House of Commons
Science and Technology Committee

Regulation of medical implants in the EU and UK

Fifth Report of Session 2012–13

Report, together with formal minutes, oral and written evidence

Additional written evidence is contained in Volume II, available on the Committee website at www.parliament.uk/science

Ordered by the House of Commons
to be printed 17 October 2012
Science and Technology Committee

The Science and Technology Committee is appointed by the House of Commons to examine the expenditure, administration and policy of the Government Office for Science and associated public bodies.

Current membership
Andrew Miller (Labour, Ellesmere Port and Neston) (Chair)
Caroline Dinenage (Conservative, Gosport)
Jim Dowd (Labour, Lewisham West and Pinge)
Gareth Johnson (Conservative, Dartford)
Stephen Metcalfe (Conservative, South Basildon and East Thurrock)
Stephen Mosley (Conservative, City of Chester)
Pamela Nash (Labour, Airdrie and Shotts)
Sarah Newton (Conservative, Truro and Falmouth)
Graham Stringer (Labour, Blackley and Broughton)
Hywel Williams (Plaid Cymru, Arfon)
Roger Williams (Liberal Democrat, Brecon and Radnorshire)

The following members were also members of the committee during the parliament:
Gavin Barwell (Conservative, Croydon Central)
Gregg McClymont (Labour, Cumbernauld, Kilsyth and Kirkintilloch East)
Stephen McPartland (Conservative, Stevenage)
David Morris (Conservative, Morecambe and Lunesdale)
Jonathan Reynolds (Labour/Co-operative, Stalybridge and Hyde)

Powers
The Committee is one of the departmental Select Committees, the powers of which are set out in House of Commons Standing Orders, principally in SO No.152. These are available on the Internet via www.parliament.uk

Publications
The Reports and evidence of the Committee are published by The Stationery Office by Order of the House. All publications of the Committee (including press notices) are on the Internet at http://www.parliament.uk/science. A list of reports from the Committee in this Parliament is included at the back of this volume.

The Reports of the Committee, the formal minutes relating to that report, oral evidence taken and some or all written evidence are available in printed volume(s). Additional written evidence may be published on the internet only.

Committee staff
The current staff of the Committee are: Dr Stephen McGinness (Clerk); Jessica Montgomery (Second Clerk); Xameerah Malik (Senior Committee Specialist); Theresa Dahn (Committee Intern); Darren Hackett (Senior Committee Assistant); Julie Storey (Committee Assistant); Henry Ayi-Hyde (Committee Office Assistant); and Nick Davies (Media Officer).

Contacts
All correspondence should be addressed to the Clerk of the Science and Technology Committee, Committee Office, 7 Millbank, London SW1P 3JA. The telephone number for general inquiries is: 020 7219 2793; the Committee’s e-mail address is: scitechcom@parliament.uk.
# Contents

## Report

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary</td>
<td>3</td>
</tr>
<tr>
<td>1 Introduction</td>
<td>5</td>
</tr>
<tr>
<td>2 Background</td>
<td>7</td>
</tr>
<tr>
<td>Regulation of medical implants</td>
<td>7</td>
</tr>
<tr>
<td>The MHRA</td>
<td>9</td>
</tr>
<tr>
<td>High profile medical device recalls</td>
<td>10</td>
</tr>
<tr>
<td>PIP breast implants</td>
<td>10</td>
</tr>
<tr>
<td>Metal-on-metal hip implants</td>
<td>11</td>
</tr>
<tr>
<td>3 Pre-market approval</td>
<td>12</td>
</tr>
<tr>
<td>Clinical data requirements</td>
<td>12</td>
</tr>
<tr>
<td>Cost and timescale of clinical trials</td>
<td>16</td>
</tr>
<tr>
<td>Transparency of evidence</td>
<td>18</td>
</tr>
<tr>
<td>Comparisons with the FDA</td>
<td>21</td>
</tr>
<tr>
<td>Notified bodies across Europe</td>
<td>22</td>
</tr>
<tr>
<td>4 Post-market surveillance</td>
<td>27</td>
</tr>
<tr>
<td>Reporting of adverse incidents</td>
<td>27</td>
</tr>
<tr>
<td>Manufacturers</td>
<td>27</td>
</tr>
<tr>
<td>Clinicians and patients</td>
<td>28</td>
</tr>
<tr>
<td>Registries</td>
<td>31</td>
</tr>
<tr>
<td>EU registry</td>
<td>32</td>
</tr>
<tr>
<td>Responding to adverse incidents</td>
<td>34</td>
</tr>
<tr>
<td>Auditing manufacturers</td>
<td>36</td>
</tr>
<tr>
<td>5 Conclusions</td>
<td>39</td>
</tr>
<tr>
<td>The MHRA</td>
<td>39</td>
</tr>
<tr>
<td>The regulation of medical implants</td>
<td>40</td>
</tr>
<tr>
<td>Conclusions and recommendations</td>
<td>42</td>
</tr>
<tr>
<td>Formal Minutes</td>
<td>47</td>
</tr>
<tr>
<td>Witnesses</td>
<td>48</td>
</tr>
<tr>
<td>List of printed written evidence</td>
<td>48</td>
</tr>
<tr>
<td>List of additional written evidence</td>
<td>49</td>
</tr>
<tr>
<td>List of Reports from the Committee during the current Parliament</td>
<td>50</td>
</tr>
</tbody>
</table>
Regulation of medical implants in the EU and UK
Summary

Effective regulation of medical implants is of paramount importance to patient safety in the UK and EU. The regulatory framework governing medical devices, which include medical implants, is undergoing revision in the European Commission. Public attention has been drawn to the shortcomings of the current system by high profile cases where faulty implants have been withdrawn from the market, such as Poly Implant Prothèse (PIP) breast implants and metal-on-metal hip implants. There have been several investigations into the PIP breast implants scandal, and our inquiry has therefore focused on the regulation of medical implants more widely.

Manufacturers seeking to place a new medical implant on the EU market must provide some evidence on the safety and performance of the implant. Unlike with medicines, it is not always necessary to generate clinical evidence about the new product: it is considered acceptable to rely on “equivalence data”, in other words, published clinical investigations or studies of similar devices. Essentially this means that implants can be used across the EU on the basis of similarity to another implant rather than evidence of its own safety and performance. While this would be acceptable (albeit not ideal) in some cases, we were unimpressed with the extent to which reliance on equivalence data, rather than clinical investigations, seemed to be acceptable. We were therefore pleased that the Commission has proposed measures to make clearer what clinical information is required from manufacturers and when equivalence data would be acceptable. We are also supportive of proposals to strengthen auditing of manufacturers.

While we support the proposal that all implants placed on the EU market should be registered centrally, we do not support the Commission’s proposal to require manufacturers with new implants to formally notify a central EU authority as this increased bureaucracy could slow the approval process unnecessarily.

Transparency was a significant concern as we found that the evidence on safety and performance of implants was not fully published by manufacturers and the operation of notified bodies (who are responsible for approving manufacturers’ implants for use) was not transparent. Perceptions of secrecy can be, and have been, very damaging to public trust in the regulatory system. We have made several recommendations to improve transparency and consider that the revised Medical Devices Directive should remove the over-emphasis on confidentiality and operate from a default position of transparency and openness. In addition, we support the Commission’s proposals to strengthen the scrutiny of notified bodies across Europe.

Once implants are on the EU market, post-market surveillance is intended to pick up any faults. This requires reporting of adverse incidents by patients and healthcare professionals as well as manufacturers. As there is some evidence of under-reporting, the Government should make the reporting of adverse incidents mandatory for healthcare professionals. We consider that implants approved on equivalence should be marked in a manner similar to the Black Triangle Scheme, which is used to monitor new medicines that have been approved for use on limited clinical data.
1 Introduction

1. Effective regulation of medical implants is of paramount importance to patient safety in the UK. Recent high-profile cases where faulty medical implants were withdrawn from the market, such as the Poly Implant Prothèse (PIP) breast implant and DePuy’s Articular surface replacement (ASR) metal-on-metal hip implant, have brought into question the effectiveness of current regulations.1 The withdrawal of the PIP breast implant from the market prompted a number of reviews and inquiries in the UK. In May 2012, Lord Howe, Departmental Under Secretary of State, Department of Health (DH), published a review of the actions of the Medicines and Healthcare products Regulatory Agency (MHRA) and DH in relation to the recall of PIP breast implants.2 Sir Bruce Keogh, NHS Medical Director, appointed an Expert Group to conduct a wider review into the regulation of cosmetic interventions, which published its report on 18 June 2012.3 The House of Commons Health Select Committee published a report in March 2012 raising a number of issues that it felt ought to be considered by these reviews.4 Although investigations into the PIP breast implant will have implications for the regulation of medical devices, we decided that an inquiry focusing on the regulation of medical implants more widely would be of interest to Parliament and the public. We wanted to examine in particular how scientific evidence is used in the approval of implants for use in humans and in post-market monitoring.

2. Medical devices are products (excluding medicines) used in healthcare for the diagnosis, prevention, monitoring or treatment of illness or disability.5 Medical implants are medical devices inserted into the body and are governed by the Medical Devices Regulations 2002. The Medical Devices Directive (MDD), the basis for the Regulations, is currently undergoing revision in the European Commission. Public consultations took place in 2008 and 2010, and a proposal to revise the legal framework for medical devices was published in September 2012. The Commission intends that “this process shall lead to a fundamental revision of the existing directives in order to simplify and strengthen the current EU legal framework for medical devices”.6 We hope that our inquiry will (i) influence the UK Government’s position when negotiating the text of the Commission’s proposed revisions in Council later this year; and (ii) inform the work of the European Scrutiny Committee, which scrutinises draft EU legislation on behalf of the House of Commons.

3. We issued a call for evidence on 26 March 2012 seeking views on the following questions:

---

2 Health Committee, Sixteenth Report of Session 2010–12, PIP Breast implants and regulation of cosmetic interventions, HC 1816
3 Poly Implant Prothèse (PIP) breast implants: final report of the Expert Group, Department of Health, NHS Medical Directorate
4 Health Committee, Sixteenth Report of Session 2010–12, PIP Breast implants and regulation of cosmetic interventions, HC 1816
5 “What we regulate”, MHRA, www.mhra.gov.uk
6 “Medical devices: Regulatory Framework”, European Commission, ec.europa.eu
a) Are current legislation and regulations on safety and efficacy of medical implants fit for purpose?

b) How effectively does the MHRA implement the Medical Devices Directive in the UK?

c) How could the legislation and regulations be improved?

d) How could the European Commission ensure that potential changes to the Medical Devices Directive do not hinder the introduction of innovations in medical implants to the market?

4. The Committee received 19 written submissions. We took oral evidence from four panels across two evidence sessions. On 23 May we took evidence from researchers, clinicians and patient representatives: Dr Carl Heneghan, GP and Director of the Centre of Evidence-Based Medicine at the University of Oxford; Dr Tom Joyce, Professor of Orthopaedic Engineering in the School of Mechanical and Systems Engineering at Newcastle University; Professor Stephen Westaby, Consultant Cardiac Surgeon, John Radcliffe Hospital, Oxford; and Dr Suzette Woodward, Director of Patient Safety, National Patient Safety Agency. On 13 June we took evidence from three panels of witnesses representing implant manufacturers, notified bodies, the European Commission, and UK Government. The first panel comprised of John Howlett, Head of the British Standards Institute (BSi); Peter Ellingworth, Chief Executive of the Association of British Healthcare Industries (ABHI); and Mike Kreuzer, Technical and Regulatory Executive Director, ABHI. In the second panel we heard from Jacqueline Minor, Director of Consumer Affairs, Directorate-General for Health & Consumers, European Commission. Finally, we took evidence from Sir Kent Woods, Chief Executive of the MHRA and Lord Howe, DH.

5. We would like to thank those who provided written and oral evidence to this inquiry. We also sought to take oral evidence from device manufacturers. Although they told us that their views would be adequately represented by the Association of British Healthcare Industries (ABHI), we are very disappointed that we were not able to take oral evidence directly from manufacturers.

6. In chapter 2 of this Report we outline the requirements of the European Directives and how implants are regulated in the UK as a result. Chapter 3 will consider the process of certifying products for the EU market: whether sufficient evidence is gathered on an implant before approval for use and whether tighter pre-market requirements would introduce barriers to innovation and prevent the latest technology from reaching patients. In chapter 4 we discuss how to improve the monitoring of medical implants once they are on the market (post-market surveillance), and increasing coordination between EU Member States. Finally, in chapter 5 we draw overall conclusions.

7 “Committee announce new inquiry into the Regulation of medical implants”, News, Science and Technology Select Committee (Commons), www.parliament.uk
2 Background

Regulation of medical implants

7. The term “medical device” covers a wide range of products and instruments, such as contact lenses, hospital beds, resuscitators and syringes. There are thousands of medical devices used every day to diagnose, prevent, monitor and treat illness or disability. A medical implant is a device intended to be either totally introduced into the body or to be partially introduced into the body through surgery and to remain there for at least 30 days. Implants can be active (that is, requiring a power source, such as a pacemaker) or non-active (such as a hip implant).

8. The regulatory framework stems from three European Directives:

a) Directive 90/385/EEC on active implantable medical devices (AIMDD);

b) Directive 93/42/EEC on medical devices (MDD); and


9. These Directives have “been implemented into UK legislation by the Medical Devices Regulations 2002, which consolidated all the existing medical devices Regulations into a single piece of legislation and which came into force in June 2002”. The Directives were intended to serve the dual purpose of allowing manufacturers “a single set of regulatory requirements” with which to access the entire EU market while providing users of devices with a high level of confidence in the safety and performance of a device. The Directives “set out a list of essential requirements which all devices must meet before being placed on the market, as well as imposing various other regulatory requirements upon the manufacturer.”

