — some of the very considerable benefits we have drawn from reducing stock into ensuring that some key elements of our infrastructure are more resilient. If we lose the channels of communications with our public in particular areas then that would be a sure fire guarantee of panic buying.

Q356 Chairman: Mr Lacey do you have a plan to stem panic buying? Do you have a contingency plan? I can also imagine you might have a security and disorder problem so you would need more security guards in your shops.

Mr Lacey: We have a security department which will take each situation as it come. I am quite sure we could cope with that. As far as rationing is concerned, it is a very difficult issue and we have had some local problems in the past. If, for instance, you consider a break down in water supply when there is panic buying of bottled water we have relationships with our suppliers that enable us to get extra products into store and also restrict the number of units that each customer buys. It is a difficult balance to strike but really it has to be taken on a case by case basis rather than having a general plan for rationing.

Q357 Baroness Sharp of Guildford: On the same theme, while you move just in time and therefore your supply lines are tighter than they used to be, most homes have invested in freezers and refrigerators and there is actually more space for keeping food at home than there used to be. Would it lead to panic if the Government were to suggest that it might be useful if people, for example, stocked up a bit on pasta or put food into their freezers? Last time when you had the petrol crisis people were totally irrational in what they were buying.

Mr Hawkins: I would like to think you are right but I think the very first announcement from government which encouraged people to stock up on anything would open the flood gates. In a way I rather hope that is the last thing government does.

Q358 Lord Mitchell: How high a priority is contingency planning within the private sector and how well prepared is business for an influenza pandemic? I think you have addressed that issue as well so I will go to a couple of other points. My background is in IT and you can imagine a situation where IT systems go down. The thing you have said to me today which worries most of all is the fineness of the supply line. We saw this in the petrol crisis, just how quickly it all goes down whereas before it was much more resilient. What would happen if terrorists, seeing this happening, actually compounded the problem? That is the sort of thing I suspect they would do.

Professor Norton: Can I respond, Lord Mitchell, with an anecdote? One of our members who thought he had very extensive backup power for his facilities went round and actually checked the fuel tanks for the backup power and found the accountant had emptied them and sold the fuel on the basis that it would be easy to re-stock in a crisis.

Mr Hawkins: Our main concern is not the level of planning among the bigger retailers because we have been here before and we always learn lessons; in general terms the procedures put in place operate quickly and smoothly. What we found during the fuel crisis in particular was that many of our smaller suppliers were not so prepared. The reason why the food supply chain came so close to disaster was the fact that the smaller firms were running out of petrol and were relying on the bigger firms from the companies like ourselves to keep them going. How much readiness there is among the small businesses generally to deal with a pandemic I really do not know.

Professor Norton: One of the things we are trying to do at IOD is suggest to our members things they can do which make perfectly good business sense in the normal world anyway and should save money in normal times, but would actually make them substantially more resilient in bad times. That is things like off-site backing up; things like being able to have a degree of working from home. Those actually save money and so they really ought to be no brainers. That process helps to improve resilience rather than simply tackling the resilience issue head on.

Q359 Chairman: You have highlighted these problems that you see. A slight silver lining to this is that it is waking people up to bad practice. What mechanisms are there to get through to small companies? Do you have any formal procedures by which you can inform and advise small companies?

Professor Norton: We certainly do through our network of members. I know the Federation of Small Business does the same as well. I think the challenge for anyone who is running a small business is the
number of things competing for their attention and the sheer difficulty of keeping head above water means that unless it is really important and pressing it does not tend to get dealt with.

Q360 Lord Taverne: What about the cost of all this contingency planning? How many small companies say, “Well, if we take into account the possibility that it may not happen at all, the cost of planning against it, let’s stick our head in the sand and do nothing”? 

Professor Norton: That is why I say there are many actions that could be taken in the normal way without having to appeal to resilience but actually do sharply increase the resilience capability. Working from home is a key example; backing up off-site is another. It is, to be blunt, commercial lunacy to run a business without proper backup to the information on which it runs. All past history suggests that something like eight out of 10 companies that lose their data never restart trading. That clearly cannot be a sensible thing. I think there is a lot that can be done—and we are certainly doing with our members—to improve resilience without saying “You have to spend X on resilience” because, as you pointed out, that is quite a difficult sell. However I can show many of those things save money in the day to day operation of the business.

Q361 Lord Taverne: There must be a lot of cost attached to contingency planning which the bigger companies are doing now. Do you have any estimates of the scale of this?

Professor Norton: I cannot estimate it. Of course, if you are a quoted company then you have quite considerable obligations, particularly on risk, to show that you are managing this well and professionally. There is a significant compliance issue there but it is also part of being a listed company. On that front we, as IOD, through our chartered director programme are actually training directors in the requirements and giving them a professional qualification if they choose to take it. If they do that they will have had to confront these issues. If you are running a small business which is not a listed company the same framework does not apply and, indeed, it may be very difficult for reasons we have explored.

Q362 Lord Howie of Troon: Obviously a good deal of planning has been done based on your experience of earlier crises of one sort or another. Can you tell me to what extent these plans have actually been tested?

Professor Norton: Going back to that IOD survey which is a year old, of the 50 per cent who did have plans, 62 per cent have tested them inside the last 12 months and 81 per cent had given specific training to staff in the execution of those plans. That was a reasonable result. It is certainly clearly important to exercise those plans otherwise, as in the case of my man with no oil for his backup power tank, you do not discover it unless you test them.

Q363 Lord Howie of Troon: Many companies—big and small—test their fire precautions quite regularly. Can they test disaster precautions regularly?

Professor Norton: Certainly if you are a listed company it would be mandatory to do so. Many companies that I know would have a major annual exercise where they declare, for example, critical systems have failed; they would be forced to switch over and prove that their backup strategies and relocation strategies work. That is the large tier of companies who are not the key concern here.

Q364 Lord Taverne: Do you get any reaction from some of the companies such as, “Well, we’re used to these scares”? 

Professor Norton: I have a very simple answer to it, Lord Taverne, and that is that in 1996 I had my headquarters wiped out by the IRA Docklands bombing so I actually had to do a complete disaster recovery. The date and time is certainly engraved on my memory. We got a lot of it right; we got some things wrong. One of the things I do is go round our members explaining that. When you have been through such an event you have slightly more credibility in telling people to take precautions.

Q365 Chairman: Mr Lacey, has Sainsbury tested the procedures?

Mr Lacey: Yes, we have major exercises to test our business continuity programme.

Q366 Baroness Finlay of Llandaff: We have been talking a lot about food and food distribution and focussing on that. I backup organisations to you such as the banks or whatever did not continue with trying to maintain service but actually responded in a crisis by battening down the hatches and closing have you built in any contingency plan of any sort for that type of situation? Are there some third lines and fourth lines as part of the industrial sector where it is actually essential to you that they do not do that and they have the same thoughts about trying to maintain the services as we have been talking about?

Mr Lacey: As part of our relationship with suppliers and contractors they are part of our contingency planning. As far as our suppliers are concerned in a situation such as we are facing now we start looking for alternatives in case there is a problem with a particular supplier or a particular part of the world that we draw a product from. Then we will have alternatives established, identified and ready to kick in when necessary.
PANDEMIC INFLUENZA: EVIDENCE

3 November 2005

Professor Jim Norton, Mr Kevin Hawkins and Mr Alan Lacey

Professor Norton: It is also a key element in a larger company. The evaluation of risk is what is called “supply chain risk”. It is not “Have I got plans in place?” but “Have my suppliers and my distributors got plans in place?”

Mr Hawkins: I agree with my two colleagues. I think there is just one caveat I would add and that is to remain oneself of Field Marshal von Moltke’s famous rumination that no battle plan ever survives contact with the enemy and all contingency planning is based to a great extent on known scenarios, on hard-won experience in the past. The problem with a pandemic is that none of us have had experience of it and we do not know until it starts exactly what the depth of the crisis will be and how many people will be laid low by it. Everything that we have said and all the planning that rightly happens is subject to that caveat.

Q367 Baroness Sharp of Guildford: Have you had any advice from the Government or from the Health Protection Agency on your planning?

Mr Hawkins: We have had no advice either from the Health Protection Agency or the Department of Health. That is ourselves as a trade association and as far as we know none of our major members have had direct advice either. We, as the British Retail Consortium and some of our member companies, have had meetings with Defra officials who have briefed us on their own contingency plan. We first met them two months ago to talk about avian flu but we found ourselves talking to the specialists in Defra who focus on disease control and not those responsible for business continuity. I think it is also worth pointing out, without being critical of Defra, that this meeting took place at our request not at theirs. We seem to have to take the initiative every time in order to get answers to questions. That goes back to what I said earlier about proactivity—or the lack of it—from government departments.

Q368 Lord Soulsby of Swaffham Prior: Do you find it very disappointing that you have to go to government departments to get information and action rather than them approaching you?

Mr Hawkins: It is not that we expect any government department to be able to answer all our questions at any one time, but it would be reassuring if there was a little more proactivity on their part because, after all, they do have overall responsibility for the food supply chain—that is of course Defra—and one would have thought it would have been in their own interests to initiate an early dialogue with the key parties within that supply chain.

Q369 Lord Taverne: Does this mean that companies are taking their own initiatives, for example in stocking antiviral drugs?

Mr Hawkins: I am really not in a position to answer that question; I will find out if you wish.

Q370 Baroness Sharp of Guildford: Can I take it that when you say you have had no contact with government departments this applies also to local authorities?

Mr Hawkins: Yes.

Q371 Baroness Sharp of Guildford: We have just been hearing about all these regional resilience teams so these have not yet percolated down to involving you.

Mr Hawkins: Not yet.

Q372 Lord Howie of Troon: Do you propose to ask for further meetings with the government departments?

Mr Hawkins: Yes, most certainly. The alternative is to wait for something worse to happen, which we do not really want to do.

Q373 Baroness Finlay of Llandaff: Can I just be clear on this, the resilience teams have not been talking to you about maintaining the food supplies in an emergency that goes on for several days and weeks.

Mr Lacey: That is correct.

Q374 Lord Soulsby of Swaffham Prior: What action would you like to see from the Government to support business in preparing for a possible pandemic, both legally and financially?

Mr Hawkins: Following on from what I have just said, more willingness on the part of those departments and health officials who are responsible for drawing up emergency plans to engage with us in the food industry—not just the retailers but the industry as a whole—to get a better understanding of how the food supply chain works; we believe the understanding is limited. Secondly, while Defra always focuses on disease control—and I think generally does a good job there—I do not think it thinks enough about the practical issues of moving forward around the country. With the assistance of the Institute of Grocery Distribution (which represents all parties in the food supply chain) over the years we have encouraged and arranged for ministers and senior officials in Defra to walk the food supply chain to see in the course of one visit how the different parts of it link together. We still do not seem to have the response we would like from officials. We saw all these problems during the foot and mouth crisis when the Ministry of Agriculture was still in charge and things do not seem to have progressed a lot since then. I think the third point is that Defra has made it clear that their contingency plans only apply to England; what happens in Scotland, Wales and Northern Ireland is down to the
Mr Hawkins: Yes, but I suspect not enough to cover any real shortfall.

Q378 Baroness Finlay of Llandaff: You have told us what you think you would like the Government to do and so on; has there been any forum between the major food suppliers such as Sainsbury, Tesco, Asda and a few others to develop a food supply contingency plan? Has there been any initiative like that at all that has occurred? Or do the different retailers remain in competition?