10. The Directives are implemented by a “competent authority” in each Member State: in the UK it is the Medicines and Healthcare products Regulatory Agency (MHRA), an executive agency of the Department of Health (DH). The competent authority designates notified bodies in that Member State to undertake specific tasks identified within EU directives. Notified bodies assess higher-risk devices (such as implants) submitted for...
approval by manufacturers. A notified body must be qualified to perform all the functions for which it is designated, and notified body status may be withdrawn if the body fails to meet expected criteria.\textsuperscript{19}

11. In the UK, the MHRA oversees six notified bodies. These are: Amtac Certification Services Ltd, BSi Healthcare, Intertek Testing and Certification Ltd, Lloyd’s Register Quality Assurance Ltd, SGS United Kingdom Ltd and UL International (UK) Ltd, all of which are private companies.\textsuperscript{20} There are 78 notified bodies in Europe.\textsuperscript{21} Manufacturers are free to seek verification of their medical device from any notified body capable of carrying out the desired conformity assessment procedure, regardless of which Member State it is in.\textsuperscript{22} According to the MHRA, demands for manufacturers to seek verification from notified bodies overseen by their national competent authority “would not only be contrary to EC law but also against the principles of the single market”.\textsuperscript{23} The MHRA also explained why the “crucial role for assessing the safety of devices is delegated to Notified Bodies and not undertaken by publicly employed experts”:

The rationale for employing such a system is largely down to the size and breadth of the market for medical devices – a typical estimate is that there are in excess of 400,000 different medical devices on the market in the EU. The medical devices sector is constantly innovating, and new technologies appear at far greater rates than they do in pharmaceuticals. Individual Notified Bodies are able to specialise in certain areas and react to market demand, adding expertise and capacity where required in a way that would not be possible for public sector bodies. The result is a system that is efficient and able to rapidly undertake pre-market assessment; the EU is widely recognised as being an innovation-friendly environment largely due to this regulatory structure, and the Notified Body model of third-party involvement is increasingly being adopted in various forms by regulatory authorities outside Europe.\textsuperscript{24}

12. Medical devices are classified by the Directives according to the level of risk they pose to the patient. There are four classes of risk (I, IIa, IIb, and III), with the lowest risk devices, such as stethoscopes, falling into Class I. Dental fillings, for example, are a Class IIa device.\textsuperscript{25} Medical implants are always classified as Class IIb or III, because they are placed within the body, require invasive surgery, and are designed to be in continuous use. The risk category in which a device is placed determines (i) how a manufacturer would need to demonstrate conformity with the relevant Directive; and (ii) the level of assessment required.\textsuperscript{26} Class IIb and III devices must be assessed and verified by a notified body\textsuperscript{27} before they can be placed on the EU market.\textsuperscript{28}

\textsuperscript{19} “The Notified Body: Bulletin No. 6”, MHRA, January 2006
\textsuperscript{20} “UK Notified Bodies under the Medical Devices Directives”, MHRA, www.mhra.gov.uk
\textsuperscript{21} Q 56
\textsuperscript{22} “The Notified Body: Bulletin No. 6”, MHRA, January 2006
\textsuperscript{23} “The Notified Body: Bulletin No. 6”, MHRA, January 2006
\textsuperscript{24} Ev 35, para 29
\textsuperscript{25} Ev 39, para A5
\textsuperscript{26} Ev 33, para 11
13. Once compliance with the essential requirements has been established, the manufacturer places a CE mark on the device and “is free to place the device on the market in all EU countries without further controls”. The CE mark also represents a declaration from the manufacturer that appropriate post-market surveillance measures are in place to monitor the device’s performance once it is in use. The CE mark is not used solely for medical implants; other products such as toys and machinery that are subject to EU directives must also be CE-marked. The Health Select Committee noted in its report *PIP Breast implants and regulation of cosmetic interventions* that “recent concern about the safety of metal-on-metal hip implants suggest there is [...] cause for strengthening CE mark requirements”. The Committee also considered that with regards to the PIP implant, “the real issue [...] is the failure of the CE mark to provide adequate assurance that the product [...] was appropriate to use” and made recommendations to strengthen the CE mark system. Pre-market approval will be discussed in more detail in chapter 3; including whether there is enough transparency and public understanding of the approval system.

14. Once a device is on the market it is the manufacturer’s responsibility to ensure it is performing as intended by collecting data about adverse events related to the device. The manufacturer is required to report any incidents and update safety information, for example, field safety corrective actions to the competent authority in the country in which the incident occurred. Field safety corrective actions include product recalls, design changes, software upgrades, and amended instructions for use, including patient management for implants. The manufacturer must also alert:

- the competent authorities of all countries in which the device is used;
- the competent authority in their own country; and
- the notified body that undertook the conformity assessment of the product.

### The MHRA

15. The MHRA is “responsible for ensuring that medicines and medical devices work, and are acceptably safe”. Its role is to “implement the provisions of the Directives, to appoint and control Notified Bodies, to assess and authorise clinical investigations of non-CE marked devices and to monitor and investigate adverse events and field safety corrective actions”. Notified bodies are explained further in paragraph 10.

---

27 Notified bodies are explained further in paragraph 10

28 Ev 32, para 5

29 Ev 32, para 7


34 Medical devices Guidance document: Guidelines on a Medical Devices Vigilance System. Revision 7 of MEDDEV 2.12-1, March 2012

35 “About us”, MHRA, www.mhra.gov.uk
actions (including recalls) occurring in [the UK]”. The MHRA explained that “clinical investigations are generally likely to be required for medical implants” and that “the role of the MHRA is to assess the technical and clinical evidence provided by the manufacturer to ensure that there are no public health or public policy reasons whereby the proposed clinical investigation should not proceed”.

16. Once a device is on the market, the MHRA has responsibility for investigating adverse incidents reported either by manufacturers (who are responsible for post market surveillance) or by healthcare professionals and members of the public. As a result of these investigations the MHRA “will take further action as appropriate, including recalling faulty products and offering advice to the health service, primarily through Medical Device Alerts, but also through safety pamphlets, posters, and bulletins”. The MHRA considers that it “has an important role in working with professionals and the public, not only to inform but also to influence their behaviour”.

**High profile medical device recalls**

17. Subsequent chapters of this report will discuss the regulatory framework for medical implants in more detail. However it is worth briefly setting out background information on the recall of PIP breast implants in early 2012 and recall of the DePuy metal-on-metal hip implant systems in 2010 as these two cases were frequently raised.

**PIP breast implants**

18. In March 2010, the French regulator Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) found that the French company Poly Implant Prothèses (PIP) had been using non-authorised silicone in the manufacture of breast implants. The CE mark for PIP implants was consequently withdrawn and the MHRA indicated that the implants should no longer be used in the UK. In relation to the PIP implant recall, Lord Howe, Parliamentary Under-Secretary of State, Department of Health, stated “we must always remember that we are dealing there with a clear case of fraud. It was clear from my investigation that no amount of regulation could have prevented deliberate fraud of that kind”. He added “there is no criticism of the notified body in relation to the PIP manufacturer; they did their job as far as we can see perfectly adequately, but the manufacturer was out to hoodwink everybody”.

19. As stated previously, this inquiry was not intended to examine the PIP implant issue directly as there have been several investigations into the matter.

---

36 Ev 32, para 9
37 Ev 33, para 20
38 Ev 34, para 21
39 Ibid.
40 Ibid.
42 Q 148
43 Q 148
Metal-on-metal hip implants

20. The hip is one of the largest joints in the human body and is a “ball-and-socket joint”. In healthy hips the bones are covered with smooth cartilage that enables the femoral head (the ball) and the acetabulum (the socket) “to glide painlessly against each other”. The bones are connected to each other with ligaments (bands of tissue) that are lubricated with fluid to reduce friction. Hip replacement can become necessary when the joint is damaged, for example because of arthritis. Hip implants can either be total hip replacements or hip resurfacing implants and in metal-on-metal hip implants both the ball and socket are made from metal. A hip resurfacing implant is smaller and does not require as much of the femur (thighbone) to be removed as a total hip replacement. It is therefore thought to be more suitable for younger patients, who are more likely to need another replacement; because of natural wear, hip implants typically last 10-20 years. Hip implants can be made from a range of metal alloys, high-grade plastics and polymeric materials.

21. In August 2010, two metal-on-metal hip implants manufactured by DePuy were recalled worldwide because data from the National Joint Registry (NJR) of England and Wales showed that more people than anticipated had experienced problems and required a second hip replacement surgery. These implants were not the only metal-on-metal hip implants in use, but metal-on-metal hip implants with a large diameter, such as DePuy’s implants, appeared to cause more problems. Both the DePuy ASR hip resurfacing and total hip replacement implants had been certified for the EU market by the UK’s British Standards Institute (BSi) in 2003. In the next chapter we will consider pre-market approval in more detail, including differences between the EU and FDA regulatory systems.

44 “Hip resurfacing”, American Academy of Orthopaedic Surgeons, orthoinfo.aaos.org
46 “Inflammatory arthritis of the hip”, American Academy of Orthopaedic Surgeons, orthoinfo.aaos.org
47 “Metal-on-metal hip implants”, US Food and Drug Administration, www.fda.gov
48 “Hip resurfacing”, American Academy of Orthopaedic Surgeons, orthoinfo.aaos.org
49 “Hip implants”, American Academy of Orthopaedic Surgeons, orthoinfo.aaos.org
51 “Metal-on-metal hip implants”, MHRA, www.mhra.gov.uk
52 Articular surface replacement
3 Pre-market approval

Clinical data requirements

23. The regulatory framework for medical implants must strike a balance between ensuring patient safety and encouraging innovation, so as to ensure timely patient access to safe and effective technology. Although medicines and medical devices are both regulated in the UK by the Medicines and Healthcare products Regulatory Agency (MHRA), their regulation differs in several crucial ways. Medicines must receive a licence, or market authorisation, from the MHRA before they can be sold in the UK. The MHRA must also authorise clinical trials of new medicines, if the trials are to be conducted in the UK. Medicines are normally subject to three phases of trial before reaching market:

- Phase 1 trials are relatively small trials (less than 100 participants) to test for side effects at different doses. They are normally conducted on healthy individuals.
- Phase 2 trials are larger (several hundred participants) and include patients with particular conditions. They test how the medicine works in patient populations and identify common side-effects.
- Phase 3 trials are large-scale trials that can include hundreds or even thousands of participants. They test the medicine in the general population. These trials gather detailed information about side effects and efficacy, and the results inform the labelling and patient information provided when the medicine is made available on the market.

24. The clinical data requirements for medical devices to be sold on the European market are significantly less stringent. Medical devices are not automatically subject to a clinical trial, although they are always tested for mechanical and/or electrical safety before use in patients. Before a medical device can be sold on the European market, the manufacturer must verify that the device conforms to essential requirements for medical devices, which concern the “the safety and performance of the device and the amount and type of information given to the user of the device by way of the label and instructions for use”. Manufacturers of Class I devices can verify this through self-certification, but for all other devices verification by a notified body is required. Given that medical implants always fall into the highest risk categories (Class IIb or III), manufacturers must submit clinical data to a notified body for evaluation before selling their products on the EU market. Although the decision on whether to run a new clinical trial of the device is made by the manufacturer, the notified body can challenge this decision. Based on the information

54 “What we regulate”, MHRA, www.mhra.gov.uk
58 Ev 32, para 4
59 Ev 32, para 5
60 Ev 33, para 11
61 Q 44
provided by manufacturers, notified bodies then assess a device’s short-term compliance with the essential requirements based on the technical data submitted.\(^{62}\) Clinical data provided by manufacturers can come from:

- published clinical investigations or other studies of similar devices in the scientific literature (this is referred to as equivalence data\(^ {63}\));
- clinical experience of the medical device or a similar device; or
- the results of a specifically designed clinical investigation of the device: these would typically be required where a medical implant has new design features or uses new materials.\(^ {64}\)

25. As part of the pre-market approval process, notified bodies also audit manufacturers to ensure their facilities comply with the essential requirements of the Directives. The MHRA explained that:

> When undertaking conformity assessment for class IIb implants a Notified Body typically carries out a detailed assessment of the manufacturing facility to look into design, manufacturing and inspection of the devices concerned. They also cover other general requirements such as staff training and the handling of complaints. They will also sample technical documentation for compliance from the range of products being manufactured. These assessments normally take place annually to ensure ongoing compliance with the requirements of the legislation.

For class III implants, as well as the assessments at the facilities as outlined for the class IIb products, there is also a requirement for the Notified Body to review the technical documentation of each product to ensure that it is in compliance with the essential requirements. Dependent upon the product this will cover such areas as safety, performance, biological properties, sterilisation, software and labelling.\(^ {65}\)

26. We heard concerns about relying on equivalence data for pre-market approval of medical implants. The Centre for Evidence-Based Medicine and the British Medical Journal (BMJ) considered that “the normal level of evidence required to demonstrate the effectiveness or safety” of new medicines is “not required for medical devices under the current legislation”.\(^ {66}\) They stated that “the level of clinical data required for a new device can be minimal [...] and could be obtained in a few days, contrasting markedly with the type and extent of clinical trial data required for new drugs”.\(^ {67}\) Furthermore, they considered that “regulators find it incredibly difficult to judge if a device is ‘equivalent’ to another on the market” and that as a result, “the current system of ‘equivalence’ and the acceptance of studies of other devices reported in the scientific literature are one of the

\(^ {62}\) Q 49 
\(^ {63}\) Q 43 
\(^ {64}\) Ev 33, para 15 
\(^ {65}\) Ev 33, paras 13–14 
\(^ {66}\) Ev w4 
\(^ {67}\) Ibid.
main drivers of poor quality under-researched devices on the market today”. The Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians stated that use of equivalence data was flawed because “there may be unpublished safety issues” with the already certified device and that “subtle differences” between the two devices may “result in safety and effectiveness differences that are not explored clinically prior to marketing the [new] device”. Additionally, “as time goes on, each iteration of a device rests its case on a previous iteration, each a little different to the next one: after several years, devices may be approved that are very different to the original marketed device”. Professor Stephen Westaby, cardiac surgeon at the John Radcliffe Hospital, Oxford, also emphasised the importance of gathering evidence from human clinical trials, noting that devices tested in animal studies would not necessarily work in a human in the same way. The perception that manufacturers of medical devices do not need to provide “proof that they work” has also been reported in mainstream media.