Mr Lacey: There is always a commercial aspect but clearly we work through the British Retail Consortium and I would guess—if you would allow me to do that—that our major competitors have very similar systems and plans in place, similar networks of supply. We made a point about HGV drivers and distribution and the need for a contingency plan throughout the United Kingdom and that is a real consideration for us because it is a fairly topical issue that food tends to travel fairly large distances and we have depots, for instance, in Scotland that supply our stores in Northern Ireland; in England they supply Wales. There is a lot of transfer of stock around the UK. One of our concerns when we have been considering transfer of management from one store to another in the event of it being particularly badly hit by an outbreak is whether there is a risk of transferring our colleagues from an area where there is no local infection into an area where there is an outbreak. We get the commercial imperatives conflicting then with the epidemiological considerations of this sort of situation.

Mr Hawkins: After the fuel crisis in October 2000 Defra did set up an emergency contingency planning group on which BRC and the manufacturing representatives were represented and it has from time to time met ever since. However I think in real life what would happen in the event of an emergency of this kind is that we, as BRC, would call together the leading food retailers and the IGD would probably set up a parallel body involving food retailers, manufacturers and transport companies and that is really where the co-ordinating work would be done.

Q376 Lord Taverne: Say 2,000 for a company like Sainsbury, multiply that by seven or eight, is that the sort of figure you have overall?

Mr Hawkins: Some HGV drivers are directly employed by supermarkets; others are employed by third party specialists like Christian Salvesen and so on because some of the depots are run by third parties. We can let you have more detailed figures.

Chairman: It did strike me that it was a speciality that could get us into trouble quite quickly.

Q377 Chairman: Presumably the forces would have drivers as well.
Written Evidence

Memorandum by the Academy of Medical Sciences

This submission was prepared in consultation with Academy Fellows drawn from across the Fellowship, from laboratory to clinic. We have also drawn upon the report of the Academy’s meeting with the Chief Medical Officer, Sir Liam Donaldson FMedSci, which took place on 20 September 2005. We are much indebted to Sir Liam for sharing his thoughts and concerns with us and much of the discussion is reproduced here.

The evidence presented here is endorsed by the Academy’s Officers.

The Risk

How is the risk of pandemic influenza emerging in south east Asia, and reaching the UK, being assessed; and how can this assessment be improved?

How great are the risks, and what confidence can be placed in these figures?

How is the UK working with international bodies to: monitor the development of the virus; and reduce the risk of pandemic influenza emerging and spreading?

1. Evidence shows that H5 bird flu is spreading ever wider and it is now acknowledged that it is not a matter of whether a pandemic will occur, but more a matter of when. It seems most likely that a pandemic will originate in south east Asia. There are significant concerns about the lack of surveillance in likely pandemic influenza source countries. Following the SARS episode, China took advice from the UK Health Protection Agency (HPA), World Health Organisation (WHO) and others on improving surveillance mechanisms, but progress appears to have been slow. The Government, in conjunction with WHO, must work for greater openness and improved surveillance in the relevant countries. Ultimately, it is unrealistic to suppose that an emerging infection will be contained in south east Asia.

2. It should be noted that an outbreak may not necessarily occur in the Far East. Influenza can spread via wild migrating birds, as well as poultry and people. The American experience with West Nile Virus demonstrated that migratory birds can rapidly spread infectious disease from east to west, as well as north to south. It is therefore crucial that disease in bird populations is monitored across Europe and the UK, in addition to south east Asia. Similarly, in the event of an outbreak, measures must be taken to protect British bird flocks. Current surveillance work by the Department for Environment, Food and Rural Affairs (Defra) in this area should be strengthened and communication between the human and animal health sectors encouraged.

Contingency Planning in the UK

What is the current assessment of the likely impact of pandemic influenza on the UK (both in terms of health and on wider society, including the economy)?

3. The current H5N1 strain of avian influenza circulating in south east Asia is extremely virulent, killing approximately half of those people infected. Although this information is based on only small number of human infections (~120) it is reinforced by the viruses’ very aggressive behaviour in vitro. If virulence does not diminish when the virus achieves human-to-human transmission, mortality will be significantly greater than the 1968 pandemic. The Academy therefore considers that the Government should plan for more than the currently estimated 50,000 pandemic flu cases.

4. Pandemic flu, unlike seasonal strains, does not disproportionately affect older people, but will impact on all age groups. However, morbidity and mortality are likely to be particularly high in already vulnerable populations such as those with diabetes, cardiovascular disease and those taking immunosuppressants. Babies under one year old are also especially vulnerable.
How well co-ordinated are health, emergency and other essential services for responding to a pandemic?

5. As mentioned previously, the Academy is concerned that an under-estimate of the likely number of UK pandemic flu cases will prevent effective co-ordination of health and other services. A significant concern is the assumption that local healthcare managers have robust local plans for coping with a flu pandemic. The Government should consider potential difficulties in switching largely devolved health administrations to a centralised system of “command and control” for the duration of the outbreak.

6. The Academy is particularly concerned about the lack of planning for management of critical care services in the event of a flu pandemic. Modelling work carried out by the Professor David Menon et al has shown that an eight-week pandemic with 25 per cent attack rate could create a demand for critical care beds at 208 per cent of current capacity. An optimistic estimation of impact factors (50 per cent reduction in critical care demand with neuraminidase inhibitors and upgrading of some beds to critical care levels), results in critical care bed occupancy at 75 per cent. It should be noted that staff illness rates of 25 per cent will severely undermine normal, let alone enhanced, critical care services.

7. However, critical care capacity can be expanded, for instance by co-opting surgical recovery areas and/or operating theatres. There is a further problem that current critical care bed density does not reflect population density and may not reflect the geography of an outbreak. The need to transfer both patients and staff must therefore be examined.

8. Planning for the management of critical care services during a pandemic should include:
   - Creation of libraries of equipment to be mobilised if an expansion of critical care services is needed;
   - Details of how critical care departments could expand into theatre recovery areas and some operating theatres;
   - Provisions to transfer patients and staff between critical care facilities;
   - Careful logging of non-NHS critical care resources;
   - Clear recognition of triggers to signal the cancellation of elective surgery (and planning for the period of catch up in the months following a pandemic);
   - The impact of how the critical care focus on influenza will negatively affect facilities available for other services;
   - Expansion of mortuary facilities.

What is being done to ensure that the general public are aware of the risks and likely effects of a pandemic, and of how they should react?

9. The Academy considers public understanding of the risks and effects of a pandemic to be crucial. There appears to be a general lack of understanding about the nature of pandemic flu and its relationship/differences with bird flu and “normal” seasonal flu. There also appears to be a lack of appreciation amongst the public that some harm will result from a pandemic, whatever measures are put in place. The Government must be explicit in communicating that a pandemic cannot be entirely prevented, but work can be done to limit the damage. Public health measures such as school closures and patient isolations will operate more effectively if there is full public understanding of the issues involved. Effective communication will be crucial in potential instances where measures appear counter-intuitive to journalists and the wider public. For instance, preventing incoming flights from affected countries might provide public reassurance, but there is little evidence that such social controls of movement are effective in preventing the spread of infection.

10. Care should be taken to ensure that public messages regarding a pandemic are accurate. For instance, the public should be aware of the true number of antiviral doses available and who will receive them. Issues relating to “essential workers” are relevant to this and are discussed below.

Is the UK’s stockpile of antiviral treatments adequate, and how will it be distributed? What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?

11. Current Government information indicates that the target stockpile of 14 million antiviral doses will be reached in approximately one year (covering 25 per cent of total UK population). The Academy is concerned by the lack of detailed plans on who should receive antiviral treatments and when. A key element is defining an “essential worker”, upon which Government policy is unclear. Essential workers are not necessarily restricted to the public sector, for instance supermarket lorry drivers would provide a key service in delivering

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food during a pandemic. The size of the “essential worker” population must be known in order to assess the impact on the antiviral stockpile. The identification of key workers within health care institutions and those who should hold a limited antiviral supply is particularly important.

12. It is also unclear how the Government intends to use antivirals in a pandemic situation. Relatively little is known about the impact of antivirals on disease outbreaks, with the only available data originating from Japan. Therapeutic and prophylactic treatment would require a supply of one week and up to six weeks per individual respectively. Current Government policy does not appear to favour prophylactic antiviral use, which would deplete the stockpile very rapidly. Rather, antivirals would be given to people displaying early flu symptoms, in order to reduce severity, infectivity and mortality. However, it might be considered unreasonable to ask essential workers to expose themselves to infection without prophylaxis. If essential workers are to be given prophylactic antivirals, the longer duration of treatment will significantly impact on the number of doses available.

13. A programme of research on the effects of antivirals is therefore very important. While the mechanism of antiviral action allows viral replication, it is unknown whether this elicits immunity to re-infection. It is also unknown how long any such immunity would last. Viruses that become resistant to antiviral treatment show a considerable drop in neuraminidase activity. However, more research is needed into the transmissibility of resistant strains. It would also be useful to know if antiviral treatment reduces transmissibility within households.

14. Effective distribution of, and access to, antivirals must be ensured. Similarly, essential workers who may be required to “self-diagnose” and commence antiviral treatment will require clear and robust guidance. Pressure on those holding small antiviral supplies may become intense in a pandemic situation. It is essential that such people receive effective guidance and support.

15. The Government should review the licensing arrangements for antivirals. For instance, neuraminidase inhibitors are not licensed in babies, who would be particularly vulnerable in a pandemic situation.

What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?

16. Government policy on vaccination accepts the inherent difficulty that the particular strain of a pandemic can never be known in advance. Policy is therefore focused on early identification of the strain and shortening the time for vaccine production. However, it appears that this position has evolved and the Government has now tendered for one to two million doses of vaccine active against the current H5N1 bird flu strain.

17. There is a question of whether, in mutating to a human transmissible form, vaccines against current bird flu virus would be rendered ineffective. Alternatively, the mutation may be small enough to allow some vaccine protection. The Academy therefore welcomes the Government’s initiative and recommends that expansion of vaccination with current bird flu vaccines should be considered. We understand that the Government has considered adding the bird flu vaccine to the seasonal flu jab, but manufacturing difficulties have prevented taking this further.

18. However, further R&D must be undertaken to establish an optimal vaccination strategy. The Academy is concerned that the Department of Health (DH) is not sufficiently active in the field of vaccine R&D to confront an emerging threat. The UK has previously been at the forefront of work on the development and assessment of candidate pandemic flu vaccines. Research on an avian H5 Duck Singapore virus vaccine, as well as on an H9 vaccine highlighted several challenges. Current H5 flu vaccines are poorly immunogenic when given in conventional subunit form (ie as currently manufactured), with 80–90µg protein required to elicit an immune response. This significantly reduces the number of available doses.

19. It cannot be assumed that a new vaccine is safe, especially if it is very different from existing vaccines. It is likely that immunising a large proportion of the population would give rise to side effects. It is therefore essential that safety and efficacy trials on potential H5 vaccines be performed in advance of an epidemic.

20. The Academy urges the DH to initiate studies to:

- Investigate different vaccine formulations (adjuvanted and non-adjuvanted, subunit and whole virion);
- Investigate different vaccine doses;
- Evaluate priming to a future antigenic variant;
- Evaluate safety and antigenicity in different populations (children, adults, older people).
21. When planning R&D strategies it is important to consider that pharmaceutical companies are committed to making conventional vaccines for both northern and southern hemisphere countries and only have a short period available each year to research “experimental” avian flu vaccines. Researchers also stress that generic difficulties with the regulatory framework for clinical research may prevent studies being approved and undertaken quickly.