27. Conversely, there was opposition to adopting the pharmaceutical approach of gathering data from clinical trials. Professor Alan Murray, Professor of Cardiovascular Physics, Newcastle University, stated that conducting the “same style of clinical trial as for drugs [...] is often not possible, because with drugs small doses can be given initially to assess tolerance and side effects, and the drug can be stopped at any time. Once a medical device has been implanted it is very difficult [to] remove”. Another problem is the time needed to run a clinical trial: John Howlett, Head of BSi, explained that as medical implants are designed to last for several years, a clinical trial assessing the wear of such an implant would similarly have to last for several years. He stated that “short-term compliance on wear and fatigue is all carried out in the design phase” and that data on long-term performance must be collected once the implant is in use (post-market surveillance; see chapter 4 for further discussion). Dr Thomas Joyce, Reader in Biotribology, Newcastle University, agreed but argued that the wear of implants such as artificial joints should be more routinely tested, and that data generated from these tests should be publicly available. Professor Westaby added:

With long-term medical implants such as hips and blood pumps—artificial lungs are on the way—and all sorts of exciting technology, you would have to embargo widespread use for something like 10 to 15 years before you got your outcome data [...] you simply cannot say [to patients], ‘We have to wait 10 years for long-term trial data’.

28. The MHRA stated “medical devices are unlike pharmaceuticals, in that their development is generally based on principles of engineering, rather than of chemistry and

---

68 Ibid.
69 Ev w14
70 Ibid.
71 Q 6
72 For example, “Are diet pills too good to be true?”, Glamour, July 2012, p270
73 Ev w10, para 1
74 Q 49
75 Ev 44
76 Q 7
pharmacology” and, “as such, greater reliance can be placed on laboratory tests rather than clinical studies in patients”. Sir Kent Woods, Chief Executive of the MHRA, gave three reasons for the differences in regulation of medical devices and medicines:

First, the way they are innovated. They are innovated in a rather iterative way with progressive, relatively small changes in technology and refinement, perhaps as frequently as every year or two, which is quite unlike the situation with pharmaceuticals.

The second point is about their sheer multiplicity. When we look at pharmaceuticals we are talking about the low thousands; when we look at medical devices we are looking at hundreds of thousands in the EU. Therefore, the regulatory system has to be able to cope with that.

The third and perhaps most important difference is the way in which they fail when they give rise to problems. In contrast to pharmaceuticals, the areas where medical devices give us problems are, first, in relation to sporadic manufacturing problems, which are not easily picked up at the market authorisation step; and, secondly, particularly in terms of implantable devices, the way they wear over time, and all of them will over time. Again, that is on a time scale that is not easy to pick up in pre-clinical studies.

The long-term success of a medical implant also depends on idiosyncratic factors such as “the way they are used and the way patients are selected for particular devices”, as well as the skill of the surgeon implanting the device, and patient compliance with caring for the medical implant following the operation (such as taking medication to prevent blood clotting following the insertion of a heart valve).

29. Sir Kent added that the MHRA’s view has been that, “in principle, the Medical Devices Directives under the new approach are appropriate”, but that there are areas where it would like to see a “greater degree of consistency of application and rigour across the piece in certain areas”. For example, the MHRA considered that “reducing the extent to which manufacturers are able to rely on equivalence” was “critical”. The Commission’s 2012 Proposal for a Regulation on medical devices introduced the regulatory instrument of “common technical specification” (CTS), to allow the Commission to “further specify the general safety and performance requirements […] and the requirements on clinical evaluation and post-market clinical follow-up”. However equivalence remains an option as the requirements still “leave manufacturers the possibility of adopting other solutions

---

77 Ev 34, para 26  
78 Q 123  
79 Q 123  
80 Ev 51  
81 Q 20  
82 Q 123  
83 Ev 36, para 38  
that ensure at least an equivalent level of safety and performance”. The proposal stated that:

Equivalence can only be demonstrated when the device that is subject to clinical evaluation and the device to which the existing clinical data relates have the same intended purpose and when the technical and biological characteristics of the devices and the medical procedures applied are similar to such an extent that there would be not a clinically significant difference in the safety and performance of the devices.

In the case of implantable devices and devices falling within class III, clinical investigations shall be performed unless it is duly justified to rely on existing clinical data alone. Demonstration of equivalence [...] shall generally not be considered as sufficient justification within the meaning of the [previous sentence].

**Cost and timescale of clinical trials**

30. Clinical trials take a significant amount of time to set up. For studies taking place in NHS settings, approval is needed both from the National Research Ethics Service, and for each local NHS site taking part in the study. The MHRA must also approve clinical protocols for studies of non-CE marked products. Professor Westaby suggested that gaining ethical approval for clinical trials in the UK was difficult, and that “there are very definitely tendencies to direct your research to areas where you are likely to get ethics permission early for certain things”. He stated: “I can do far more in Greece that is wholly ethical much faster than I can in the UK [...] I can get ethics approval for [clinical research] in Greece, where it would take me two years in Oxford”. He also lamented the cost of conducting trials:

[An] artificial heart is an example of the epitome of implantable devices [...] to test one of these miniature artificial hearts costs a company $1 million per week [...] I have a device, and I want it to go into humans soon, but my little company cannot afford $1 million, full stop [...] the clinical trials have got to be made accessible and far cheaper than they are now, because right now it just does not work [...] In my view, the NHS has got to support it far better than it does.

31. The decision on whether to run a new clinical trial of a device is, in the first instance, made by the manufacturer. Dr Carl Heneghan, Centre of Evidence-Based Medicine, University of Oxford, pointed out that such high costs do not incentivise manufacturers to

---

88 Ev 32, para 9
89 Q 16
90 Q 16
91 Q 9
92 Q 44
run trials, when equivalence data is often acceptable.\textsuperscript{93} Mr Howlett, BSi, agreed that manufacturers could be disincentivised from running new trials because clinical trials are expensive to run and could delay patient access to life-saving technology.\textsuperscript{94} However he added that although “trials are by nature costly for the manufacturer to set up” the BSi as a notified body would “challenge the manufacturer on the availability of the data”.\textsuperscript{95} The Association of British Healthcare Industries (ABHI), representing medical devices manufacturers, stated that:

Clinical evaluation of a device is required when demonstrating conformity with relevant essential requirements. For medical implants, this process is particularly important, as the characteristics of a device when implanted in the body need to be understood and documented. ABHI believes the revision of the MDDs should see the system become more prescriptive in setting out when manufacturers need to undertake clinical investigations, or to what extent they are able to rely on existing scientific literature claiming equivalence with an existing device.\textsuperscript{96}

The ABHI added that since “notified bodies are responsible for assessing clinical evaluation by manufacturers as part of conformity assessment, ensuring that appropriate clinical investigations have taken place” it believed that “by improving the coordination of Notified Bodies, the scrutiny of clinical evaluation will be greatly improved”.\textsuperscript{97}

32. Jacqueline Minor, Director of Consumer Affairs, Directorate-General for Health & Consumers, European Commission, stated that the Commission was considering how to make early scientific advice available to “producers” and to notified bodies and stated “we will have a scientific panel, and anyone developing a novel technology will be able to go to that scientific panel to ask about the kinds of evidence they will need to bring forward to support its safety when the time comes for conformity assessment and placing it on the market”.\textsuperscript{98}

33. The difficulty of conducting clinical trials in the UK is not a newly identified problem and our predecessor Committee regularly encountered criticisms of the system.\textsuperscript{99} In January 2011 the Academy of Medical Sciences published \textit{A new pathway for the regulation and governance of health research}.\textsuperscript{100} A key recommendation was to create a Health Research Agency (HRA) to improve the UK environment for clinical trials, including working with the MHRA and the National Institute for Health Research (NIHR) to unify the process by which ethical approval is given to studies.\textsuperscript{101} Other recommendations included improving “access to patient data that protects individual interests and allows

\textsuperscript{93} Q 6
\textsuperscript{94} Q 44 and 49
\textsuperscript{95} Q 44
\textsuperscript{96} Ev 43, para 19
\textsuperscript{97} Ev 43, para 20
\textsuperscript{98} Q 107
\textsuperscript{99} For example, Science and Technology Committee, Seventh Report of Session 2009–10, \textit{Bioengineering}, HC 220
\textsuperscript{100} “A new pathway for the regulation and governance of health research”, \textit{The Academy of Medical Sciences, January 2011}
\textsuperscript{101} “Health Research Authority”, \textit{Health Research Authority, www.hra.nhs.uk}
approved research to proceed effectively”, and embedding “a culture that values research within the NHS”.\textsuperscript{102} The HRA was established in December 2011 as a Special Health Authority, and acquired the existing National Research Ethics Service (NRES).\textsuperscript{103} The Queen’s Speech in May this year included a draft bill to modernise adult care and support in England: as part of this draft bill the HRA would be established as a non-departmental public body (NDPB).\textsuperscript{104} The Clinical Trials Directive is also being revised by the European Commission, which, in July 2012, proposed a Regulation to boost the EU’s attractiveness as a place to do clinical research.\textsuperscript{105} The legislative proposal will be discussed in the European Parliament and in the Council and is expected to come into effect in 2016.\textsuperscript{106}

34. Ideally, all medical implants approved for use on the EU market would be subject to rigorous clinical investigations prior to introduction but it is not practical to do this for every implant and there are circumstances where reliance on equivalence data may be acceptable. Nonetheless, it appears that the existing regulatory framework may have the effect of encouraging manufacturers to rely on equivalence data rather than evidence from clinical trials. This is compounded by the difficulties of conducting clinical trials in the UK. We do not advocate a pharmaceutical style approach to regulation. We endorse the approaches already being taken: (i) the proposed revisions to the Medical Devices Directive make clearer when equivalence data is or isn’t acceptable and strengthen scrutiny and challenge of manufacturers’ decisions; and (ii) the environment for clinical trials should be improved, not just in the UK but across Europe.

35. We welcome the European Commission’s proposal to make scientific advice available to manufacturers and notified bodies when placing new implants on the market.

36. The establishment of the Health Research Authority (HRA) is a welcome step towards improving the regulation and governance of health research. We expect the HRA to tackle the difficulties of setting up clinical trials in the UK. We intend to scrutinise the HRA and its work and we recommend that the Government publishes an update on the progress of the HRA in improving the environment for clinical trials in December 2012, a year after its establishment.

\textbf{Transparency of evidence}

37. According to the MHRA, “very little information is available about a medical device throughout its lifetime – clinical evaluations, conformity assessment, adverse incidents and post-market surveillance plans, for example, are generally not published”.\textsuperscript{107} This

\begin{itemize}
\item \textsuperscript{102} “A new pathway for the regulation and governance of health research”, \textit{The Academy of Medical Sciences, January 2011}
\item \textsuperscript{103} “Health Research Authority”, \textit{Health Research Authority, www.hra.nhs.uk}
\item \textsuperscript{104} “Draft Bill to modernise adult care and support in England included in Queen’s Speech”, \textit{Department of Health, 9 May 2012, www.dh.gov.uk}
\item \textsuperscript{105} “Fostering EU’s attractiveness in clinical research: Commission proposes to revamp rules on trials with medicines”, \textit{European Commission press release, 17 July 2012}
\item \textsuperscript{106} “Clinical trials”, \textit{European Commission, ec.europa.eu}
\item \textsuperscript{107} Ev 37, para 52
\end{itemize}
“opaqueness” was considered to “contribute […] to a degree of unease about the regulatory system”. Dr Heneghan Centre for Evidence-Based Medicine, expressed frustration that the transparency of pre-market clinical data is much greater in the US than in Europe. The joint submission from the Centre for Evidence-Based Medicine and the British Medical Journal (BMJ) stated:

In the absence of publicly available regulatory data, it is left to the device manufacturers to decide what enters the public domain on their website or as a scientific publication. This means that clinicians are dependent on the manufacturers to provide them with data about their implant and what they decide to publish […] The lack of data does not help clinical decision making. Indeed, the lack of clinical studies or trials makes it an almost impossible task for health technology appraisal […] In the worst case scenarios, patients may be subject to an intervention that is not appropriate for them. In addition the lack of clinical data means it is difficult if not impossible for commissioners of health care to understand the true cost of interventions beyond the initial cost impact analysis.

Professor Westaby explained that clinicians like him did not have access to the clinical data used in approving a medical device for the European market. When we asked Professor Westaby about how increased transparency might assist clinicians choosing an implant for their patients, he explained that published data from medical implants was available in journals, but that "a lot of what is published in terms of clinical trial is done by enthusiasts in the best units under ideal conditions". This refers to the practice of "cherry picking", or selective publishing, of clinical data whereby positive results are reported and negative results are not. This problem goes beyond medical implants to many areas of medicine and has led to calls for clinical trial registers. Professor Westaby considered that the data collected after a medical implant has been placed on the market—post-market surveillance—was "more instructive" than clinical trials and that the use of registries to track patients and implants in post-market surveillance was "very important". Post-market surveillance and registries are discussed in chapter 4.

38. Mr Howlett, BSi, stated that “the notified bodies cannot make [clinical] information public, but, in the interests of transparency, I would support that”. He considered that the way an implant was approved for sale should be made clearer, so that “the public, in the interests of patient safety, can visibly see the route and compliance either through clinical literature or trials”. Dr Suzette Woodward, Director of Patient Safety, National Patient Safety Agency, did not consider that increased transparency would pose a problem for patient confidentiality, provided the data were passed through “certain level of filter so that

---

108 Ibid.
109 Q 5
110 Ev w3
111 Q 13
112 Q 13
113 Q 13
114 Q 45
115 Q 45
individual patients would not recognise themselves in something that was made public”. Sir Kent Woods acknowledged that greater transparency “will influence the way clinicians do their jobs; it will influence the way patients make decisions about healthcare”. He explained that the Directives require “that information obtained by regulators is confidential”, but that he would support a change to this in the revision of the Directives. The MHRA was clear that “the revision of the Medical Devices Directives provides an opportunity for a substantial change in the availability of information about medical devices and the regulatory system” and that “a key aim for the UK in the revision is therefore to drive far greater publication of information in a format that is useful for the public, as well as regulators and manufacturers”. This was generally prohibited by explicit confidentiality requirements currently within the Directives that the MHRA wished to see removed (this is further explored in paragraph 93).

39. The importance of transparency has been recognised by the European Commission. Ms Minor stated:

> It is very difficult [...] for anyone to know what devices are on the market; what evidence was used to support their safety; and what information is available about the associated risks and the incidents they might have provoked. We are planning to have a central registry in which all manufacturers and all devices will have to be listed. For each device, there will be some standard information, such as the name of the notified bodies, the class of risk, and the unique device identifier, when we have that. There will also be a summary of performance and clinical data. For the first time, for example, clinicians will be able to have access to the clinical data which supported the certificate granted to the device.

The Commission’s published proposal stated that a lack of transparency is “one of the main shortcomings of the current system” and proposes “an obligation for manufacturers of high-risk devices to make publicly available a summary of safety and performance with key elements of the supporting clinical data.”

40. Transparency should be the default position in the approval of medical implants: it is particularly important where some of the key players influencing public health—manufacturers and notified bodies—are private organisations not accountable to Parliament or subject to Freedom of Information requests. Greater transparency would improve public confidence in the system and support decision-making by patients and healthcare professionals. We are disappointed that there is a lack of transparency in the current regulatory system and we urge the UK Government to take a lead in increasing transparency.

---

116 Q 15
117 Q 137
118 Q 133
119 Ev 37, para 52
120 Ibid.
121 Q 109
41. The Commission’s proposals are a step in the right direction, but do not go far enough. All clinical data used in the approval of a medical implant should be made publicly available without identifying patients or clinical trial participants. For products currently on the market, data should be published immediately. It should be clear when medical implants have been approved using equivalence data and when clinical investigations have been conducted on that implant prior to market approval.

42. In addition, regardless of whether an implant is approved for use or not, any new clinical data generated about that implant should be published. It is as scientifically useful to know what doesn’t work as it is to know what does work.

**Comparisons with the FDA**

43. Comparisons were made with the Food and Drugs Administration (FDA), the public body that conducts pre-market approval for medical devices in the USA. Dr Heneghan, Centre for Evidence-Based Medicine, University of Oxford, provided examples of several medical implants that were rejected by the Food and Drugs Administration (FDA) but were approved for the European market. As stated in chapter 2, one of the implants rejected by the FDA but approved in the EU was the DePuy metal-on-metal ASR hip resurfacing implant. The US Food and Drugs Administration (FDA) also approved the total hip replacement, although it rejected the resurfacing implant. The New York Times reported that the FDA had told Johnson & Johnson (DePuy’s parent company) in August 2009 “that company studies and clinical data submitted to gain approval in the United States to sell the model available overseas were inadequate to determine the [resurfacing] implant’s safety and effectiveness”. Another DePuy metal-on-metal hip implant, the ASR total hip replacement system, was approved in both the US and EU. Both of these implants were recalled worldwide in 2010 due to higher than expected revision rates. The MHRA pointed out that “the DePuy ASR hip was placed on the market in both the US and the EU, having satisfied the pre-market requirements of both regulatory frameworks and yet [...] problems with the implant were first identified in the UK”.

44. Further to this, Professor Westaby explained that because of the differing evidence requirements, some US companies used the European market to run clinical trials of their medical implants. Data from these trials are then presented to the FDA for approval in the US. Professor Westaby considered this to be of benefit to patients, and stated “I can use sophisticated devices many years before my colleagues in the States and Japan”, in other words, current regulations allow EU patients access to new medical devices several years before other countries. He cautioned against increasing the requirements for approving

---

123  Ev 38, para 54
124  Q 4
127  “ASR hip replacement recall guide”, DePuy, www.depuy.com; Revision rates refer to the additional surgery required when an implant needs to be repaired or replaced.
128  Ev 38, para 54
129  Q 5
130  Q 2
Regulation of medical implants in the EU and UK

devices, stating “the NHS is becoming so stiff in bureaucracy that it can hardly move. If we are not very careful, it will just grind to a halt.”\textsuperscript{131} The Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians explained that “on average, the [FDA] process delays approval of medical implants [...] by two years compared to the EU, and that there have been no safety issues identified post-approval in the EU that were “caught” by the longer and more rigorous approval process in the US”.\textsuperscript{132} Sir Kent Woods, MHRA, considered that “currently that balance is about right”.\textsuperscript{133}

45. There is insufficient evidence that the Food and Drugs Administration’s (FDA) more onerous procedures for granting market approval to medical implants have resulted in greater patient safety. The FDA system also operates more slowly and thus delays patient access to medical implants, which is, in itself, a threat to patient safety.

Notified bodies across Europe

46. Notified bodies play a key role in the regulation of medical implants, having responsibility for approving implants for use on the EU market. UK notified bodies are private companies, and the competence and transparency of notified bodies was questioned. For example, Dr Heneghan stated that “nobody knows the make-up of notified bodies or their skill base, and nobody knows their [...] process of approving”.\textsuperscript{134} Mr Howlett, BSi, explained that the BSi had:

> in excess of 200 assessors around the world doing medical and conformity assessments. [...] As to our expertise, we have highly qualified reviewers from industry and the universities where they have been involved in the design and development of those particular products.\textsuperscript{135}

Concerns appeared to focus not on the UK’s notified bodies but those in other European countries that might not perform to the same standards, thus posing a threat to patient safety (including in the UK). The ABHI stated that currently “the control and oversight by National Competent Authorities of their Notified Bodies depends largely on voluntary and national approaches rather than on consistent, mandatory EU level rules and standards”.\textsuperscript{136} The Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians stated that “some notified bodies are not expert enough in the assessment of clinical data, of likely safety risks in clinical use [...] to make an effective critical assessment of whether a [new] clinical trial is needed and whether long-term safety data should be gathered in a formal way”.\textsuperscript{137} A consequence of the differences between notified bodies is that less scrupulous manufacturers may use this to their advantage. The Royal College of Surgeons (RCS) outlined its concerns over “the current potential for variability in the standards and

\textsuperscript{131} Q 33
\textsuperscript{132} Ev w13
\textsuperscript{133} Qq 126–127
\textsuperscript{134} Q 5
\textsuperscript{135} Q 48
\textsuperscript{136} Ev 42, para 15
\textsuperscript{137} Ev w13
expertise of national Competent Authorities and the Notified Bodies to which they delegate responsibility for approving medical devices”. The RCS added:

This scope for variation presents the possibility that a device failing to meet the approval criteria of one Notified Body may gain approval from another less stringent Notified Body elsewhere. We see this as not only a public protection risk, but also a major barrier to increasing public confidence in the system.

The practice of getting products assessed by a notified body thought more likely to provide a favourable opinion was referred to as “forum shopping”. The BSi wrote to the European Commission stating that “if forum shopping exists it is direct consequence of inconsistency between Member States and Competent Authorities that leads to an environment where Notified Bodies are not consistent”. Mr Howlett, BSi, explained that

There is the potential for a manufacturer, faced with demands from the Notified Body to submit more comprehensive information, particularly clinical data to support device safety, to withdraw an application and seek another [notified body]. BSI has been aware of situations where a manufacturer had withdrawn an application and had “been successful just a few months later, clearly without any further clinical data, to gain certification through another [notified body]”.

47. He clarified that the BSi had experienced this seven times over the past five years, and further emphasised that “the instances of this nature are relatively rare but the consequences of each individual case could be very significant in respect of patient safety”. Due to the lack of transparency, it was difficult for us to evaluate how common forum shopping was beyond this anecdotal information.

48. Differences between notified bodies across Europe are a key weakness in the current regulatory system and can result in “forum shopping”, whereby manufacturers choose notified bodies more likely to provide approval for a device. Forum shopping is facilitated by a lack of transparency and therefore accountability. Notified bodies should consider publishing records of all approaches by manufacturers, regardless of whether applications were completed or not.

49. The European Commission plans to address regulatory inconsistencies by moving from Directives to Regulations. Ms Minor claimed that this would have “the effect of meaning that no national legislation is required to translate the rules into the legal systems of the member states, which will eliminate to some degree differences of interpretation or of application”. Ms Minor explained that the revision to the Directives will include “a system where responsibility for designating a notified body remains with the competent

138 Ev w25
139 Ibid.
140 For example, Q 141 [Sir Kent Woods]
141 “Recast of the Medical Devices Directive consultation, Comments from BSI – UK Notified Body”, BSI, ec.europa.eu
142 Ev 51
143 Ibid.
144 Q 88
145 Q 88
member state, but prior to that designation there would be a joint inspection” by several Member States, which would serve to reduce the discrepancies between different notified bodies across Europe.\footnote{146} This process would be overseen by a central European Medical Devices Expert Group.\footnote{147} The Commission’s proposal considers that such “joint assessments” would “ensure effective control at Union level”.\footnote{148} In its written evidence the MHRA stated that involving experts from more than one Member States in designating notified bodies would “drive a consistently high level of oversight of Notified Bodies, ensuring that they are designated on the basis of proven competence for the devices that they will be assessing”.\footnote{149} A likely consequence of this new designation process was thought to be a reduction in the number of notified bodies in Europe.\footnote{150} However, the costs of pre-market approval would increase as fees charged by notified bodies for approving medical implants are likely to increase.\footnote{151} Ms Minor stated that the industry had been consulted regarding this proposal and that “they feel this is a cost which the industry must bear […] in order to improve confidence in the system and restore trust”.\footnote{152} We asked whether the additional cost might prohibit small companies bringing a product to market in Europe and Ms Minor responded:

I honestly do not think so, because we are talking about a notified body, as you have heard, which is designated for a number of years. A number of manufacturers go to them for certificates, so when it is spread across all the certificates and all the manufacturers, I do not think it would amount to a substantive increase.\footnote{153}

Sir Kent, MHRA, stated that while “there will be an increased cost of doing more clinical studies pre-market authorisation […] we should not allow that to become so burdensome that it shuts off the innovation process”.\footnote{154}

50. In the proposed revision to the Directive, manufacturers of Class III devices (the highest risk category) wishing to bring this device to the EU market will have to “notify their intention centrally”.\footnote{155} Ms Minor explained that:

At that point, competent authorities in all the member states would learn of something that is approaching the point at which it will be placed on the market […] When that notification is made, it will be examined by our scientific experts. The scientific opinion would go to the central committee, the medical device expert

\footnotesize{\begin{itemize}
\item \footnote{146}  Q 91
\item \footnote{147}  Q 92
\item \footnote{149}  Ev 35, para 33
\item \footnote{150}  Q 93
\item \footnote{151}  Q 95
\item \footnote{152}  Q 96
\item \footnote{153}  Q 97
\item \footnote{154}  Q 143
\item \footnote{155}  Q 107
\end{itemize}}
group, and they would offer an opinion as to the [clinical] evidence [for the device] presented, which would then go back to the notified body.156

The Commission’s proposal, published in September 2012:

introduces the obligation for notified bodies to notify an expert committee [...] of new applications for conformity assessment of high-risk devices. On scientifically valid health grounds, the expert committee will have the power to request the notified body to submit a preliminary assessment on which the committee can issue comments within a deadline of 60 days, before the notified body can issue a certificate. This scrutiny mechanism empowers the authorities to have a ‘second look’ at individual assessments and make their views heard before a device is placed on the market. A similar procedure is currently already applied for medical devices manufactured utilising animal tissues (Commission Directive 2003/32/EC19). Its use should be the exception rather than the rule and should follow clear and transparent criteria.157

51. While the notion of greater coordination at European level was broadly welcomed, there were mixed views on whether pre-market approval of medical devices should be conducted by a centralised EU body. The Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians considered that:

A central body approving and overseeing notified bodies may be not be readily accepted by industry, although it would reduce inconsistency and increase fairness. It would likely increase the demand for clinical trial data for some Class IIb and Class III devices, which industry may see as overly onerous. However, if a new system of approving higher risk devices increases patient safety and public confidence, this would have long-term societal and industrial benefits.158

The ABHI, representing the industry, was in favour of the current decentralised approach and stated:

Today the EU oversight of medical devices is decentralised and this European approach makes it possible to manage what is a highly innovative and diverse industrial sector in terms of products, technologies and services. The decentralised approach is best placed to provide the capacity to efficiently deal with the many applications related to over 400,000 products on the market from over 22,000 medical technology businesses, 80% of which are SMEs.

The decentralised approach, which is the essence of the current system, should remain a basic principle of the future legislative framework for medical devices in order to preserve safety, flexibility and pace. However, the current system does suffer from disparate national approaches. It needs improved coordination at EU level to

156 Q 107
158 Ev w13
ensure uniform application by Member States, especially in the areas of Notified Bodies and vigilance.  

52. Lord Howe, Departmental Under Secretary of State, Department of Health, also considered that medical device manufacturers would prefer coordination between EU Member States rather than a centralised body because “they fear that a centralised European mechanism could act as a brake on innovation and add to costs unnecessarily.” The Minister added “we would prefer to see a model involving much more efficient co-operation between member states”. The MHRA explained that “whilst the idea for using the [European Medicines Agency] has since been disregarded, it seems likely that the Commission will include a proposal for some sort of central EU scrutiny of new class III devices in addition to assessment by a Notified Body before they are placed on the market”. The MHRA’s principal concerns were that this would result in duplication of the work of notified bodies and that “it is unclear to what extent a central EU resource will be able to scrutinise this in any meaningful way, without requiring a substantial investment in staff”. In addition, “introducing this additional step could serve to muddy the water in relation to where responsibility lies for pre-market scrutiny, and risks reducing the onus on a Notified Body to undertake their activities properly.”