What is the long-term strategy for reducing the threat of pandemic influenza?

22. Long term strategies for reducing the threat of pandemic influenza must be multi-faceted. Research needs and opportunities are the focus of this response. It is crucial that research agencies and funders consider in advance what research questions should be carried out during a pandemic, as it will be extremely difficult to conduct research in an emergency situation. Current work in this area by the DH and Medical Research Council should be strengthened. It may be the case that researchers working in other areas would be keen to switch to flu-related research in a pandemic situation. The DH should compile a list of such researchers.

23. In the event of a pandemic, the Government should consider the collection and fractionation of serum from convalescent patients (as soon as they exist), perhaps to provide a bank of immune immunoglobulin for future prophylaxis. Similarly, it will be important to know whether there are any genetic associations with mortality, morbidity or survival with pandemic influenza. Preparations should be made to collect and store DNA samples for future association studies.

Acknowledgements
The Academy is extremely grateful to Sir John Skehel FRS FMedSci for assistance in preparing this response. We also thank Professor David Menon FMedSci and Professor Karl Nicholson for their contributions.

Letter from Dr Peter Bailey
I have followed with interest the work of the Science and Technology Committee as it has investigated the response to the threat of pandemic influenza.

My practice has around 5,000 patients, and there is a staff team of around 20 including doctors, nurses and administrators. We have kept ourselves fully informed about the emerging pandemic of avian influenza and have studied the history and epidemiology of previous pandemics in humans.

The Health Protection Agency’s revised advice in the event of pandemic influenza guesses at an attack rate of 25 per cent and a case fatality rate of 0.37 per cent, giving an excess mortality of 53,700 for the UK as a whole. In view of the 50 per cent death rate for cases of avian influenza in the few humans known to have contracted the disease, this could be a serious underestimate. In 1918, the pandemic was caused by a virus of avian origin and had a case fatality rate of 2 per cent. It would seem prudent to base our plans for dealing with the next pandemic on a pessimistic assumption rather than rely on the most optimistic figures taken from the mildest of recent pandemics.

Using an attack rate of 30 per cent and a case fatality rate of 3 per cent the UK would see over 17 million cases of influenza and there would be over half a million deaths.

My practice would expect to see 45 excess deaths during the pandemic. The work load of the practice would rise to unsustainable levels. The Chief Medical Officer’s advice of having two separate waiting areas and two separate treatment teams, one dealing with influenza cases and one dealing with “the rest” is unworkable.

Among our own clinical team, attack rates are likely to be higher because of constant exposure to the virus. It would seem reasonable to use a figure of double the population average. This would suggest that at least half of the doctors and nurses and administrative staff would become unwell. There is a greater than 1:4 probability that the practice would experience the death of a team member.

It seems to me that there are many pressing questions that are not answered by the plans that have been prepared so far:

— What model is proposed for calculating the number of doses of antivirals to be provided to each practice?
— When will stocks be made available to the practices?
— How will stocks be distributed?
— How should stocks be protected?
—— Who should be given treatment courses (signs, symptoms, duration of illness, risk exposures etc)?
—— What arrangements have been made for out of hours access, given that treatment should be started within 48 hours according to the data sheet for oseltamivir?
—— Have any plans been made to treat front line Primary Care staff with prophylactic antivirals during the course of the pandemic?
—— How many additional doses of antivirals will be distributed for prophylaxis and who will be eligible for such treatment?
—— Will non-essential staff be expected to come to work?
—— Who will determine who is “non-essential”?
—— How should Primary Care teams respond to demands for prophylactic treatment in families in which cases occur?
—— What is the status of existing H5N1 vaccines?
—— Are there any plans for protecting Primary Care teams using existing vaccines?

And perhaps the most important question of all:
—— What behavioural responses to perceived risk are expected in doctors, nurses, ancillary staff and the general public?
   — Altruism;
   — Generosity;
   — Volunteering for overtime without pay;
   — Good neighbourliness;
   — Voluntary quarantine by infected cases;
   — Family support strengthened.
Or:
   — Fear;
   — Anxiety;
   — Abandonment of influenza victims;
   — Violent protectionism;
   — Absenteeism in all sectors but especially health care;
   — Civil disorder and breakdown of infrastructure (utilities, transport, food supplies, education, broadcasting, law enforcement, mortuary and cremation facilities);
   — Violence against Primary Care staff and pharmacists;
   — Theft from treatment centres.

All these questions require sensible answers and Primary Care teams must be fully engaged in any solutions that are proposed.

November 2005

Memorandum by Dr Alan Hay, Director of the World Influenza Centre

Assessment of Risk

1. The WHO Global Influenza Programme takes responsibility for co-ordinating international efforts to monitor the emergence and spread of potential pandemic influenza viruses, provides up-to-date information on recent developments and advises on strategic actions to mitigate the impact of an influenza pandemic. In this, the WHO works closely with other international organisations with responsibilities for animal health, OIE and FAO, and national authorities, to optimize information on the epidemiological and virological links between human and avian (and animal) infection.

2. The WHO Global Influenza Surveillance Network provides the international framework: for monitoring the incidence of human infection by novel (animal/avian) influenza viruses, such as the H5N1, H9N2 or H7N7 viruses, and the capacity of these viruses to spread from one person to another and more widely within the community; to assess the potential significance of changes in the viruses, including genetic reassortment with circulating human or animal viruses, which may be associated with adaptation to the human host; and for assisting early intervention which might reduce the chance of emergence or the spread of a pandemic virus.
3. Enhanced surveillance in southeast Asia in recent years, especially in response to the SARS outbreaks and more recently to H5N1, has enabled detection of human infection by avian H5N1 (and other avian/animal) viruses, the detailed genetic characterization of the viruses and provided an understanding of the interrelationships between the viruses responsible for human infections and those causing outbreaks in domestic poultry. However, there is still relatively little definite information on the true extent of human infections, especially subclinical or mild infections, particularly among rural communities (in Vietnam) and the role of domestic ducks, with asymptomatic infection, and other animals in spreading disease.

4. Intensive collaboration between many agencies, from diagnostic labs to national public health/veterinary authorities to international agencies (WHO, OIE, FAO) has been essential to facilitate the necessary scientific investigations in the context of both local and international interests. Future increased co-operation, supported by the provision of necessary financial resources, particularly in south east Asia, is essential to enhance our understanding of the epidemiology of these viruses and the links between animal disease and the risk of human infection, to allow a more objective assessment of the present pandemic threat posed by these viruses and to monitor their future significance. A role for migratory birds in spreading the H5N1 viruses to other regions is supported by the similarities between viruses isolated from wild and domestic birds in distant geographical locations and has led to calls for more intensive international surveillance.

Level of Risk

5. Since 1997 there have been a number of “outbreaks” of human infection by avian influenza viruses associated with outbreaks of disease in domestic poultry: by H5N1 subtype viruses in Hong Kong in 1997, in southern China in 2003 and during 2004 and 2005 in Vietnam, Thailand, Cambodia and more recently Indonesia; by H9N2 viruses in Hong Kong in 1999 and 2002; and by H7N7 viruses in the Netherlands in 2003. In contrast to the high fatality associated with H5N1 infection, infections by the H9N2 and H7N7 (which like H5N1 is highly pathogenic for chickens) viruses were, with one exception, relatively mild. Evidence indicates that most infections were contracted directly from infected birds. The H5N1 viruses have not spread readily from one person to another and evaluation of clusters of cases have provided only limited evidence of human-to-human transmission. Thus removal of the source of infection, by culling the birds in Hong Kong in 1997 or controlling the outbreak in the Netherlands in 2003, halted cases of human infection. Although greater efforts and resources to control the outbreaks in poultry would lessen the risk of human infection, the H5N1 viruses are now endemic in a number of countries in eastern Asia and recent wider spread of the viruses in poultry in western Asia and their potential intercontinental spread by infected migratory birds (or other means) provide the bases for a more persistent pandemic threat, requiring maintained heightened surveillance.

6. To date all the human isolates have been exclusively avian in genetic makeup and there is no evidence for genetic reassortment with human viruses, as occurred to produce the H2N2 and H3N2 subtypes which caused the 1957 and 1968 pandemics, respectively. However, H5N1 human infections have occurred co-incidentally with outbreaks of normal human influenza. There is also little evidence to date that the H5N1 viruses adapt during human infection to acquire a greater capacity for human infection or human-to-human transmission. However, the virus isolated from the single fatal human case of H7N7 in the Netherlands in 2003 had undergone significant change during prolonged infection, indicative of adaptation which may have increased its pandemic potential. Thus, the greater the number of human infections and the longer they persist, together with an increase in the number of variants of H5N1 viruses responsible, will increase the risk that one will emerge with a greater capacity for human infection and transmission.

7. H5N1 infection of pigs, and other animals such as cats, provides the possibility that these animals might act as intermediate hosts in the emergence of a human pandemic virus. The recent emergence in pigs in North America of reassortant viruses possessing genes of human, swine and avian virus origin, together with the frequency of human infection associated with outbreaks of influenza in pigs, lends credence to this mechanism.

International Interaction

8. The World Influenza Centre (WIC) was established at the MRC National Institute for Medical Research in 1948, at the behest of the newly established WHO, and has a long history of international collaboration in influenza. Today it is one of five WHO Collaborating Centres for Reference and Research on human and animal influenza which together with some 112 WHO National Influenza Centres (NICs), including the HPA Centre for Infections, Colindale (HPA-CFI), in over 80 countries worldwide comprises the WHO Global Influenza Surveillance Network. The WIC receives viruses from many of these laboratories in different parts of the world, to monitor changes in influenza viruses circulating in the human population and advise WHO (biannually) on its recommendations for the compositions of influenza vaccines, and to detect (as early as
possible) and characterise novel human influenza viruses, from animal or avian sources, which may have the potential to cause a pandemic.

9. The WIC is one of the WHO H5 Reference Laboratories and participates in the characterisation of the antigenic and genetic properties of the recent H5 (N1) viruses. Of particular interest are:

   (i) the genetic relationships between the human isolates and avian (and animal) viruses and the significance of changes which might indicate adaptation of the avian virus to the human (or animal) host and increased potential for human-to-human transmission and to cause a pandemic;

   (ii) changes/differences in the antigenic characteristics of recent human viruses in relation to suitability of prototype vaccine strains;

   (iii) changes in drug susceptibility. Together with the National Institute for Biological Standards and the HPA-CFI, it has been involved in the selection and evaluation of potential pandemic vaccines.

10. The WIC works closely with many NICs and laboratories of the European Influenza Surveillance Scheme and provides advice on the characteristics of H5N1 and other potential pandemic influenza viruses and provision of reference reagents for their detection. Also, as members of the international Neuraminidase Inhibitor Susceptibility Network and a European antiviral drug resistance network (VIRGIL), the WIC and the HPA-CFI have international responsibilities for monitoring the emergence of drug resistance in relation to anti-influenza drug use.