53. We support the proposal to use teams of experts drawn from Member States to oversee the designation of notified bodies in order to minimise differences and raise and harmonise standards across Europe.

54. Beyond this, we do not support further centralisation of medical device regulation in the EU, as increased bureaucracy could slow device approvals unnecessarily. The speed of device approval is a strength of the current system. The emphasis should be on raising the standards and accountability of notified bodies and we are opposed to pre-market approval processes being transferred to or being duplicated at European level. Therefore we do not support the European Commission’s proposal to require a central notification of intent from manufacturers seeking approval for new devices. We urge the Government to oppose this proposal during Council negotiations.

55. Manufacturers may be charged increased fees by notified bodies if more coordinated oversight leads to a reduction in the number of notified bodies. We are not fully convinced by reassurances provided by the Government or Commission that this would not hinder small companies bringing products to market. The Commission and Government should explain how they intend to support small, innovative companies in the medical devices sector if pre-market approval becomes prohibitively costly.

---

159 Ev 43-44, paras 26-27
160 Q 130
161 Qs 126 and 128
162 Ev 36, para 39
163 Ev 36, para 40
164 Ibid.
4 Post-market surveillance

56. The process of gathering data to monitor an implant in use is called post-market surveillance. As indicated in the previous chapter, post-market surveillance is a crucial element of the current regulatory system that adds to the evidence base about how well implants work in real world conditions. The MHRA considered that improvements to post-market surveillance were a “key area that needs to be addressed in the revision of the Directives”.

Reporting of adverse incidents

Manufacturers

57. Once an implant has been approved for the European market, the Directives require manufacturers to undertake post-market surveillance. The MHRA explained that because “it is not feasible to run pre-market clinical investigations for the expected lifetime of an implant, nor is it usually possible or appropriate to carry out randomised clinical trials such as is done with pharmaceuticals”, a “critical aspect of ensuring the safety of implants is therefore a manufacturer’s responsibility to ensure that adequate post-market surveillance is in place once an implant has met the relevant requirements for CE marking.” John Howlett, Head of the British Standards Institute (BSi) explained that:

The medium and long-term effects [of medical implants] have to be coming from post-market. It is unreasonable to think that we can predict 10-year performance if we are looking at hip joints and, say, 90% success after 10 years. It is not reasonable to think that you can do that through a clinical trial. It is a combination of test data and doing all you can to demonstrate patient safety in the short term, and then monitoring for any further medium to long-term effects through the post-marketing phase.

He stated that the essential elements of post-market surveillance are “early warning systems, gathering of data and registries”. Mr Howlett also explained that when seeking pre-market approval for a medical implant, manufacturers must present a “robust plan” of how they will gather post-market data. Post-market data largely come from reports of adverse incidents but notified bodies also actively take part in post-market vigilance through auditing manufacturers and periodically reviewing product certificates. In the UK, the MHRA investigates both the “mandatory serious adverse event reports from

165 Ev 36, para 42
166 Ibid.
167 Ev 33, para 16
168 Q 49
169 Q 49
170 Q 71
171 Q 19
172 Q 71
manufacturers” as well as “adverse events reported voluntarily by healthcare professionals and members of the public”; thereby actively monitoring implants once they are on the market.173

58. The MHRA considered that while “the Medical Devices Directives require manufacturers to undertake post-market surveillance” this is in “rather general and imprecise terms and, as such, it is undertaken with variable rigour”. 174 The Centre for Evidence-Based Medicine and the British Medical Journal (BMJ) considered that there were:

many vested interests that disincentivise manufacturers and clinicians from highlighting problems as they arise [...] The extent to which manufacturers undertake post-marketing surveillance is currently unknown. Rather than have large post-marketing studies, manufacturers may rely simply on feedback from users.175

59. Manufacturers should publish the results of post-market surveillance studies.

60. Echoing some of the concerns set out in the previous chapter, the ABHI considered that the key problem lay with notified bodies, that had “not been designated or controlled with sufficient rigour” and that therefore “this aspect of the device regulatory system must be improved”.176 Medtronic Ltd, a devices manufacturer, also considered that “the oversight of these notified bodies by Member States differs enormously again causing consistency problems for industry”.177

Clinicians and patients

61. Effective post-market surveillance requires that patients and clinicians—the users—report problems as they arise; although this is not mandatory. Dr Suzette Woodward, Director of Patient Safety, National Patient Safety Agency (NPSA), outlined a number of barriers limiting effective reporting by clinicians:

There is the lack of feedback. If you report something and you hear nothing back, you say, ‘What was the point in me doing that?’

There is the issue of immediacy. If something is going wrong, you deal with what is going wrong. You deal with the patient, the family and the issues. By the time you have done all that and ended your shift, you will want to go off and do not necessarily come back and fill out an incident report. Incident reporting systems are seen as highly bureaucratic.

Performance management systems make you end up feeling that you as a person or your colleague are being blamed, rather than the organisation, the group or team that

172  Ev 34, para 21
173  Ev 33, para 16 and Ev 36, para 42
174  Ev w3
175  Ev w17, para 11
you are in saying, ‘This has obviously gone wrong. Let’s see if we can learn from it.’ We need a culture of learning rather than punishment.\textsuperscript{178}

She stated that to encourage clinicians and healthcare professionals to report faults more often, we need to “make it feel worthwhile, give them lots of feedback, make it a learning system and make them feel supported when things have gone wrong”.\textsuperscript{179} Carol Holland, Altogether Hip Support, stated that:

Surgeons should have a legal obligation to notify the Joint Registry of exactly what joints are being fitted and of any problems reported. Then those joints with more problems would be flagged earlier. It seems, at present, surgeons are loathe to admit problems in case it appears to make them look incompetent.\textsuperscript{180}

62. The Royal College of Surgeons also considered that “there is great potential for surgeons to fulfil a mandatory implant monitoring duty through audit and procedure registries”, adding “there is evidence to suggest that where audits and registries are well established, it is possible to identify problems with specific implants and devices as well as assess clinical outcomes and surgical performance more broadly”.\textsuperscript{181} The British Standards Institute (BSi) agreed that reporting by healthcare professionals should be mandatory to “ensure that all reports are made available to the appropriate medical device manufacturers so that manufacturers can fulfil their vigilance reporting and incident investigation obligations”.\textsuperscript{182} Registries are further explored from paragraph 68.

63. The MHRA has an online reporting system for reporting adverse incidents with medical devices.\textsuperscript{183} Dr Thomas Joyce and Dr Pauline McCormack from Newcastle University stated that “we have repeated reports from patients that their concerns over symptoms from their hip implants were dismissed and/or ignored by medical professionals”.\textsuperscript{184} They considered that the Yellow Card System should include users of medical devices.\textsuperscript{185} The Yellow Card Scheme is the main adverse drug reaction reporting scheme in the UK. It is intended to help the MHRA monitor the safety of the medicines and vaccines that are on the market and provides a way for patients and healthcare providers to report side effects of medicines to the MHRA.\textsuperscript{186} Sir Kent stated that the MHRA had taken action to “make it easier to report adverse incidents related to medical devices”; it had “created an IT system that makes it easier for manufacturers to deliver [...] reports” to the MHRA, and in the middle of the MHRA website “there is a button about medical device adverse incident reports” which can be used by clinicians and patients alike:

\textsuperscript{178} Q 19
\textsuperscript{179} Q 19
\textsuperscript{180} Ev w9, para 3
\textsuperscript{181} Ev w25
\textsuperscript{182} Ev 50
\textsuperscript{183} “Reporting adverse incidents involving medical devices”, MHRA, www.mhra.gov.uk
\textsuperscript{184} Ev 46
\textsuperscript{185} Ibid.
\textsuperscript{186} “Yellow Card”, MHRA, yellowcard.mhra.gov.uk
the incident report is sent directly to the MHRA database for analysis.\textsuperscript{187} He also stated that the MHRA has “electronic yellow card reporting now, too” for devices.\textsuperscript{188}

64. The MHRA uses a Black Triangle Scheme to monitor newly licensed medicines that have been approved for use on limited clinical data.\textsuperscript{189} Such medicines are marked with a black triangle symbol to indicate to healthcare professionals that their side-effects and associated adverse incidents should be closely monitored and reported to the MHRA.\textsuperscript{190} Nuffield Health, a UK health charity, considered that “fundamental lessons learnt from medicine regulation” had not been “transferred to implantable medical device regulation” and that the Black Triangle status sends a clear signal to healthcare professionals that a particular product “requires an intense level of reporting”.\textsuperscript{191} The Independent Healthcare Advisory Services (IHAS) recommended that an “analogy to the Black Triangle process for medicines should be adopted”.\textsuperscript{192}

65. Although web-based reporting has the advantage of being able to “reach across both hospital and community settings”, Dr Armitage, University of Bradford, considered that “patients have specific concerns about web based reporting”.\textsuperscript{193} The reasons for this included:

> The need to maintain confidentiality; the requirement for a quick and personalised response; a coding mechanism which can triage the patient’s concerns; an option to report positive as well as negative comments; and that a relative can report on behalf of a patient (who is officially nominated by that patient).\textsuperscript{194}

66. We are satisfied that the mechanisms exist to enable patients to report adverse incidents directly to the MHRA online if desired. In practice, patients are more likely to approach healthcare professionals in the first instance and this places a duty on healthcare professionals to report incidents of suspected device failure or side effects to the MHRA. However, there is evidence of under-reporting by healthcare professionals. To incentivise reporting, the Government should consider making the reporting of adverse incidents by healthcare professionals compulsory. This should generate more evidence on the risks associated with devices, which would ultimately benefit patients.

67. For medical implants (Class Ib or III medical devices) where equivalence data has been used in place of clinical trials or evaluations of the specific implant, the Black Triangle Scheme (or an equivalent system) should be adopted in the UK. This would mean that devices approved on equivalence alone would be subject to stronger post-market monitoring.

\textsuperscript{187} Q 147
\textsuperscript{188} Q 147
\textsuperscript{189} “Black Triangle Scheme”, MHRA, www.mhra.gov.uk
\textsuperscript{190} “Medicines & Medical Devices Regulation: What you need to know”, MHRA, www.mhra.gov.uk
\textsuperscript{191} Ev w18
\textsuperscript{192} Ev w29
\textsuperscript{193} Ev w35, para 6
\textsuperscript{194} Ibid.
Registries

68. The National Joint Registry (NJR) for England and Wales was established by the Department of Health and the Welsh Assembly Government in 2002 to collect “data on all hip, knee, ankle, elbow and shoulder joint replacements across the NHS and independent healthcare sector.”\(^\text{195}\) It is mandatory for clinicians to report information to the NJR.\(^\text{196}\) Sir Kent stated:

The National Joint Registry is the biggest in the world now. It has over a million hip, knee and ankle replacements in its register, and it produces an annual report, which sets out in very great detail the follow-up results of those procedures by type of operation, type of device and manufacturer of device. That is a valuable resource for changing clinical practice. That is the way in which accumulating information on outcome is fed back to improving care and, therefore, improving outcomes.\(^\text{197}\)

In August 2010 DePuy had to issue a worldwide recall of their ASR hip resurfacing implant because data from the NJR showed that more people than anticipated had experienced problems and required a second hip replacement surgery.\(^\text{198}\) This demonstrated that implant registries can be a powerful contributor to effective post-market surveillance.\(^\text{199}\)

69. The NJR covers joint replacements. Professor Murray explained that while there are currently no requirements for other implants to be registered, some “professional bodies have developed their own databases and voluntary recording systems.”\(^\text{200}\) Registries do not always succeed: the MHRA funded a National Breast Implant Registry between 1993 and 2006,\(^\text{201}\) which failed because “the completeness of registration was totally inadequate, and, secondly, the willingness of patients [...] to give follow-up information was far too low to allow conclusions to be drawn”.\(^\text{202}\) Nevertheless, the Health Committee recommended in their recent report on PIP breast implants that registry of all implants should be compulsory.\(^\text{203}\)

70. Although Sir Kent stated that “the transparency that now exists around the outcomes of joint replacement surgery through the National Joint Registry is a model of what might be achieved in other areas were there to be better follow-up data presented in a more coherent and consistent way”,\(^\text{204}\) there have been calls for greater transparency even with the NJR. Dr Thomas Joyce and Dr Pauline McCormack from Newcastle University suggested that “we should consider whether the raw data contained in [the NJR] could be made more

\(^{195}\) “About the NJR”, National Joint Registry, www.njrcentre.org.uk

\(^{196}\) Q 78

\(^{197}\) Q 134

\(^{198}\) “ASR hip replacement recall media guide”, Depuy, www.depuy.com

\(^{199}\) Q 18, Q 146

\(^{200}\) Ev w10

\(^{201}\) Health Committee, Sixteenth Report of Session 2010–12, PIP Breast implants and regulation of cosmetic interventions, HC 1816, para 66

\(^{202}\) Q 146 [Sir Kent Woods]

\(^{203}\) Health Committee, Sixteenth Report of Session 2010–12, PIP Breast implants and regulation of cosmetic interventions, HC 1816, para 69

\(^{204}\) Q 134
readily available”.205 They also pointed out the value of keeping explanted joints (implanted joints that have been subsequently removed):

Examination of explanted joints that have failed or caused problems in the body is one of the most valuable sources of data about how and why implants fail—they can be thought of as the ‘black box’. Revision operations, which remove such problem implants have to be reported to the National Joint Registry (NJR) but conservation of the failed joint itself is not required and many are simply thrown away [...]. We call for the conservation and analysis of explanted joints to be made mandatory as part of the NJR reporting procedure.206

71. The Government should ensure that raw data from the National Joint Registry (NJR) is published where possible. In addition, explanted joints should be analysed, and subsequent data generated should be reported to the NJR and published.