11. The WIC and the Central Veterinary Laboratories Agency (VLA), Weybridge, the OIE European Reference Laboratory for avian influenza, collaborate with other members of the recently formed WHO Working Group on Influenza Research at the Human/Animal Interface which co-ordinates the surveillance and research interests of WHO, OIE and FAO laboratories in relation to the emergence of potential pandemic viruses. The VLA is also a member of OFFLU, a network co-ordinating the efforts of OIE and FAO laboratories on avian influenza. The WIC also has a specific, Wellcome Trust supported, collaboration with the University of Hong Kong and Massey University, New Zealand, on the epidemiology and zoonotic potential of avian influenza viruses in southeastern China.

26 September 2005

Memorandum by the Institute for Animal Health and the Roslin Institute

1. We will address the question that was posed by the committee: What is the long-term strategy for reducing the threat of pandemic influenza?

2. The threat of pandemic influenza in man seems very likely to be related to the level of infections sustained in poultry. Waterfowl are the natural host for avian influenza viruses and it is believed that spread into poultry represents episodic events that may be sustained in the poultry population for varying periods of time. We submit that it is prolonged human contact with infected waterfowl or poultry that increases the risk of pandemic influenza in man—so control in the avian host is critical. Control by depopulation is an obvious option but due to the uncertain nature of pandemic influenza this does not seem viable thus control through alternative means is our focus.

3. We propose approaches towards reducing AI in the avian host by:

   — Generation of novel vaccines and their testing under controlled conditions to enable control of infection during outbreaks of infection;
   — Screening for differences in the responses of poultry to traditional and new vaccines to promote the breeding of birds with optimal protection following vaccination;
   — Identification of differences in susceptibility of poultry to influenza virus infection so that it may be possible to breed chickens with a reduced potential for spread of the virus;
   — Fundamental work to uncover the details of host interactions with avian influenza to give future prospects for control.

Generation of novel vaccines and their testing under controlled conditions

4. Vaccination is the major method of control for many viruses in the poultry industry, which has experience in developing and administering live and killed viral vaccines. Traditional and new vaccines against avian influenza viruses have mixed success and can cause problems if they result in protection from disease signs and yet fail to block virus transmission.
5. Substantial advances in our understanding of the immune response of poultry have been made over recent years with the discovery of genes and proteins that control the immune response. Through our knowledge of these we hope to improve the efficacy of vaccines against avian influenza viruses effective in the avian (poultry) host. Particular discoveries that bear on novel vaccines are the description of proteins that act as molecular adjuvants (such as cytokines and toll-like receptors) to induce the correct immune responses.

6. It is not just the genes and proteins that are important to vaccines but vaccines need to deliver the right response to the right place at the right time, and there is increasing knowledge about these parameters. Identification of the right viral proteins, the best vectors, the more appropriate adjuvants, and the best immunisation procedures are crucial for improving the efficacy of vaccination. Another desirable feature of such vaccines would be that they protect against many serotypes, that is to say they are sustainable.

7. It is essential therefore that infection of poultry flocks with viruses is determined swiftly, so that timely slaughter and vaccination can be carried out. Masking the infection by vaccination without eliminating shedding of active virus potentially leads to a situation with the virus out of control—as in south east Asia. New vaccines must totally eliminate or reduce shedding to minimal levels to be effective in the long term. New vaccines will need to be developed since there are doubts about the efficacy of current vaccines outside the laboratory environment.

**Identification of differences in susceptibility of poultry to influenza virus infection**

8. The management of poultry breeding and production makes it exceptionally well suited to exploiting genetic variants for a useful trait and establishing it in the poultry population; such a trait may be disease resistance. From the field there is little evidence for resistance to avian influenza virus infection since, once established, highly pathogenic strains of avian influenza virus (HPAI viruses) will spread and kill poultry indiscriminately. However this does not imply that all poultry strains are equally susceptible to infection and able to transmit infection. A successful strategy may be to select poultry that (a) need a higher infectious dose of virus or (b) produce less virus when infected. Both strategies effectively reducing the potential of the virus to spread infection and could reduce the risk of pandemic influenza.

**Screening of the responses of poultry to traditional and new vaccines**

9. Host genetics may also play a role in the selection of poultry that respond well to vaccination. There is much evidence that different chickens respond differently to various vaccines. In some cases this may be a general trait towards many vaccines and in other cases may be specific for the particular pathogen or vaccine. It is already known that some current AI vaccines efficiently immunise some chickens but not others. The selection by poultry breeding of those genes which allow the best response to the traditional and any novel vaccines is a desirable goal.

10. Antiviral innate resistance whether through the interferon system, with its antiviral response, or through other mechanical barriers, is worthy of investigation to be used as part of a suite of traits that could be considered.

**Fundamental work to uncover the details of host interactions with avian influenza to give future prospects for control**

11. The viruses circulating in poultry and waterfowl in south east Asia are lethal for poultry. It is unusual for such HPAI viruses to be isolated from wildfowl and these strains are a cause of special concern. In infected poultry HPAI viruses are not restricted to replication in the respiratory and alimentary tracts of birds but cause a systemic infection which results in rapid death. How applicable this model is to human infection is not known, but it is clearly a very serious risk factor relating to the severity of the disease. The risks can be considered enormous should the virus acquire the ability to spread to humans more efficiently and then spread from human to human without losing its pathogenic potential. An additional risk might be that the virus does not spread to humans but the pig could act as a source of infection. Even if we get no immediate pandemic, there may be a chronic threat from AI or AI viruses in pigs to transmit to humans, with lethal consequences, and yet still maintaining the potential for starting a future pandemic.
12. In the long term, greater understanding of the interactions between the host and avian influenza will be important in our ability to control the spread of this disease. We need answers to questions like:

— what factors limit replication and transmission of AI strains within and between different avian and mammalian species?

— why are some strains pathogenic in geese and ducks but others are not?

13. In recent years the rapid development in genomics and genetics has increased our knowledge of the biology of avian influenza. There has never been a better time to exploit these new tools to increase our knowledge of how the host responds to and may limit avian influenza virus infections. International projects to sequence the genomes of ducks and other hosts will provide information about host defence and susceptibility genes. These sequences will be used to develop the tools to examine host responses in terms of changes in gene expression (“DNA chips”) and protein differences (“Proteomics”). The sequence will also be used to screen for genetic variation in host genes and search for associations with susceptibility to infection, and with the ability to shed and spread AI infections.

14. Avian influenza is a particularly high-risk virus because it mutates at a high rate and if transmitted to another host species, even at a low rate, may adapt to evolve into a more virulent strain. It is therefore of interest to examine the responses of different host species to avian influenza viruses. Surveillance has detected avian influenza virus strains in a wide range of species, including wildfowl (ducks and geese), shorebirds (gulls and terns), poultry (chicken, turkey, quail) and other birds, mammals (not only pigs, horses, and humans, but also seals, whales, mink, and, more recently, cats and tigers).

15. Increased knowledge of the genes and proteins of the host that limit infection may also identify new targets for drugs or vaccine design. Antiviral drugs might therefore be targeted against virus proteins that counter the host antiviral response.

16. Finally, the application of novel vaccines, drugs or selected strains of poultry in the field need to be approached with caution. It is important to develop new models of infection at the individual and population level to predict the consequences of their use. Critically, there will be a need to develop infrastructure in additional laboratories to handle the LPAI and HPAI viruses and ensure secure and safe access to these resources. Currently within BBSRC only IAH Compton has facilities to handle highly pathogenic avian influenza viruses, and to our knowledge is one of only five laboratories so equipped and licensed within the UK.

Memorandum from Research Councils UK

INTRODUCTION

1. Research Councils UK (RCUK) is a strategic partnership that champions the research supported by the eight UK Research Councils. Through RCUK the Research Councils are creating a common framework for research, training and knowledge transfer.

2. This memorandum is submitted by Research Councils UK on behalf of four of the Research Councils (the Biotechnology and Biological Sciences Research Council, Economic and Social Research Council, Medical Research Council and Natural Environment Research Council) and represents our independent views. It does not include or necessarily reflect the views of the Office of Science and Technology (OST). RCUK welcomes the opportunity to respond to the Committee’s Inquiry.

3. This memorandum provides evidence from RCUK in response to the questions outlined in the inquiry document, in addition to supplementary information from:

   Biotechnology and Biological Sciences Research Council (BBSRC)  
   Economic and Social Research Council (ESRC)  
   Medical Research Council (MRC)  
   Natural Environment Research Council (NERC)

Because of their different interests, Councils have focused on different questions below, and the responses are attributed accordingly. We emphasise that the annexes contain important additional information about specific research aims and collaborations.
The Risk

How is the risk of pandemic influenza emerging in south east Asia, and reaching the UK, being assessed; and how can this assessment be improved?

MRC

4. The WHO works closely with individual countries and the international community to monitor and verify the emergence of new flu strains and suspected human cases of zoonotic strains. It coordinates the WHO Global Influenza Surveillance Network2, established in 1952, which now links four international WHO Collaborating Centres (of which the WIC at NIMR is one, see paragraph 1 of Annex 3) with some 112 National Influenza Centres. The Network makes recommendations to the WHO on influenza vaccine formulation and acts as a global alert mechanism for new and dangerous influenza strains. The rapid control of Severe Acute Respiratory Syndrome virus (SARS) in 2003–04 owes much to the effectiveness of the WHO Network.

5. Strong surveillance and reporting systems in affected countries are crucial. The WHO reports that some affected countries do not yet have the requisite laboratory and epidemiological capacity. International collaborative support for affected countries in strengthening their capacity for national and local surveillance, active case-finding and rapid response is a critical investment for the world.

6. Collaboration with south east Asian partners to maximise the rapid collection and analysis of high-quality clinical data and samples in the pre- and early pandemic periods is crucial. International efforts must support rather than compete with national research aspirations and development of capacity in surveillance and research. The international community must take every opportunity to promote strong science and health protection strategies, and every effort must be made to mitigate conflicts that arise between international and local interests.

7. Reliable and rapid diagnostic tests that are robust under field conditions could be especially valuable in south east Asia. The OST’s Foresight Project on the Detection & Identification of Infectious Disease may provide valuable insights into smart, adaptable technologies: the Project is due to report later in 2005. The potential value of testing at home (“self-tests”) and in healthcare settings needs to be considered also in the context of a UK epidemic.

8. UK mathematical modelling of outbreaks is at the international forefront. Professor Neil Ferguson (Imperial College) and others have published a strategy for the containment of a pandemic strain in south east Asia,3 pinpointing the importance of rapid (within days) recognition of small clusters of cases and intervention with antiviral drugs and other measures such as geographic and social separation. It is less clear how effective these strategies would be in the face of a gradual evolution of strains with more efficient human-to-human transmission, and/or diffuse emergence on a widely dispersed geographic front in remote districts with poor communications.

9. There are significant questions about the appropriate intervention strategies at different stages of an outbreak and pandemic. For instance, would antiviral drugs be more effectively used as a prophylactic, or for early treatment (allowing a degree of exposure to the virus and potentially engagement of the immune system)—and under what circumstances? UK laboratories could contribute to answering such questions through collaborative research with clinical teams in south east Asia.

NERC

10. Assessment is largely based on co-ordination of the information obtained from serological studies combined with molecular analysis, virus isolation, epidemiological observation in birds and in humans and assessment of the impact of control measures based on animal slaughter, and the use of antivirals. The quality of assessments could be improved by extending the range of virological studies in south east Asia and in Europe, including the UK. See Annex 4 for detailed suggestions.

11. In particular, it is important that UK wildlife species, especially birds, be monitored for relevant antibodies before, during and after the arrival of any pandemic influenza virus—work in train at the Centre for Ecology and Hydrology. The possibility that strains other than H5N1 might pose a threat (see paragraph 15) makes such monitoring all the more important. For it to be carried out effectively, virologists must have access to the relevant viruses. This need should be borne in mind when controls are imposed for biosecurity purposes, so that circulating viruses are not unnecessarily over-classified, making it hard for many researchers

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2 http://www.who.int/csr/disease/influenza/surveillance/en/
to carry out survey work. A library of avian, equine, porcine and human influenza viruses, freely available to all virologists in the UK (not just to a limited number of laboratories), would greatly facilitate the gathering of survey data.

**BBSRC**

12. **BBSRC** is funding research to examine the epidemiology of the influenza virus related to the genetic structure of the virus population, both within an individual and in a host population, and the underlying genetic factors that allow strains of the virus to change host organism, which are thought to be related to suppression of virus replication in the host cells. This work is essential to support efforts to successfully predict the spread of avian influenza through populations.

*How great are the risks, and what confidence can be placed in these figures?*

**MRC**

13. **Avian Influenza: Assessing the Pandemic Threat**, published by WHO in January 2005 concluded that “The confirmation of human cases gave the outbreaks in poultry a new dimension. They were now a health threat to populations in affected countries and, possibly, throughout the world. All prerequisites for the start of a pandemic had been met save one, namely the onset of efficient human-to-human transmission. Should the virus improve its transmissibility, everyone in the world would be vulnerable to infection by a pathogen—passed along by a cough or a sneeze—entirely foreign to the human immune system.” It could be argued that the N1 (neuraminidase) component of H5N1 is not entirely foreign, since it has been circulating in other strains for several years, and that residual antibodies could reduce disease severity, but the degree of protection that previous exposure to N1 would offer is uncertain.

14. The fact that viruses of avian origin contributed to all three 20th Century pandemics suggests that the likelihood of another zoonotic strain becoming efficiently transmissible between people is high. Population vulnerability to H5N1 and other strains that are not susceptible to existing neutralising antibodies is likely to be high. The WHO considers it likely that an antigenically novel, efficiently transmitted zoonotic strain would very rapidly spread, causing high morbidity and mortality, and seriously threatening the capacity of health systems to respond.

15. However, much remains uncertain about the biology, clinical characteristics and epidemiology on which risk estimates are based. Consequently, while experts believe that a pandemic will occur, parameters such as timing, spread and scale are unpredictable. Further, despite the current focus on avian H5N1, there is no guarantee that the next pandemic challenge will be from either avian H5N1 or indeed an H5 strain.

16. The WHO is coordinating action to strengthen surveillance systems regionally in southeast Asia and its advice to countries is readily accessible. In relation to the zoonotic threat to human health, the WHO works with the World Organisation for Animal Health (OIE) and the Food and Agriculture Organisation (FAO). The OIE and FAO have in recent years been assisting countries in southeast Asia to control the severe avian influenza epidemic in poultry. The culling in 1997 of the entire national poultry flock of 1.5 million birds in the Hong Kong Special Administrative Region is considered by the WHO to have averted a human pandemic. Effective surveillance of bird populations, outbreak and panzootic prevention and response are all essential to the protection of human health. This work needs to be underpinned by strong research that fully exploits the opportunities for collaboration between human and veterinary research.

17. The containment, despite its rapid intercontinental spread, of SARS offers some comfort as well as lessons. However, influenza is more highly contagious than SARS and is considered less likely to be contained by public health measures than was SARS.

**NERC**

18. Current evidence indicates that the avian viruses in Asia have retained their preference for avian hosts. This implies that unless the situation changes the risk of human pandemic influenza emerging in south east Asia is not as great as might initially have been anticipated. However, it is difficult to estimate reliably the risk because there is insufficient knowledge concerning the likelihood of the appropriate genetic exchange or mutation required to produce a human pandemic virus. The risk is not negligible because of the high number of exposures of humans to avian influenza viruses in south east Asia, and if a high-virulence human strain emerges in south east Asia, the risk of it reaching the UK is likely to be high.

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How is the UK working with international bodies to: monitor the development of the virus; and reduce the risk of pandemic influenza emerging and spreading?

MRC

19. As described in paragraphs 4 above and paragraph 1 of Annex 3, the WHO World Influenza Centre at the NIMR plays a significant collaborative role internationally in meeting the challenges for human health of potentially pandemic viruses.

ESRC

20. Spontaneous changes in micro-organisms that potentially lead to pandemics are unpredictable so it is vital to take a broad view in order to identify the most important risks associated with infectious diseases, such as avian flu. The pathways by which the disease can spread are often influenced by socio-economic drivers, which might include governance systems, conflict, or poverty. These are complex, multifactorial systems. The risks also depend on the socio-economic factors that influence the chances of a change occurring in infectious agents in the first place. Much of what the UK can do to prevent the spread of disease would be contingent on how it handled these socio-economic interactions and drivers both within the UK and beyond its borders. From Foot and Mouth Disease (FMD) experience, researchers have shown the importance of informal and opportunistic behaviour in the presence of a sudden threat. Undue emphasis should not be given to considering only formal communication, nor should public spiritedness be assumed.

Contingency Planning in the UK

21. Contingency planning is led by the UK Health Departments. Research Councils have a role in underpinning those plans with scientific advice (eg through the DH Scientific Advisory Group on Pandemic Influenza) and generating new knowledge and in developing and evaluating new technologies. It is crucial to build a strong evidential base to public health interventions—whether medical or non-medical.

What is the current assessment of the likely impact of pandemic influenza on the UK (both in terms of health and on wider society, including the economy)?

ESRC

22. The following important issues have been widely documented and the Research Councils are aware that the Department of Health has them under review. In the event of a pandemic, national authorities would need to rapidly obtain numerous pharmaceutical products including vaccines, to store and equitably distribute them and to manage demand for health services (primary and secondary) and social care. There would be a need to maintain social and economic functions bearing in mind that if predominantly working-age adults were affected by the pandemic, this would have a more severe impact on the continuation of services and businesses. Closure of schools would also impact on the number of adults at work and have a knock-on effect on services and businesses.

23. The UK Influenza Pandemic Contingency Plan acknowledges that it is possible that movement and gatherings of people would be affected. This could include both local and international movement and could either be enforced through contingency planning policy, or result from people choosing not to travel or from the need to scale down transport systems due to the effects of the pandemic on their workforce and the availability of fuel. The first of these three scenarios needs careful consideration in order to balance the rights of citizens to freedom of movement with the need to contain a pandemic.

24. A pandemic might also affect international trade routes, and the possible effect of this on the economy needs to be considered.
Are the measures described in the revised UK Influenza Pandemic Contingency Plan adequate to minimise the effects of a pandemic? What more could be done?

ESRC

25. The measures described in the UK Influenza Pandemic Contingency Plan may be adequate to minimise the effects of a pandemic as far as they can be foreseen. However, in relation to contingency arrangements concerning hygiene, the following observations are pertinent. The reception of what are intended as health-promotion initiatives will vary according to public trust in those giving the message. Local health professionals are more trusted than politicians, for example. Vulnerable communities are likely to show patterns of trust different from those of majority communities.

How well prepared and co-ordinated are health, emergency and other essential services for responding to a pandemic?

ESRC

26. The effect of a pandemic on the whole community and the need for sustained support should be considered. Medically there is a need to think more widely than simply the supply of drugs. The provision of nursing support and social care must also be considered, including provision for those who live in more remote areas or who are incapacitated. Support by volunteers and NGOs could be considered in this context. The role of the military services in supporting the emergency services and medical staff could also be considered. It would be interesting to know if the potential for businesses and industry to support essential services has been explored.

What is being done to ensure that the general public are aware of the risks and likely effects of a pandemic, and of how they should react?

ESRC

27. Development of best practice in terms of public reaction and individual behaviour to a pandemic situation does not necessarily mean that individuals will react in the way planned. The public, or various publics, are diverse and this diversity is important when considering the preparedness of the public and the communication of warning information. Social science has a number of findings relevant to appropriate risk communication. As we have seen with BSE, salmonella in eggs and GMOs, poor communication can elevate a problem to crisis levels. There is therefore a need to ensure that public perception of the risks associated with avian flu is proportionate. Public reaction to information about risks and immediate danger depends on many social, cultural, environmental and psychological factors. For example, the degree to which individuals have pre-existing knowledge about the hazard and the appropriate response, education, socio-economic status, experience, resources to facilitate response, physiological constraints, geographical proximity to the danger, source of information and characteristics of social networks will all affect the ways that the public or publics react to information about a pandemic and the associated risk.

28. It is important to understand how individuals perceive levels of risk and how this differs between individuals. Social science research has shown that hazardous events interact with psychological, social, institutional and cultural processes to attenuate or amplify perceptions of risk and through this shape behaviour and physical consequences. Further social science research shows that people do not draw personal implications from risk information; they tend to perceive negative events as less likely and positive events as more likely to themselves than to others. This can hinder the adoption of preventative interventions and undermine health-promotion efforts. These complex interactions mean that a direct causal link cannot necessarily be drawn between education of risks and level of risky behaviour.

Pidgeon, N (1 August 1999) Risk Decision and Policy, Volume 4, Number 2, pp 145–159.
Is the UK’s stockpile of antiviral treatments adequate, and how will it be distributed? What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?

ESRC

29. Given the possibility of shortage of vaccine and antiviral medicine, or at least the likelihood that treating all those in need will take some time, care must be taken to prioritise, and be seen to prioritise, treatment in a fair, robust and transparent fashion. Those particularly at risk should be identified in advance and distribution to all areas, including rural areas and areas with little or no communication should be considered.

30. Although stockpiling of vaccine and antiviral medicine can go some way to facilitating a quick response to the sudden threat of an influenza pandemic, the exact requirements for treatment will depend on the strain of influenza. This, together with the fact that not every affected country will have been able to stockpile sufficient medication, is likely to lead to inequality in supply for countries lacking facilities to manufacture vaccines or lacking resources to purchase supplies at a time when their cost is likely to increase. These international inequalities in the basic defence against the effects of a pandemic need to be addressed by the pharmaceutical industry and international governments in advance of a pandemic.

What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?

BBSRC

31. Although BBSRC does not fund research directly concerned with the practical aspects of manufacture and distribution of vaccines, it supports the underpinning research required to develop new, more effective vaccines to tackle influenza.

32. In particular, BBSRC funds work that aims to understand the fundamental biology of the influenza virus, both in isolation and in its interaction with the host cell. BBSRC supports research that examines host-pathogen interactions at a range of scales from the molecular level, the cellular level and up to the level of tissues/organs and the whole organism. Recent advances in Genomics and Genetics in a number of species of poultry and waterfowl allow us to develop a greater understanding of host-pathogen interactions in these systems and to begin to understand variable host susceptibility to infection. Using this knowledge researchers hope to understand the action of the virus and the immune response of the host and thereby identify new targets for vaccines and antiviral drugs to more effectively combat the disease. Work to this effect is discussed in the response from the Institute of Animal Health and the Roslin Institute. In particular, the production of novel vaccines based upon our knowledge of the genes and proteins involved in the immune response of poultry will be vital.

MRC

33. See also Annex 3 for current MRC Programmes in Influenza (eg item 6) and Interim Scientific Priorities (eg bullet 4).

What is the long-term strategy for reducing the threat of pandemic influenza?