**EU registry**

72. Ms Minor from the European Commission informed us that the revisions to the Directive included plans for developing the European databank on medical devices (Eudamed) into an EU-wide medical devices registry. Ms Minor explained that this would serve to increase access to and transparency of clinical data, as well as improve post-market surveillance:

We are planning to have a central registry in which all manufacturers and all devices will have to be listed. For each device, there will be some standard information, such as the name of the notified bodies, the class of risk, and the unique device identifier, when we have that. There will also be a summary of performance and clinical data. For the first time, for example, clinicians will be able to have access to the clinical data which supported the certificate granted to the device.207

This registry would cover all medical devices (that is, Classes I to III), and would therefore include thousands of items.208 There would also be a fee for manufacturers associated with it, but Ms Minor pointed out that currently manufacturers are faced with the “possibility of having to register 27 times, because a number of member states have set up registries”209 so a central registry should ideally reduce both overall cost and bureaucratic burden associated with registries across the EU.210

73. According to the National Institute of Health and Clinical Excellence (NICE), “it is difficult to set up new registers”.211 The Minister stated that the England and Wales NJR is expensive to maintain and costs “about £3 million a year”.212 He compared this with “the
£10 million spent on the whole of the MHRA’s devices-related work”.213 Ms Minor explained that the start-up and maintenance costs of the proposed EU registry would be covered by the European Commission, and that the registry would be “available when the new regulatory framework goes live” which would be towards “the end of 2014-15”.214

74. Ms Minor also explained that the proposed changes to the Eudamed database would include an EU portal for reporting faults, so that “every serious incident would be reported directly at European level”.215 She stated:

I hope that would enable us to pick up more quickly any emerging trend that gave concern in relation to a device. We also hope to make some funds available to have some central trend analysis, so that we would have scientists working in our joint research centre looking at the data coming in and being able to check it and sound the alarm more quickly than has been the case in the past.216

75. This portal will be designed for manufacturers to report faults, but the European Commission is looking to include provisions for healthcare professionals and patients to use it as well.217 Ms Minor also considered that reporting faults should be mandatory for healthcare professionals.218 Lord Howe was supportive of greater coordination of communication between EU Member States, but stated:

If we can get greater sharing of data between member states, maybe even have an EU portal where data can be fed in when there is an adverse report on a device so that it is clearly on view to all member states, that would be much more efficient and effective and much less cumbersome [than establishing an EU body overseeing these functions].219

76. The MHRA had been pushing the Commission “to require registration of all devices placed on the EU market […] on a central EU portal” (currently the responsibility of member states) and “the development [of] an effective and efficient electronic communication and information support tool to support co-ordinated post-market surveillance across the EU”.220 Improving co-ordination, both within the EU and globally “is an aspect of the Commission’s ‘joint plan for immediate action’ and will also feature in the revision of the Medical Devices Directives”.221

77. An additional proposal is that each device would be marked with a Unique Device Identification (UDI), which, according to the ABHI, would:

---

213 Q 146
214 Q 100; Ev 48, para 4; Q 85
215 Q 98
216 Q 98
217 Q 106
218 Q 105
219 Q 128
220 Ev 37, paras 49–50
221 Ibid.
enable a particular implant to be linked to the patient who receives it and will greatly assist in the setting up of databases and registries. UDI will be based on internationally accepted standards and will eventually become a global requirement for devices as it is also the subject of legislation in North America, Australia and other regions.\(^{222}\)

78. For Sir Kent the key issue was “to make sure that the data are captured at the time the procedure is done”.\(^{223}\) He agreed that “the key to that would be to have a unique device identifier so that there is a recognised code that describes a device. That is something that is very much in the Commission’s thinking for the revision of the directives”.\(^{224}\) The Commission’s September 2012 proposal includes:

a requirement that manufacturers fit their devices with a Unique Device Identification (UDI) which allows traceability. The UDI system will be implemented gradually and proportionate to the risk class of the devices; [and]

a requirement that manufacturers/authorised representatives and importers must register themselves and the devices they place on the EU market in a central European database.\(^{225}\)

79. The National Joint Registry (NJR) proved useful in identifying high revision rates of metal-on-metal hip implants and should serve as the gold standard for implant registries. Part of its success is due to contributions from clinicians being mandatory. As such, we welcome the Commission’s proposal that manufacturers, authorised representatives and importers must register themselves and devices placed on the EU market on a central European database.

80. We support the European Commission’s plans to expand Eudamed to include an EU registry of medical devices in classes IIa, IIb and III, but we would not advocate Eudamed replacing the National Joint Registry in England and Wales in the foreseeable future. The Government must ensure that the proposed Eudamed registry achieves or exceeds the successes of the NJR before any replacement of the NJR is considered. These successes include, but are not limited to, the breadth of clinical data collected, the ease of reporting incidents by clinicians, and access to the data by clinicians and researchers for analysis.

81. We recommend that the inclusion of data from explanted medical implants should be a requirement of the Eudamed registry.

**Responding to adverse incidents**

82. The MHRA’s role, as the UK’s competent authority, is to monitor and investigate adverse events and field safety corrective actions (including recalls) occurring in the UK.\(^{226}\)
It is also responsible for “recalling faulty products and offering advice to the health service, primarily through Medical Device Alerts, but also through safety pamphlets, posters, and bulletins.”

83. There were mixed views on the MHRA’s speed of response to reports of faulty medical implants. Professor Stephen Westaby, Consultant Cardiac Surgeon, John Radcliffe Hospital, Oxford, was impressed with the MHRA’s response to a concern he raised about a heart valve:

I am very positive about MHRA and how it works. I took a concern to it about [a] particular heart valve [...] Its response was very prompt and effective; it did a very good job in preventing the sort of scandal, which would have been completely inappropriate, that we saw in the PIP implants.

On the other hand, some criticised the MHRA for being slow to respond to incident reports. For example, an article in the British Medical Journal (BMJ) reported that problems with the now-recalled DePuy ASR metal-on-metal hip implant systems were first noticed by the Australian National Joint Replacement Registry in 2007. These hip implants were removed from the Australian market in December 2009, but the worldwide recall was not issued until August 2010, following analysis of data from the National Joint Registry of England and Wales. The BSi, a UK notified body, certified these hip implants for the EU market. Sheila Sunley, member of the Altogether Hip Patient Support Group, considered that the MHRA should have responded more quickly than it did to the concerns raised in Australia. Dr Heneghan and the BMJ considered that “the failure in some cases to evaluate rapidly devices in which concerns have been expressed seems quite unacceptable. Doctors have said that the MHRA is slow to respond when they do raise concerns”. We asked some of our witnesses whether the recall of metal-on-metal hip implants represented a success or failure of the regulatory system. Dr Joyce, Newcastle University, stated “it is a failure. We speak to many thousands of people, and these lives have been absolutely ruined”. Dr Woodward, NPSA, suggested:

If you take the aviation industry as the gold standard and places such as Toyota, they have a system whereby, if something goes wrong with one airline or even one flight, it is known throughout the system within about 12 hours. That is what we need for the NHS—a system whereby, if you pick up really quickly that something is going wrong, rather than wait for months and months, you need to be able to spread it around really quickly [...] What we would want to happen when somebody picks up

---

227  Ev 34, para 21
228  Q 5
231  Ev w3, para 2
232  Ev w3, para 4
233  Q 18
that things are going wrong is that you stop any future surgery or implanting or whatever, until you know that it is safe to start again.234

84. Sir Kent Woods, MHRA, explained that competent authorities “have an obligation to notify [other] competent authorities” if they “hear of serious adverse incidents that might affect products on the market in the other countries of Europe”.235 He stated:

I do not think in practice [that communication] is as regular and detailed as it could be. One of the aspects of the legislative review has been how to improve the interaction between the national competent authorities across the 27 member states. As you might expect, some of the national competent authorities are larger; they have better resources and more data, but we are dealing in a European system and it is important that we draw on experience from the whole population of 500 million and share our resources. We have been exploring among ourselves as heads of the national competent authorities how best to do this.236

The Minister did not express concerns over the MHRA’s response to the problems with metal-on-metal hip implants and in fact considered it to be “probably a good news story”, as “in this country we were able to react very swiftly with the medical community to influence clinical practice when concerns became apparent”.237 Ms Minor explained that the revisions to the Directive included centralising the risk analysis of reported faults. The aim was to implement a unified approach amongst Member States in response to large-scale incidents with medical implants, such that a “common European recommendation as to how it should be addressed” can be made.238

85. We are satisfied that the Commission intends to propose greater coordination across EU Member States when adverse incidents are reported. However, global coordination and collaboration are also essential. It is disappointing that problems with metal-on-metal hip implants were picked up several years before the worldwide recall and it appears that the MHRA was slow in responding to data emerging from Australia. Because of that delay, many patients have suffered needlessly. The Minister’s view that the MHRA’s response to the problems with metal-on-metal hip implants was a “good news story” shows some complacency. The European Commission and UK Government must improve the speed with which information from adverse incident reporting abroad is handled and acted upon.

Auditing manufacturers

86. As discussed in paragraph 25, notified bodies audit manufacturers prior to certifying new medical implants for the EU market: this includes assessing manufacturers’ facilities and technical documents. Auditing continues after market approval: the MHRA explained

---

234 Q 18
235 Q 136
236 Q 136
237 Q 148
238 Q 103
that “these assessments normally take place annually to ensure ongoing compliance with the requirements of the legislation”. Mr Howlett, BSi, explained that:

When we are looking at situations where a manufacturer is found wanting, the first line of approach as a notified body is to bring that manufacturer into compliance. We do not want to be denying the patient the product; we want that product, if it is a good one, to be brought to the market in a safe condition. We would work with them and agree corrective action plans.240

87. The recent withdrawal of PIP breast implants highlighted the need to conduct regular inspections of manufacturers’ facilities. PIP breast implants were certified for the EU market in 2000 by the German notified body TUV Rheinland.241 The interim report by Bruce Keogh, NHS Medical Director, noted that “concerns began to emerge among cosmetic surgeons about the performance of PIP implants” from 2006.242 However, it was not until the French competent authority conducted an inspection of the PIP manufacturing facilities in March 2010 that it was discovered that the manufacturer was using an unapproved implant filler.243 The MHRA had raised concerns with the PIP manufacturers several times between 2006 and 2010.244 The Minister stated that “it was clear from my investigation that no amount of regulation could have prevented deliberate fraud of that kind”.245 Professor Westaby agreed that it was a “fraudulence issue” and that “If the regulatory authorities are told that a certain content is present in a device, they are justified in taking that as accepted”.246

88. Nevertheless, there was a desire to improve the auditing process. The Independent Healthcare Advisory Services (IHAS) suggested that:

Increasing the frequency and depth of inspections carried out at both the ‘legal manufacturer’ and the actual producer’s sites would naturally lead to a raise in standards across the medical device industry. Options include more frequent unannounced inspections, more detailed audits and tougher sanctions.247

89. The Harley Medical Group stated that “the testing that currently takes place after commercialisation is not adequate [...] The visits to the manufacturer must be unannounced and must take place several times a year”.248 The MHRA stated that the European Commission aims to improve the audits carried out by notified bodies, “with a

---

239  Ev 33, para 13
240  Q 56
241  Health Committee, Sixteenth Report of Session 2010-12, PIP Breast implants and regulation of cosmetic interventions, HC 1816
243  “Poly Implant Prothèse (PIP) silicone breast implants: Review of the actions of the Medicines and Healthcare products Regulatory Agency (MHRA) and Department of Health”, Department of Health, 14 May 2010, p87
244  “Poly Implant Prothèse (PIP) silicone breast implants: Review of the actions of the Medicines and Healthcare products Regulatory Agency (MHRA) and Department of Health”, Department of Health, 14 May 2010, p72-87
245  Q 148
246  Q 3
247  Ev w27, para 3.7
248  Ev w 3, para 2
particular focus on ensuring that Notified Bodies undertake unannounced inspections of manufacturers”. The Minister stated:

There is also a case for specifying in greater detail how notified bodies should undertake conformity assessments and ongoing monitoring of manufacturers, and the use of unannounced inspections and audits, perhaps requiring physical checks of devices. I know this takes us into the territory of greater prescription, but perhaps there is a case for looking at that more closely if we really want to see greater consistency of performance across Europe.

The Commission has proposed that:

the position of notified bodies vis-à-vis manufacturers will be significantly strengthened, including their right and duty to carry out unannounced factory inspections and to conduct physical or laboratory tests on devices. The proposal also requires rotation of the notified body’s personnel involved in the assessment of medical devices at appropriate intervals to strike a reasonable balance between the knowledge and experience required to carry out thorough assessments and the need to ensure continuous objectivity and neutrality in relation to the manufacturer subject to those assessments.

90. We are supportive of proposals to enforce unannounced audits of manufacturers by notified bodies, and recommend that in addition, audits should take place at least annually. Frequent and unannounced auditing of manufacturers by notified bodies should be enforced by competent authorities.

91. Although we have not received evidence to suggest that notified bodies face a conflict of interest in auditing manufacturers whose devices they have approved, it may be a risk. We welcome the proposal to rotate notified bodies’ personnel to increase objectivity and neutrality, but we suggest that audits of a manufacturer by a notified body that did not approve that manufacturer’s devices should also take place.