BBSRC

34. The strategy must include research to enhance our knowledge of disease processes through the study of fundamental biology of the virus and host. This is important because a long-term strategy to reduce the threat of a pandemic should include three parts: firstly the source of infection (in this case the disease in the animal hosts) needs to be removed or reduced, and the development of intelligently designed, novel vaccines is essential here. BBSRC funds research into identifying specific proteins involved with pathogenicity and replication of the virus, both of which could be targets for vaccines. This is discussed above and in detail in the response from BBSRC Institutes. Secondly, the transmission of virus from the host organism to humans must be controlled. Again, BBSRC research can contribute to the production of effective vaccines that will prevent transmission from hosts. Thirdly, the transmission of the virus between people must be controlled. Although this final aspect is outside BBSRC’s remit it is important to consider all three aspects when developing a strategy.
ESRC
35. The long-term strategy should take into account the points raised (by ESRC) above. It should recognise the international context and consider the root causes of such an epidemic as well as contingency measures should a pandemic occur. There are clearly roles for social science professionals such as medical anthropologists in, for example, understanding the role that human behaviour plays in disease spread or in communicating with and mediating between biomedical professionals and local communities. In ensuring that policy-makers receive the best support and advice on issues such as pandemic influenza we must strive to recognise and value contributions from the full range of social science disciplines in order to achieve a well-rounded view of the full array of socio-economic factors involved. Furthermore, appropriate social science professionals need to be embedded within interdisciplinary teams from the outset so that, through cross-fertilisation of ideas with natural scientists, questions are framed and response strategies developed based on as full an understanding of the situation as possible.

MRC
36. Research is required across the board both in relation to questions needing answers in the short term, and longer-term issues:
   — Biological mechanisms—as a basis for new and better drugs and vaccines. The current ability of drugs and vaccines to stem a pandemic is extremely precarious. Better drugs and vaccines are also required for seasonal influenza;
   — Clinical and translational research—to understand the respective host and virus-mediated contributions to clinical disease and outcome;
   — Epidemiology—to support risk assessment and effective intervention. Mathematical and epidemiological modelling to underpin prevention and control strategies;
   — Better delivery of vaccines—e.g. more rapid scale-up of strain-specific vaccines in response to the emergence of dangerous novel strains; antigen sparing strategies; novel adjuvants;
   — Development and evaluation of public health intervention strategies and technologies—for application in healthcare and community settings.

37. Industry has a crucial role to play in vaccine research and development, but it is likely to do so only with the right incentive structures. There may be room for further European and national action to strengthen the market in Europe for seasonal flu vaccine.

38. MRC’s interim priorities for emerging infections with epidemic and pandemic potential are set out in Annex 3.

September 2005

Annex 1

Additional information from the Biotechnology and Biological Sciences Research Council (BBSRC)

INTRODUCTION
1. BBSRC is the principal UK funder of research across the biosciences. This includes a number of areas of relevance to this inquiry, including the fundamental biology of viruses; host-pathogen interactions; control of infectious diseases in animals; and zoonotic diseases. Between 2001 and 2004 BBSRC research funding directly on influenza totalled £1.8 million: including responsive-mode research grants, Core Strategic Grant (CSG) to BBSRC-sponsored Institutes, and studentships. The primary focus is on basic research aimed at advancing our knowledge of the virus and its interactions with host animals, both avian and mammalian.

2. Also, BBSRC’s Advisor for Animal Health, Professor Paul-Pierre Pastoret, keeps a watching brief on developments regarding Avian Influenza through OIE and FAO.

BBSRC INSTITUTES
3. BBSRC provides CSG funding to seven Research Institutes, these also receiving some support from other organisations. The Institutes are instrumental in the delivery of long-term, strategic research for BBSRC. Together with BBSRC scientists at UK universities they provide a focal point for research and a critical mass of expertise that can be called upon to give independent advice to Government: they are also an important national capability that can be brought to bear on issues of concern.
4. The Institute for Animal Health (IAH) and Roslin Institute (RI) both have programmes of relevance to pandemic influenza research:
   — IAH receives the majority of the CSG funding in this area. It operates a programme specifically investigating influenza biology and the response of avian hosts to infection;
   — Through RI, BBSRC are at the forefront of efforts to sequence the chicken genome. The results of these efforts will help to identify factors involved in host-pathogen interactions and may enable the development of novel vaccines, antiviral drugs and new strategies to control avian flu.

5. IAH and RI are submitting a separate response to the inquiry.

**Particular relevance of BBSRC funding**

6. BBSRC’s funding of research into the control of infectious diseases, including influenza, includes epidemiology and the dynamics of infection. In these and other areas BBSRC is positioned to provide funding to enhance our knowledge of disease processes through the study of fundamental biology of the virus and host. This is important for a long-term strategy for reducing the threat of pandemic influenza.

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**Annex 2**

**Additional information from the Economic and Social Research Council (ESRC)**

**Introduction**

1. The Economic and Social Research Council (ESRC) is the UK’s leading research funding and training agency addressing economic and social concerns. We aim to provide high-quality research on issues of importance to business, the public sector and government.

**Detection and identification of infectious diseases Foresight Project**

2. In the context of risk, the ESRC Centre for social and economic research on innovation in genomics (Innogen) is involved in the risk work package of the detection and identification of infectious diseases Foresight Project. The Project aims to draw on the best available evidence to review and compare future risks from infectious diseases using a common set of metrics to: identify the factors driving changes in risk; assess how the size and nature of risks are evolving; and indicate the range of plausible future patterns of risk, taking account of the needs and views of the wider stakeholder community. The work will cover plant, animal and human infectious diseases, in Africa, China and the UK, but has not yet formally reported.

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**Annex 3**

**Additional information from the Medical Research Council (MRC)**

**MRC’s contribution to influenza research**

1. The MRC has made a long, sustained and significant contribution to influenza research. The human influenza virus was identified in 1933 at the MRC National Institute of Medical Research (NIMR). In 1948, the World Influenza Centre (WIC) was established at the NIMR at the behest of the then newly established World Health Organisation (WHO). The Centre, now directed by Dr Alan Hay, has continued to work with a network of collaborating laboratories to detect and characterise the emergence of new influenza viruses anywhere in the world. For instance, the Centre helped detect the avian H5N1 and H9N2 viruses that caused human infections in Hong Kong in 1997, 1999 and 2003. The Centre also has a key role advising the WHO on the composition of seasonal influenza vaccine. Sir John Skehel, Dr Hay and colleagues at the NIMR are also at the forefront of international research to discover how molecular changes in the virus affect its ability to infect people and cause disease.

2. The Council is committed to sustaining and developing its world-leading influenza research programmes and to galvanizing UK biomedical research to meet the challenges of pandemic influenza. Our current investment in influenza research is in the order of £1.6 million per annum. The programme portfolio is summarised briefly below.
Development of research strategy

3. MRC’s Council considered in July 2005 the public health threat of pandemic influenza. It recognised the action being taken by the UK Health Departments and of health protection agencies nationally and internationally to prevent and plan for a pandemic, and the MRC’s own contribution in this area. It approved activities for the MRC Infections & Immunity Board, chaired by Professor Andrew McMichael (Director of the MRC Human Immunology Unit), to review Council’s strategy for emerging infections with epidemic and pandemic potential. Professor McMichael will lead a Council scientific mission to south east Asia in October 2005, focused on emerging infections. The mission will be followed by an expert & stakeholders’ meeting in London in December. The Board’s recommendations will be considered by Council in March 2006.

4. To cover the interim period, the MRC has issued a Highlight Notice (see “Interim Scientific Priorities” below), inviting research proposals from the research community on emerging infections with epidemic or pandemic potential. The Council is keen to stimulate new research, and welcomes collaborative proposals, including proposals with overseas or industry partners. As an innovation, the Infections & Immunity Board is willing to consider in principle funding for “readiness protocols.” These will be to support research that can be put into effect only in the early stages of an epidemic—for example, clinical work on a newly circulating strain.

5. We are working with BBSRC, the Wellcome Trust, the Health Departments and the Health Protection Agency to survey the UK’s main influenza research programmes. The survey will be resource for all the partners and contribute to MRC’s strategy development in influenza. We anticipate the survey will be placed in the public domain.

Coordination of research

6. The Department of Health published a National Pandemic Influenza Contingency Plan in March this year. It subsequently established a Scientific Advisory Group on Pandemic Influenza, on which MRC is represented. MRC officials are in regular informal contact with counterparts from the Health Departments, the Department for International Development, the Department for Environment, Food & Rural Affairs, the Health Protection Agency, the BBSRC and ESRC, the OST, the Wellcome Trust, and the Academy of Medical Sciences.

7. Professor Blakemore (MRC Chief Executive) has regular contact with senior officials of the Chinese Academy of Sciences. Together with the Chairman and Deputy Chairman of the MRC’s Infections & Immunity Board, he recently met Dr Jeremy Farrar, Director of the Oxford Clinical Research Unit in Vietnam. The meeting informed plans for the MRC’s Emerging Infections mission to Vietnam and China, when Professor Blakemore will also be in China.

8. Research issues in the field are also reviewed by Heads of International biomedical Research Organisations (HIROs). This informal grouping, which meets six-monthly, brings together the heads of MRC, the USA National Institutes of Health, and counterparts from Canada, Australia, New Zealand, several European national funders and China (represented by a Vice President of the Chinese Academy of Sciences).

Current MRC programmes in influenza

i. The MRC currently invests £1.6 million per annum on flu research.

ii. The MRC’s principal investment in influenza research is at the National Institute for Medical Research (NIMR). The NIMR programme was recognised as being internationally outstanding in a recent a quinquennial review.

iii. Sir John Skehel’s programme focuses on the structural and functional characteristics of the virus surface that enable it to infect cells; and on the mechanism by which anti-haemagglutinin antibodies neutralise viral infectivity. His team recently explained how the haemagglutinin (HA) of the 1918 virus both retained receptor binding site amino acids characteristic of an avian precursor HA, and was able to bind to human receptors and how, as a consequence, the virus was able to spread in the human population. The programme has produced other major insights into the molecular basis of host range, pathogenicity and human-to-human transmission and into the pandemic potential of different influenza subtypes.

iv. Dr Alan Hay leads the World Influenza Centre at the NIMR, monitoring changes in the virus that have significance for human health and protection as those changes occur: this work makes an important contribution to public health internationally. Dr Hay works closely with the HPA and with WHO Collaborating Centres in the USA, Japan and Australia and the global network of...
National Influenza Centres. Dr Hay also leads a programme of basic research on the mechanisms of action of resistance to antiviral drugs, including the structural basis of M2-channel activity. Dr Hay also participates in international and EU networks concerned with viral drug resistance.

v. The NIMR has ACDP Category 4 facilities and the Council is keenly aware of the need to make appropriate high containment arrangements in renewing the Institute in partnership with UCL. The renewal and partnership strategy offer significant advantages over current arrangements at Mill Hill in terms of strengthening translational research and integration with world-class physical sciences.

vi. The Council also funds a programme of research at the University of Oxford (Professor George Brownlee) to study transcription and regulation of influenza A virus. This is fine-grained, basic molecular work on how the segmented RNA viral genome is copied in a regulated manner, and has the potential to lead in the longer term to production of novel influenza antivirals and vaccines.

**INTERIM SCIENTIFIC PRIORITIES**

Based on input from the community and expert discussion, the Infections & Immunity Board will formally define its emerging infections priorities early in 2006. Until then, the following questions—as applied to influenza—describe the Board’s interim priority research themes:

— What is the current risk posed by avian flu to the human population? How robust are the data and systems on which risks are being estimated? What are the specific modes of transmission? What do ecology, epidemiology and clinical research reveal about the critical points for preventive (pre-pandemic) or responsive (pandemic) action?