---

249 Ev 35, para 35
250 Q 141
5 Conclusions

The MHRA

92. Although much responsibility for medical implant regulation is delegated to notified bodies and manufacturers, the MHRA plays a key role in the UK. We heard mixed views on the MHRA’s overall performance in medical devices regulation. For example, Medtronic Ltd, a manufacturer of medical devices, stated that “compared to some other national Competent Authorities, MHRA is well-resourced, has technically competent staff, and maintains vigilant oversight of clinical trials conducted in the UK, post market surveillance and Notified Bodies it designates”.252 The Association of British Healthcare Industries also considered that “the MHRA does a very effective job in implementing the Directives” and that it was “often considered to be the pre-eminent Device authority in the EU and is well respected throughout Europe and beyond among those concerned with efforts to achieve global harmonization in device regulation”.253 However, Dr Stephen O’Connor from the Institute of Physics and Engineering in Medicine (IPEM) considered that the MHRA was overly bureaucratic relative to other competent authorities in the EU, inefficient and difficult to deal with.254 We also heard from a number of patients from the Altogether Hip Patient Support Group, who considered that MHRA did not prioritise patient wellbeing. This patient-led group was established in February 2011 for patients fitted with DePuy ASR metal-on-metal hip implants, as a source of information and support.255 Members of this patient group stated that “the MHRA seems to be a totally ineffective body working on behalf of the corporations rather than patients”256 and that “the MHRA is a toothless organisation influenced by manufacturers not patient care”.257 In a recent editorial, the medical journal The Lancet stated that the failure of PIP breast implants and metal-on-metal hip implants resulted from “MHRA’s paralysis and inability to address the shortcomings of a badly flawed system” and that “there is an urgent need for reform of the MHRA”.258

93. The lack of transparency of the MHRA’s operations was also heavily criticised. The MHRA has a Committee on the Safety of Devices (CSD), which “is a group of 25 external experts from clinical and scientific disciplines”.259 The CSD was established in 2001 and meets two to three times a year.260 It supports the Devices sector of the MHRA in its aim to “protect public health and safeguard the interest of patients and users”.261 It achieves this by “ensuring that medical devices and equipment meet appropriate standards of safety,

252  Ev w16, para 6
253  Ev 42, para 12
254  Ev w1
256  Ev w9, para 2
257  Ev w3, para 2
259  Q 132
quality and performance and that they comply with relevant Directives of the European Union”.262 Nuffield Health pointed out that the CSD “can make recommendations however, since the committee does not make decisions, it is not subject to independent review or audit”.263 The MHRA website states that “the work of the Committee must remain confidential at all times. There could be serious consequences to industry if any leaks occurred from committee meetings”.264 We asked Sir Kent Woods about this and he explained that this lack of transparency was due to obligations of confidentiality placed on the MHRA by the Medical Devices Directives (MDD), but that he would like to see this changed.265 The MDD states that:

> Without prejudice to the existing national provisions and practices on medical secrets, Member States shall ensure that all the parties involved in the application of this Directive are bound to observe confidentiality with regard to all information obtained in carrying out their tasks. This does not affect the obligation of Member States and notified bodies with regard to mutual information and the dissemination of warnings, nor the obligations of the persons concerned to provide information under criminal law.266

94. Any revision to the Directives should include removing the over-emphasis on confidentiality. The default should be transparency and openness, unless there is a compelling reason otherwise. Perceptions of secrecy can be, and have been, very damaging to public trust in the regulatory system. Transparency also enables more effective external scrutiny of the system and the parties involved.

95. It is impossible to evaluate the performance of the MHRA’s Committee on the Safety of Devices (CSD) when its work is kept secret. We recommend that the MHRA improves the transparency of the CSD, for example by publishing the minutes of its meetings as well as the advice it provides.

The regulation of medical implants

96. Effective regulation of medical implants is paramount to patient safety in the UK and EU. Patients and healthcare providers alike should feel confident that medical implants available for use in the EU conform to a high standard of safety and quality, while still granting patients access to the latest innovations. One of the key questions is whether the PIP breast implant and metal-on-metal hip implant recalls have been exceptional, albeit unfortunate, incidents, or whether they represent deeper weaknesses in the regulatory system. The MHRA stated that:

> Issues with PIP silicone breast implants and metal-on-metal hips stem from very different root causes—the first from deliberate subversion of the regulatory system and the second from unanticipated wear over a long time-period. However, this

263 Ev w23
265 Q 133
illustrates that picking isolated examples and attributing them to regulatory failure should not be the basis on which to advocate widespread changes to a system.267

97. We accept that the PIP breast implant case stemmed from deliberate fraud that would have been extremely difficult to prevent. In addition, we are aware that thousands of implants are used by patients every day, mostly without problem. **We have not advocated widespread changes to the regulatory system other than significantly increasing transparency.** However in practice there are several areas of weakness. We are pleased that the Commission’s proposed revisions to the Medical Devices Directive generally aim to address the weaknesses we identified in the regulation of medical devices, although we do not support all of the proposed measures.

98. It would not be possible to detect all possible adverse consequences in pre-market assessment and therefore there is an emphasis on post market surveillance of medical implants. However, we were unimpressed with the extent to which reliance on equivalence data, rather than on more rigorous sources of evidence such as clinical trials, seemed acceptable in pre-market assessment. The utility of post-market surveillance should not detract from the priority of ensuring implants are safe and effective before they are used in patients.

99. During this inquiry we have been disappointed with the lack of transparency and accountability of the regulatory process and the organisations involved. Our strongest recommendations are to increase transparency and accountability across the entire regulatory framework and to improve the coordination and communication between Member States. We have welcomed many of the proposed changes to the Directives, although we caution against excessive European centralisation.

100. The EU regulatory framework for medical devices was developed with the desire to create a free market, and the emphasis on public health followed. We consider that safeguarding public health should be the primary aim of the regulatory system.

101. When negotiating on the proposed revisions, the UK Government should use this Report to press for greater transparency and a more evidence-based approach to the regulation of medical devices, particularly implants.
Conclusions and recommendations

1. Although they told us that their views would be adequately represented by the Association of British Healthcare Industries (ABHI), we are very disappointed that we were not able to take oral evidence directly from manufacturers. (Paragraph 5)

Pre-market approval

2. Ideally, all medical implants approved for use on the EU market would be subject to rigorous clinical investigations prior to introduction but it is not practical to do this for every implant and there are circumstances where reliance on equivalence data may be acceptable. Nonetheless, it appears that the existing regulatory framework may have the effect of encouraging manufacturers to rely on equivalence data rather than evidence from clinical trials. This is compounded by the difficulties of conducting clinical trials in the UK. We do not advocate a pharmaceutical style approach to regulation. We endorse the approaches already being taken: (i) the proposed revisions to the Medical Devices Directive make clearer when equivalence data is or isn’t acceptable and strengthen scrutiny and challenge of manufacturers’ decisions; and (ii) the environment for clinical trials should be improved, not just in the UK but across Europe. (Paragraph 34)

3. We welcome the European Commission’s proposal to make scientific advice available to manufacturers and notified bodies when placing new implants on the market. (Paragraph 35)

4. The establishment of the Health Research Authority (HRA) is a welcome step towards improving the regulation and governance of health research. We expect the HRA to tackle the difficulties of setting up clinical trials in the UK. We intend to scrutinise the HRA and its work and we recommend that the Government publishes an update on the progress of the HRA in improving the environment for clinical trials in December 2012, a year after its establishment. (Paragraph 36)

Transparency of evidence

5. Transparency should be the default position in the approval of medical implants: it is particularly important where some of the key players influencing public health—manufacturers and notified bodies—are private organisations not accountable to Parliament or subject to Freedom of Information requests. Greater transparency would improve public confidence in the system and support decision-making by patients and healthcare professionals. We are disappointed that there is a lack of transparency in the current regulatory system and we urge the UK Government to take a lead in increasing transparency. (Paragraph 40)

6. The Commission’s proposals are a step in the right direction, but do not go far enough. All clinical data used in the approval of a medical implant should be made publicly available without identifying patients or clinical trial participants. For products currently on the market, data should be published immediately. It should be clear when medical implants have been approved using equivalence data and
when clinical investigations have been conducted on that implant prior to market approval. (Paragraph 41)

7. In addition, regardless of whether an implant is approved for use or not, any new clinical data generated about that implant should be published. It is as scientifically useful to know what doesn’t work as it is to know what does work. (Paragraph 42)

**Comparisons with the FDA**

8. There is insufficient evidence that the Food and Drugs Administration’s (FDA) more onerous procedures for granting market approval to medical implants have resulted in greater patient safety. The FDA system also operates more slowly and thus delays patient access to medical implants, which is, in itself, a threat to patient safety. (Paragraph 45)

**Notified bodies**

9. Differences between notified bodies across Europe are a key weakness in the current regulatory system and can result in “forum shopping”, whereby manufacturers choose notified bodies more likely to provide approval for a device. Forum shopping is facilitated by a lack of transparency and therefore accountability. Notified bodies should consider publishing records of all approaches by manufacturers, regardless of whether applications were completed or not. (Paragraph 48)

10. We support the proposal to use teams of experts drawn from Member States to oversee the designation of notified bodies in order to minimise differences and raise and harmonise standards across Europe. (Paragraph 53)

11. Beyond this, we do not support further centralisation of medical device regulation in the EU, as increased bureaucracy could slow device approvals unnecessarily. The speed of device approval is a strength of the current system. The emphasis should be on raising the standards and accountability of notified bodies and we are opposed to pre-market approval processes being transferred to or being duplicated at European level. Therefore we do not support the European Commission’s proposal to require a central notification of intent from manufacturers seeking approval for new devices. We urge the Government to oppose this proposal during Council negotiations. (Paragraph 54)

12. Manufacturers may be charged increased fees by notified bodies if more coordinated oversight leads to a reduction in the number of notified bodies. We are not fully convinced by reassurances provided by the Government or Commission that this would not hinder small companies bringing products to market. The Commission and Government should explain how they intend to support small, innovative companies in the medical devices sector if pre-market approval becomes prohibitively costly. (Paragraph 55)
**Post-market surveillance**

13. Manufacturers should publish the results of post-market surveillance studies. (Paragraph 59)

14. We are satisfied that the mechanisms exist to enable patients to report adverse incidents directly to the MHRA online if desired. In practice, patients are more likely to approach healthcare professionals in the first instance and this places a duty on healthcare professionals to report incidents of suspected device failure or side effects to the MHRA. However, there is evidence of under-reporting by healthcare professionals. To incentivise reporting, the Government should consider making the reporting of adverse incidents by healthcare professionals compulsory. This should generate more evidence on the risks associated with devices, which would ultimately benefit patients. (Paragraph 66)

15. For medical implants (Class IIb or III medical devices) where equivalence data has been used in place of clinical trials or evaluations of the specific implant, the Black Triangle Scheme (or an equivalent system) should be adopted in the UK. This would mean that devices approved on equivalence alone would be subject to stronger post-market monitoring. (Paragraph 67)

**Registries**

16. The Government should ensure that raw data from the National Joint Registry (NJR) is published where possible. In addition, explanted joints should be analysed, and subsequent data generated should be reported to the NJR and published. (Paragraph 71)

17. The National Joint Registry (NJR) proved useful in identifying high revision rates of metal-on-metal hip implants and should serve as the gold standard for implant registries. Part of its success is due to contributions from clinicians being mandatory. As such, we welcome the Commission’s proposal that manufacturers, authorised representatives and importers must register themselves and devices placed on the EU market on a central European database. (Paragraph 79)

18. We support the European Commission’s plans to expand Eudamed to include an EU registry of medical devices in classes IIa, IIb and III, but we would not advocate Eudamed replacing the National Joint Registry in England and Wales in the foreseeable future. The Government must ensure that the proposed Eudamed registry achieves or exceeds the successes of the NJR before any replacement of the NJR is considered. These successes include, but are not limited to, the breadth of clinical data collected, the ease of reporting incidents by clinicians, and access to the data by clinicians and researchers for analysis. (Paragraph 80)

19. We recommend that the inclusion of data from explanted medical implants should be a requirement of the Eudamed registry. (Paragraph 81)
Responding to adverse incidents

20. We are satisfied that the Commission intends to propose greater coordination across EU Member States when adverse incidents are reported. However, global coordination and collaboration are also essential. It is disappointing that problems with metal-on-metal hip implants were picked up several years before the worldwide recall and it appears that the MHRA was slow in responding to data emerging from Australia. Because of that delay, many patients have suffered needlessly. The Minister’s view that the MHRA’s response to the problems with metal-on-metal hip implants was a “good news story” shows some complacency. The European Commission and UK Government must improve the speed with which information from adverse incident reporting abroad is handled and acted upon. (Paragraph 85)

Auditing manufacturers

21. We are supportive of proposals to enforce unannounced audits of manufacturers by notified bodies, and recommend that in addition, audits should take place at least annually. Frequent and unannounced auditing of manufacturers by notified bodies should be enforced by competent authorities. (Paragraph 90)

22. Although we have not received evidence to suggest that notified bodies face a conflict of interest in auditing manufacturers whose devices they have approved, it may be a risk. We welcome the proposal to rotate notified bodies’ personnel to increase objectivity and neutrality, but we suggest that audits of a manufacturer by a notified body that did not approve that manufacturer’s devices should also take place. (Paragraph 91)

Conclusions

23. Any revision to the Directives should include removing the over-emphasis on confidentiality. The default should be transparency and openness, unless there is a compelling reason otherwise. Perceptions of secrecy can be, and have been, very damaging to public trust in the regulatory system. Transparency also enables more effective external scrutiny of the system and the parties involved. (Paragraph 94)

24. It is impossible to evaluate the performance of the MHRA’s Committee on the Safety of Devices (CSD) when its work is kept secret. We recommend that the MHRA improves the transparency of the CSD, for example by publishing the minutes of its meetings as well as the advice it provides. (Paragraph 95)

25. We have not advocated widespread changes to the regulatory system other than significantly increasing transparency. However in practice there are several areas of weakness. We are pleased that the Commission’s proposed revisions to the Medical Devices Directive generally aim to address the weaknesses we identified in the regulation of medical devices, although we do not support all of the proposed measures. (Paragraph 97)

26. It would not be possible to detect all possible adverse consequences in pre-market assessment and therefore there is an emphasis on post market surveillance of medical
implants. However, we were unimpressed with the extent to which reliance on equivalence data, rather than on more rigorous sources of evidence such as clinical trials, seemed acceptable in pre-market assessment. The utility of post-market surveillance should not detract from the priority of ensuring implants are safe and effective before they are used in patients. (Paragraph 98)

27. During this inquiry we have been disappointed with the lack of transparency and accountability of the regulatory process and the organisations involved. Our strongest recommendations are to increase transparency and accountability across the entire regulatory framework and to improve the coordination and communication between Member States. We have welcomed many of the proposed changes to the Directives, although we caution against excessive European centralisation. (Paragraph 99)

28. The EU regulatory framework for medical devices was developed with the desire to create a free market, and the emphasis on public health followed. We consider that safeguarding public health should be the primary aim of the regulatory system. (Paragraph 100)

29. When negotiating on the proposed revisions, the UK Government should use this Report to press for greater transparency and a more evidence-based approach to the regulation of medical devices, particularly implants. (Paragraph 101)
Formal Minutes

Wednesday 17 October 2012

Members present:
Andrew Miller, in the Chair
Stephen Metcalfe
Stephen Moseley
Sarah Newton
Graham Stringer

Draft Report (Regulation of medical implants in the EU and UK), proposed by the Chair, brought up and read.