— Some flu strains are more readily transmitted from non-human species to people than are others; and strains differ in their transmissibility between people. What are the mechanisms that determine viral strain transmissibility and individual susceptibility? What are the strategies to reduce transmission effectively? What are the critical research issues?

— People with H5N1 influenza reported to the World Health Organisation in the current outbreak have a high mortality rate. But what is the full spectrum of illness? What makes people infected with H5N1 influenza become seriously ill and die? What are the genetic, molecular and cellular and immune mechanisms determining virulence, pathogenicity and protection? What are the contributions of the virus and the host and the interplay between them to clinical outcomes of infection? How can collaborative research on clinical and pathological manifestations, and the effectiveness of interventions to control and treat infection, be promoted?

— Current vaccines for seasonal flu are strain-specific. There are few effective drugs, and resistance is a threat. What characteristics do we need vaccines and drugs to exhibit to achieve effective prevention and control? What are the opportunities and strategies for innovation to develop better and new vaccines and drugs—(a) in the short term; (b) in the longer term?

— Were a pandemic to emerge, the timescale could be very rapid. How can biomedical and health research contribute to rapid and reliable collection, analysis and evaluation of surveillance data and samples? What might be the opportunities for effective intervention in the early stages of an outbreak of a dangerous flu strain, so as to prevent a pandemic?

— Similarly, what research is required to ensure that public health intervention strategies and technologies in an epidemic can be effective in healthcare and community settings? What contributions can public health modelling and behavioural research make?

The Board recognises that:

— Some crucial research questions are urgent now; others can be addressed only over a longer time-scale. Some can be addressed only at the moment a serious outbreak occurs—in which case a research protocol needs to be enacted then, without delay. MRC will consider proposals for such “preparedness protocols”;

— A broad range of disciplines and technologies need to be brought to bear on these questions;

— The MRC’s remit and capacity is such that it’s most effective contribution is likely to be to basic biomedical and health research on aetiology and mechanisms; and generalisable clinical, behavioural, public health and field research;

— Human infections that are also zoonoses require complementary and coordinated human and veterinary research strategies;

— Access to specialised models, expertise and infrastructure is critical;
— Large and small scale research have important roles to play: some questions will be best addressed through goal-oriented, research networks, collaborations or consortia; and others through focused, individual grants;
— There is strong rationale for collaborating internationally, especially with countries at high endemic risk from emerging virulent infections;
— Influenza research outputs need to be translated efficiently into implementable benefits for patients and public health globally.

Annex 4

Additional information from the Natural Environment Research Council (NERC)

1. NERC is one of the UK’s eight Research Councils. It funds and carries out impartial scientific research in the sciences of the environment. NERC trains the next generation of independent environmental scientists. Its priority research areas are: Earth’s life-support systems, climate change, and sustainable economies.

2. NERC’s research centres are: the British Antarctic Survey (BAS), the British Geological Survey (BGS), the Centre for Ecology and Hydrology (CEH) and the Proudman Oceanographic Laboratory (POL).

3. NERC’s contribution to the present submission comes from CEH.

4. In addition to addressing two of the Committee’s specific questions in the main body of the present submission, we here present our opinions of further research required in the UK.

What benefits might be expected from studying avian influenza in UK wildlife species?

5. The most obvious answer to this question is that there is very little information at the moment and we really cannot accurately predict the risk of avian influenza to humans in the UK. The benefits would be improved understanding of the possible risks, greater knowledge of the factors that determine viral epidemiological success and the possibility of controlling the pandemic at the virological level.

6. A few years ago avian influenza viruses re-emerged and they are now causing major epidemics involving high numbers of fatalities amongst wild and domestic avian species in Asia. In the late 1990’s these epidemics appeared to be confined to Hong Kong and nearby regions but by 2003 they had spread to Vietnam and China and are the epidemics currently being recorded amongst avian species throughout southern and northern Asia including Russia. There is every reason to believe that this virus dispersal will continue in a westerly direction into Europe as infected birds migrate during the autumn of 2005. Whilst this in itself presents a major threat to avian species, it is of even more concern since humans exposed to infected birds, particularly poultry, have also been fatally infected. One strain of influenza virus in particular, ie H5N1, referred to as “highly pathogenic avian influenza (HPAI)” virus, is believed to pose the most likely threat of changing its preference for birds to become a human pathogen, ie a virus that could spread efficiently amongst humans. Such a change could occur either by HPAI virus exchanging appropriate genes with human, porcine or equine strains of influenza virus or by mutation of genes within HPAI virus. If such changes do occur it is believed that a novel virus might arise that could cause an influenza pandemic equivalent to the devastating Spanish flu of 1918–19 which is estimated to have killed up to 40 million humans globally.

7. For these reasons, and also because there is a significant lack of information on the presence of these viruses in the UK, we believe it is important to investigate the current situation with regard to avian influenza virus in wildlife species, particularly but not exclusively birds, in the UK. If co-ordinated properly, such an investigation would provide us with the information required to make meaningful predictions as to the risk of pandemic influenza in the UK. Moreover, by co-ordinating the derived information with that currently being obtained throughout Europe and Asia, a deeper understanding of the factors that are most important in determining pathogenicity for humans and other mammalian species would be obtained. Hopefully, this would improve our ability to control influenza virus dispersal and pandemic in the future.

Viruses in birds in the United Kingdom

8. Scientists at CEH and others in Europe have demonstrated that several different pathogenic arthropod-borne viruses circulate in the UK and Europe. Many of these viruses have been introduced by migrant birds from Africa, eastern Europe and Asia. They have been shown to cause a wide variety of clinical manifestations from fever to encephalitis or arthritis. In contrast, there is little information concerning the presence of type A avian influenza viruses in wildlife species in the UK and we have no idea if such viruses could provide a
genetic reservoir for exchange with viruses such as highly pathogenic avian influenza (HPAI) virus to create novel human pathogens. Moreover, the HPAI virus is classified as a hazard group 3 pathogen. Therefore, if it is introduced into the UK, it can only be studied in laboratories with appropriate high-containment facilities.

9. This potential technical problem has effectively been circumvented by the development of a genetically engineered strain of influenza virus designated NIBRG-14 which will be used for the studies proposed herein. NIBRG-14 virus was engineered by Dr John Wood at NIBSC (Potters Bar, Herts) with a view to its use as a human influenza vaccine. NIBRG-14 is based on the PR8 strain of influenza A virus modified by substituting the haemagglutinin (H5) and the neuraminidase (N1) from the HPAI strain of influenza. However to ensure that this vaccine strain is safe both as a vaccine and also for laboratory diagnostic studies, the haemagglutinin has been modified (by Dr Wood) so that it lacks the polybasic cleavage site in the haemagglutinin gene. Without this cleavage site influenza viruses are of much lower virulence than the strains that contain the cleavage site. This modification reduces the efficiency of release and spread of the virus from cell to cell and host to host.

Recommendations for future study

10. Specific information is required relating to the presence of avian influenza virus in UK wildlife species—particularly birds, but not excluding other species such as bats and possibly pigs.

11. We suggest to:
   — look for specific antibodies to the highly pathogenic avian influenza (HPAI) virus using plaque reduction neutralisation tests on the sera of avian and other wildlife species;
   — look for the presence of specific viral RNA (from HPAI) in the sera and/or tissues of healthy birds and, if positive samples are obtained, identify the viruses by sequencing;
   — look for the presence of antibodies and/or specific viral RNA to related strains of influenza virus and, if positive results are obtained, identify the viruses by sequencing;
   — attempt to isolate strains of influenza virus from healthy birds, sequence them and determine whether they contain the basic cleavage site in the haemagglutinin protein that determines virus pathogenicity.

12. This approach will have to include the collection and analysis of samples taken from a wide range of areas of the UK, and should cover a wide range of avian species. Advantage should be taken of any ongoing studies by other investigators who are currently sampling bird populations and possibly maintaining stocks of frozen avian blood sera, as these will provide both current and historical perspectives.

Memorandum by the Royal Society

The Royal Society is pleased to respond to the Committee’s call for evidence for the inquiry into “UK’s preparations for a potential outbreak of pandemic influenza”. The Society would like to recommend that the Committee consider the following points when conducting its inquiry:

1. The majority of cases of pandemic influenza among human reported to date have emerged in south east Asia where avian flu is endemic. However it should be noted that pandemic influenza could emerge elsewhere in the world. For example, the USA, South Africa and Canada all reported cases of avian flu in 2004 and the Netherlands recently reported human deaths from avian flu. Furthermore, the UK is in the flight path of migratory wild fowl from Siberia and central Asia, areas in which avian flu has been reported. It is therefore essential that any assessment of risk should be considered more broadly than solely emergence from south east Asia. It is of further concern that many surveillance organisations such as the Centre for Disease Control and Prevention in the US are reporting the spread of a strain of avian flu in south east Asia with an increased pathogenicity in a wide range of bird and mammal species.

2. The Society believes the UK is strongly placed to develop modelling-based scenarios on the possible routes of human transmission and propose possible containment strategies based on these scenarios. Development of these scenarios can be used to anticipate which combinations of interventions are best applied, given the current and future availability of drugs and vaccines. Furthermore these scenarios will benefit from the addition of epidemiological and clinical data which will further inform interventions that may need to be made.
3. If an outbreak is due to a strain for which an existing vaccine is available it will be possible to offer protection as long as adequate production facilities exist. It is important to note that there is not currently a vaccine against the H5N1 strain of avian influenza that is licensed for human use in the UK. Vaccines should be developed against strains of avian influenza virus, but these may not be effective if a virus mutates into a form that is easily transmissible to and between humans. Therefore vaccines should be modified and updated to keep pace with the evolution of the viruses. To ensure that the development, manufacture and distribution of vaccines will be effective the Government needs to put mechanisms in place to ensure that the quality and supply of vaccines in the UK are maintained, rather than being bought from the private sector on the open market. It is likely that vaccine companies will not make large profits from vaccines as the costs of updating their technology compared with the potential usage could make it unviable. If necessary, the Government should consider underwriting the cost and liability of developing this new production technology.

4. In the event of a pandemic influenza outbreak it would be preferable to have a rapid and inexpensive diagnostic test available at the GP clinic and for “bedside” use. Current diagnosis is laboratory based and takes much longer for results to be available to the prescriber than the narrow window of opportunity (approximately 48 hours) that exists for effective utilisation of antivirals after exposure to influenza. Any “dip stick” style test will require an appropriate level of sensitivity and accuracy that allows a clear diagnosis and typing of the virus strain. The Government should consider allocating research funds for the development of such a test. In the mean time, further research should also be conducted to increase the accuracy and decrease the time taken for laboratory based diagnosis. The widespread availability of a rapid diagnostic test may also have implications for prescribing of treatments outside of the GP surgery in an outbreak scenario.

5. Antiviral drugs can be used in the early treatment of influenza as well as prophylactically in those at risk. Government needs to initiate research on the use of antivirals on a prophylactic basis, the development of possible resistance to an antiviral treatment and the subsequent transmission of resistant strains.

6. The Society is concerned by the loose definition in the Department of Health pandemic influenza contingency plan of an “essential worker” (someone who would receive antiviral treatment) and at what time they would receive the antiviral. This definition should include not only workers in the healthcare sector but other personnel involved in the maintenance of critical national infrastructure such as power, finance, water and government. A strategic decision on the priority of treatment given to essential workers also needs to be made. It is essential that the number of doses of antivirals and vaccines, if appropriate, available in the UK is at least sufficient to cover all essential workers identified in the contingency plans.

7. The globalisation of the economy means that infections now have the potential to spread rapidly around the world. A previously local epidemic now has the potential to become a pandemic. It is essential the UK Government does not focus entirely on stopping a pandemic at source through the use of antivirals but instead considers a broad range of interventions such as modelling based scenarios and developing new vaccine production capability.

Memorandum by Dr R L Salmon, Director, Communicable Disease Surveillance Centre, National Public Health Service for Wales

Preamble
1. The submission is substantially confined to the Sub-Committee’s particular questions. The views expressed are my own and based on 15 years as a regional epidemiologist in Wales, including some published research on the impact of the 1989 epidemic in Wales.

The Risk

How is the risk of pandemic influenza emerging in south east Asia, and reaching the UK, being assessed; and how can this assessment be improved?

2. It seems inconceivable that there will not be another influenza pandemic, given that they have occurred throughout recorded history. How soon it will occur and whether H5N1 Avian influenza strains, circulating currently in the far east, will constitute the next human pandemic strain is very uncertain and could be said to represent a (well) educated guess. Nevertheless, sufficient authoritative scientific authorities on influenza regard this to be of concern, that it would be unwise not to bring forward measures for influenza pandemic planning that are themselves necessary anyway.

3. Assessment might potentially be improved by harnessing a combination of molecular biological and information technology techniques. The ability of an influenza virus to infect a host (although not its subsequent virulence) is determined by the extent to which its haemagglutinin is adapted to bind with that host’s cell’s sialic acid receptors. Much is known both about the differences in haemagglutinin structure between avian adapted and human adapted strains and about the influenza genome and how these
differences are coded for. This could permit an assessment of which nucleotides are critical coding regions for changes that would result in greater infectivity of humans. This would allow the a priori determination of what observed changes, in the genome and/or haemagglutinin molecule of currently circulating H5N1 viruses, should suggest emerging human adaption and should trigger a wider pandemic response, notably the large scale production and administration of an H5N1 influenza vaccine. I understand that certain British research groups, notably that of Queen Mary College, London, are involved in similar work to this. It would be worth seeking information as to progress and inquiring whether, in practice, it could be adapted in the sort of ways that are proposed.

How great are the risks, and what confidence can be placed in these figures?

4. The careful documentation of the impact of the three pandemics of the last century (1918–20, 1957–58, 1968–69), not to mention of the two years where previously encountered strains reappeared after an absence of some years (1976, 1989) allow intelligent estimates of the likely scale of the potential problem.

CONTINGENCY PLANNING IN THE UK

What is the current assessment of the likely impact of pandemic influenza on the UK (both in terms of health and on wider society, including the economy)?

5. The central planning assumptions, based on historical experience, anticipate a cumulative clinical attack rate of 25 per cent as a culmination of one or two approximately annual waves of pandemic activity, each of eight to 15 weeks’ duration. This is very reasonable.

6. More speculative would appear to be some of the prognostications of wider societal breakdown. Previous pandemics in the 20th century did not result in this and it is difficult to advance the argument that society today is somehow more fragile than it was in those years. Nevertheless an influenza pandemic would be disruptive, although the historic experience suggests that this disruption is, with difficulty, manageable.

Are the measures described in the revised UK Influenza Pandemic Contingency Plan adequate to minimise the effects of a pandemic? What more could be done?

7. Work to introduce the necessary operational detail into the UK Influenza Pandemic Contingency Plan appears to be getting under way. It is necessary to recognise the critical role of the National Health Service, particularly Primary Care. The latter, which will have a key role in distributing antiviral treatments (below), is the key resource and engagement with general practitioners, community pharmacists and their representatives is vital and needs to be commenced urgently.

How well prepared and co-ordinated are health, emergency and other essential services for responding to a pandemic?

8. The development of emergency planning arrangements and local resilience fora, based on police force areas has been a helpful development, in a wider sense, for providing a focus for collaboration across the public sector more widely. However these arrangements were primarily designed to address major incidents unfolding over a few days or hours. They are less adaptable to the circumstance of pandemic flu where the problem lasts for several weeks and the key resources are in the health and related care sectors.

9. The health sector continues to digest various reorganisations and changes in contractual arrangements that are primarily aimed at reforming the delivery of personal health services rather than at public health. These affect the collaboration and co-ordination of infectious disease services, a problem that the Committee acknowledged in Fighting Infection. Thus, for example, organising the delivery of antiviral treatments and if appropriate, vaccinations, may prove to be more complicated in Wales than it might have been previously. This is, in part, a result of the abolition of the five health authorities and their replacement by 22 local health boards and of changes to the out of hours GP services brought about by the new GP contract.

What is being done to ensure that the general public are aware of the risks and likely effects of a pandemic, and of how they should react?

10. Welsh Assembly Government is, we understand, participating in the wider public communications package being organised by the Department of Health.
Is the UK’s stockpile of antiviral treatments adequate, and how will it be distributed? What steps are being taken to ensure that the UK has access to sufficient antiviral treatment and vaccine in the event of a flu pandemic?

11. Once the UK’s stockpile of 14.6 million doses is in place in April 2007, it should be adequate to treat the number of clinical cases that are likely to arise. Details of their distribution need to be worked out urgently and any potential contractual or legal obstacles ironed out.

What will be the role of vaccine development, manufacture and distribution in responding to a pandemic?

12. Traditionally, vaccines have only been available subsequent to the initial pandemic waves of a new influenza strain. They would then be incorporated into seasonal vaccination programmes.

13. A decision has to be made as to whether there is sufficient justification for vaccinating certain groups with the H5N1 vaccines being developed, at present. If not at present, then criteria for initiating such vaccination would be helpful. They could conceivably be based on molecular biological and information technology techniques (para 3 above).

23 September 2005

Memorandum by the Wellcome Trust

1. The Wellcome Trust is pleased to respond to this Call for Evidence by the House of Lords Science and Technology Committee (the “Committee”). The threat of pandemic influenza is an important issue, and the Wellcome Trust provides substantial funding for research in this area—mainly through the southeast Asia Programme, but also with a number of ad-hoc grants via our Biomedical Science and History of Medicine funding streams. The Wellcome Trust is not well placed to answer many of the specific questions within the call for evidence. However, we would like to offer the following thoughts regarding the two main areas covered by the inquiry, i.e. the risk of pandemic influenza, and contingency planning in the UK.

A. The risk of pandemic influenza

2. Most experts agree that a new influenza virus with pandemic potential will emerge in southeast Asia, and that a further pandemic is to be expected. However, as the Committee will be aware, research published recently in *Nature* and *Science* suggests that a pandemic could be avoided if local health authorities react quickly to an outbreak and provide suitable drugs to prevent it spreading. The two independent modelling studies were carried out by a team led by mathematical biologist Neil Ferguson of Imperial College London, and by a group led by biostatistician Ira Longini of Emory University in Atlanta, Georgia. Both studies agree that it would be theoretically possible to contain an emerging pandemic—if the virus was detected early, if it did not spread too fast, if sufficient antivirals were deployed rapidly around the outbreak’s epicentre, and if strict quarantine and other measures were also used.

B. Contingency planning in the UK

3. The Wellcome Trust considers that there is currently a dearth of influenza expertise within the UK research community, and that action is required to ensure that a new generation of researchers are able to fill the void created once the current crop of experts reach retirement age. The scale of the global threat to human health posed by pandemic influenza would appear to warrant additional funding to stimulate an increase in basic research into influenza in the UK.

Vaccine development

4. The Trust has not undertaken any analysis of vaccine manufacturing capability, but anecdotally we are often told that the process for developing a vaccine to deal with a new variant will need to be a lot more efficient than it currently is in order to avert a serious problem. It is widely documented that the majority of deaths from pandemic influenza are likely to occur within the first six to twelve months, so any delay in the R&D of a new vaccine will have serious consequences. Some researchers estimate that it will be possible to develop a new vaccine within three to six months. The Wellcome Trust considers that a timescale of six to twelve months is more realistic—barring any unforeseen logistical or technical issues.

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5. The Trust is aware that the Singapore government is pushing hard to establish itself in the flu vaccine field and it is setting up manufacturing capacity on a scale enabling it to become a global supplier. It could therefore make sense for the UK Government to enter into some form of agreement with Singapore regarding future flu vaccine needs, subject to satisfactory due diligence. It will be too late once an epidemic starts as there will be a massive scrabble to get vaccine pre-ordered from anywhere that has established the infrastructure to put in motion a crash programme. The UK needs to establish what in-country capability it currently has, or is prepared to invest in now; what additional capability the UK will need based on expected demand; where to source that additional capability from; and what backup arrangements are needed in the event of a logistical failure (like the incident last year when the flu vaccine production plant in Liverpool had to be closed for safety reasons and supplies were seriously disrupted).

Wellcome Trust activity related to avian flu

6. The Wellcome Trust is currently funding a project to further research into what made the virus that caused the influenza pandemic of 1918 so deadly. The project will analyse the flu virus found in tissue samples from 1918 flu victims, and from people killed by other strains, to look for differences that might explain its immense impact. Led by London-based virologist John Oxford, the project team will use recently discovered preserved lung material from flu victims from 1908–33 to examine the genetic codes of viruses that were circulating before and after the 1918 virus. This will allow the team to track the development of the virus, and so build up a picture of how it became so lethal. It is hoped that research such as this will help to devise or improve systems for predicting and handling future pandemics.

7. The Wellcome Trust has funded an international consortium led by the UK and Hong Kong since 1999 under the IPRAVE initiative (International Partnership Research Awards in Veterinary Epidemiology). This initiative sought to support research in areas of veterinary public health that were of importance in both the developed and developing world and provided investment in research and research training programmes in the field of zoonotic and food borne disease. Funding has been provided for core support and for research projects on influenza virus epidemiology, interspecies transmission and a pandemic risk assessment study of the role of Asian live poultry markets.

8. The Wellcome Trust has recently allocated funding totalling up to £36 million over the next five years to its major overseas programmes in Kenya, Thailand and Vietnam. In Vietnam, where Dr Jeremy Farrar is Programme Director, research is focused on malaria, dengue, typhoid, and infections of the central nervous system such as tetanus and tuberculous meningitis. However, more recently, the programme has played an important role in the treatment and study of people infected with the avian influenza virus, providing valuable information on this deadly new global threat to human health.

9. The Committee may wish to note that the Trust will participate in an expert scientific meeting on pandemic flu, organised by the Medical Research Council (MRC), on 7 and 8 December 2005. The outcome of this meeting, which is likely to be attended by experts such as Dr Jeremy Farrar, may be of interest to the Committee. The meeting will address the first two of the following questions, and will contribute to the MRC’s discussions with the Department of Health on the third:

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- Prevention—what reasonably swift contribution could the MRC make to south east Asian research efforts that aim to prevent a pandemic from ever happening?
- Preparedness—what long term, strategic research contribution could MRC make to achieve substantive improvements in flu surveillance, diagnosis, immunisation and treatments, such that a pandemic could be averted or better controlled?
- Response—were a pandemic to be declared, what would be the appropriate response from MRC in supporting the international and national response?