Ordered, That the draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 101 read and agreed to.

Summary agreed to.

Resolved, That the Report be the Fifth Report of the Committee to the House.

Ordered, That the Chair make the Report to the House.

Ordered, That embargoed copies of the Report be made available, in accordance with the provisions of Standing Order No. 134.

Written evidence was ordered to be reported to the House for printing with the Report.

[Adjourned till Wednesday 24 October at 9.00 am]
Witnesses

Wednesday 23 May 2012

Dr Carl Heneghan, GP and Reader in Evidence-Based Medicine, Director of the Centre for Evidence-Based Medicine, University of Oxford,
Dr Thomas Joyce, Reader in Biotribology, School of Mechanical and Systems Engineering, Newcastle University, Professor Stephen Westaby, Professor of Biomedical Science, Swansea University, Consultant Cardiac Surgeon, John Radcliffe Hospital, and Dr Suzette Woodward, Director of Patient Safety, National Patient Safety Agency

Wednesday 13 June 2012

John Howlett, Head of Notified Body, British Standards Institute (Healthcare) (BSI), Peter Ellingworth, Chief Executive, Association of British Healthcare Industries, and Mike Kreuzer, Technical and Regulatory Executive Director, Association of British Healthcare Industries

Jacqueline Minor, Director of Consumer Affairs, Directorate-General for Health & Consumers, European Commission

Sir Kent Woods, Chief Executive, Medicines and Healthcare products Regulatory Agency (MHRA), and Earl Howe, Parliamentary Under-Secretary of State, Department of Health

List of printed written evidence

1 Medicines and Healthcare products Regulatory Agency Ev 32
2 Association of British Healthcare Industries Ev 41; 51
3 Dr Thomas Joyce and Dr Pauline McCormack Ev 44
4 Professor Stephen Westaby Ev 48
5 Jacqueline Minor, European Commission Ev 48
6 BSI Healthcare Ev 49; 51
List of additional written evidence

(published in Volume II on the Committee’s website www.parliament.uk/science)

1 Jane Edwards Ev w1
2 Dr Stephen A O’Connor Ev w1
3 Sheila Sunley, Member of the Altogetherhip Patient Support Group Ev w3
4 Centre for Evidence-Based Medicine and the British Medical Journal Ev w3
5 Carol Holland, Altogether Hip Support Group Ev w9
6 Professor Alan Murray Ev w10
7 Action on Hearing Loss Ev w12
8 Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians of the United Kingdom Ev w13
9 Medtronic Ev w16
10 Nuffield Health Ev w17
11 Royal College of Surgeons Ev w25
12 Independent Healthcare Advisory Services (IHAS) Ev w26
13 The Harley Medical Group Ev w31
14 National Institute for Health and Clinical Excellence (NICE) Ev w32
15 Dr Gerry Armitage Ev w34
16 Dr Peter Wilmshurst Ev w36
17 Johnson & Johnson Ev w39
# List of Reports from the Committee during the current Parliament

The reference number of the Government’s response to each Report is printed in brackets after the HC printing number.

## Session 2012–13

<table>
<thead>
<tr>
<th>Report Type</th>
<th>Title</th>
<th>Reference Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Special Report</td>
<td>Science in the Met Office: Government Response to the Committee’s Thirteenth Report of Session 2010–12</td>
<td>HC 162</td>
</tr>
<tr>
<td>First Report</td>
<td>Devil’s bargain? Energy risks and the public</td>
<td>HC 428</td>
</tr>
<tr>
<td>Second Report</td>
<td>Pre-appointment hearing with the Government’s preferred candidate for Chair of the Medical Research Council</td>
<td>HC 510–I</td>
</tr>
<tr>
<td>Third Report</td>
<td>The Census and social science</td>
<td>HC 322</td>
</tr>
<tr>
<td>Fourth Report</td>
<td>Building scientific capacity for development</td>
<td>HC 377</td>
</tr>
</tbody>
</table>

## Session 2010–12

<table>
<thead>
<tr>
<th>Report Type</th>
<th>Title</th>
<th>Reference Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Report</td>
<td>The Reviews into the University of East Anglia’s Climatic Research Unit’s E-mails</td>
<td>HC 444 (HC 496)</td>
</tr>
<tr>
<td>Second Report</td>
<td>Technology and Innovation Centres</td>
<td>HC 618 (HC 1041)</td>
</tr>
<tr>
<td>Third Report</td>
<td>Scientific advice and evidence in emergencies</td>
<td>HC 498 (HC 1042 and HC 1139)</td>
</tr>
<tr>
<td>Second Special Report</td>
<td>The Reviews into the University of East Anglia’s Climatic Research Unit’s E-mails: Government Response to the Committee’s First Report of Session 2010–12</td>
<td>HC 496</td>
</tr>
<tr>
<td>Fourth Report</td>
<td>Astronomy and Particle Physics</td>
<td>HC 806 (HC 1425)</td>
</tr>
<tr>
<td>Fifth Report</td>
<td>Strategically important metals</td>
<td>HC 726 (HC 1479)</td>
</tr>
<tr>
<td>Third Special Report</td>
<td>Technology and Innovation Centres: Government Response to the Committee’s Second Report of Session 2010–12</td>
<td>HC 1041</td>
</tr>
<tr>
<td>Fourth Special Report</td>
<td>Scientific advice and evidence in emergencies: Government Response to the Committee’s Third Report of Session 2010–12</td>
<td>HC 1042</td>
</tr>
<tr>
<td>Sixth Report</td>
<td>UK Centre for Medical Research and Innovation (UKCMRI)</td>
<td>HC 727 (HC 1475)</td>
</tr>
<tr>
<td>Fifth Special Report</td>
<td>Bioengineering: Government Response to the Committee’s Seventh Report of 2009–10</td>
<td>HC 1138</td>
</tr>
<tr>
<td>Sixth Special Report</td>
<td>Scientific advice and evidence in emergencies: Supplementary Government Response to the</td>
<td>HC 1139</td>
</tr>
</tbody>
</table>
### Regulation of medical implants in the EU and UK

<table>
<thead>
<tr>
<th>Committee's Third Report of Session 2010–12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seventh Report: The Forensic Science Service</td>
</tr>
<tr>
<td>Eighth Report: Peer review in scientific publications</td>
</tr>
<tr>
<td>Eighth Special Report: UK Centre for Medical Research and Innovation (UKCMRI): Government Response to the Committee's Sixth Report of session 2010–12</td>
</tr>
<tr>
<td>Ninth Report: Practical experiments in school science lessons and science field trips</td>
</tr>
<tr>
<td>Ninth Special Report: Strategically important metals: Government Response to the Committee's Fifth Report of Session 2010–12</td>
</tr>
<tr>
<td>Tenth Special Report: Peer review in scientific publications: Government and Research Councils UK Responses to the Committee's Eighth Report of Session 2010–12</td>
</tr>
<tr>
<td>Tenth Report: Pre-appointment hearing with the Government's preferred candidate for Chair of the Technology Strategy Board</td>
</tr>
<tr>
<td>Eleventh Special Report: Practical experiments in school science lessons and science field trips: Government and Ofqual Responses to the Committee’s Ninth Report of Session 2010–12</td>
</tr>
<tr>
<td>Eleventh Report: Alcohol guidelines</td>
</tr>
<tr>
<td>Twelfth Report: Malware and cyber crime</td>
</tr>
<tr>
<td>Thirteenth Report: Science in the Met Office</td>
</tr>
<tr>
<td>Fourteenth Report: Pre-appointment hearing with the Government’s preferred candidate for Chair of the Engineering and Physical Sciences Research Council</td>
</tr>
</tbody>
</table>
Oral evidence

Taken before the Science and Technology Committee
on Wednesday 23 May 2012

Members present:
Andrew Miller (Chair)
Gareth Johnson Pamela Nash
Stephen Metcalfe Graham Stringer
Stephen Mosley Hywel Williams

Examination of Witnesses

Witnesses: Dr Carl Heneghan, GP and Reader in Evidence-Based Medicine, Director of the Centre of Evidence-Based Medicine, University of Oxford, Dr Thomas Joyce, Reader in Biostatistics, School of Mechanical and Systems Engineering, Newcastle University, Professor Stephen Westaby, Professor of Biomedical Science, Swansea University, Consultant Cardiac Surgeon, John Radcliffe Hospital, and Dr Suzette Woodward, Director of Patient Safety, National Patient Safety Agency, gave evidence.

Q1 Chair: I welcome our panel of witnesses this morning. Just for the record, may I ask the four of you to introduce yourselves.

Dr Heneghan: My name is Dr Carl Heneghan. I am from the University of Oxford.

Dr Joyce: I am Dr Tom Joyce from Newcastle University.

Professor Westaby: I am Steve Westaby from Oxford and also from the Institute of Biomedical Sciences at the University of Swansea.

Dr Woodward: I am Dr Suzette Woodward. I am from the National Patient Safety Agency.

Q2 Chair: Thank you very much. I have a series of questions for you and I will start on the issue of regulation in the field of medical implants. We have a regulatory structure that has a UK component, and it operates within the broader EU arena. Does that relationship—the decentralised nature of the structure—give you any concerns about safety in this field?

Professor Westaby: To a degree it does in that, as you already know, there are more than 80 regulatory bodies throughout the EU, and in order to obtain a CE mark you can go to virtually any of them. Once you have a CE mark for an implantable device, you can use it in any European country. The MHRA supervises the UK very carefully, and I have lots of evidence with my own endeavours to back that up. Compared with the United States and Japan, for instance, where I have substantial interface with medical devices, we are very fortunate indeed, because I can use sophisticated devices many years before my colleagues in the States and Japan, for instance.

Dr Heneghan: I have spent about three or four years trying to get my head around regulation and how it works, looking in terms of the evidence requirement. The key is to understand, from the three European directives, how the evidence is brought about. You submit your device—a design dossier—to one of the notified bodies. There are 76 across Europe; you submit to one—wherever the country is—and you get access to the whole of the European market. When you submit that design dossier, you submit your potential technical standards and clinical data. When you dig down into it, what does clinical data mean? There is a crucial issue called equivalence. All manufacturers more or less use it. In the US they use it about 95% of the time; here, I don’t know, but I expect it would be round about 100% of the time. Equivalence means that you can write a literature review that says, “My device is very similar to somebody else’s on the market and so I should have access to the whole of the European market.” That is then looked at by a notified body. As of now, that is a non-transparent process between the manufacturer and a private company, and nobody, including the MHRA, gets to see the quality of that data, as submitted, what it looks like and how much it establishes effectiveness. I am not going to come to safety yet—we will come to that later. Is this device equivalent or is it better than something on the market? Right now, probably nobody in the European Union has a perspective on that, because it is a non-transparent process that hides behind commercial confidentiality. I have access to that in an ongoing case right now, as an expert witness in evidence in transvaginal tape meshes, where I have the information submitted, and that is the only way I can get access. That non-transparency in the quality of evidence is a real problem.

Q3 Chair: Professor Westaby, going back to your response, are there examples you can give of approvals that have been given by one of the 80 regulatory bodies that specifically give you concerns?

Professor Westaby: To be honest, not in my field. I am sure that the recent PIP breast implant is the focus of attention here, but I think that was a fraudulence issue. If the regulatory authorities are told that a certain content is present in a device, they are justified in taking that as accepted. I don’t personally have experience with a device that I think should not have been used. I have had experience with a heart valve that was licensed and then caused issues. There were two well-known ones. The LabCor valve was implanted at six or seven centres in the UK; it was a safe and durable device, but it was sterilised in a...
material that could cause corrosion of biological materials. There were clear instructions as to how long that particular valve should be washed before it was implanted. In certain cases, because of certain techniques, the valve was not washed for long enough; there were nurses in the operating theatres whose English was not good enough to scrutinise the instructions before use, and there were issues, but it was not the valve itself. I have not actually used a product that was questionable from the point of regulation.

**Dr Joyce:** Much of my work has been concerned with a group of devices—metal-on-metal hips. Within this group, we are seeing substantial revision rates and substantial failure rates—certainly a lot more than would be expected from conventional types of artificial hip joint. Those that have failed have all been through the regulatory process and have been CE marked and checked, but when it comes to pass, they have failed a massive amount. That is with hips. If we look at something like finger joints, they have been fitted in relatively small numbers. If we look at the literature, the LPM finger prosthesis failed in about 50% of cases after about 15 to 18 months, and the Mathys finger prosthesis failed in 76% of cases, at 15 months again. Although these are small numbers, they are substantial failures and they have presumably been CE marked and checked, yet they are going into patients and performing incredibly poorly.

**Q4 Chair:** Is there any evidence that the regulatory structures outside Europe—say, in the US or Japan, or indeed anywhere else—are better than the European one?

**Dr Heneghan:** I can answer that. The US system is slightly different in that they have two systems. They have one called the 510(k) route, which is their equivalence route, but they have a second route called the PMA approval process, which they use for the highest-risk devices. The idea there is to say, “I’m sorry but you can’t use equivalence and you have to establish clinical trial data to use this product in our population.” I can give you a whole list of about six different ones that have not been cleared in America but were used in the European market.

Hips are a classic example. You had a 3% failure rate, which is a very impressive revision rate, at about 10 years, and then a new device comes along on equivalence—and it is a technical equivalence, not a clinical improvement—and now you have failure rates of 13% or 15%. Whoever is responsible for the regulatory framework there is in trouble, because their job is to catch that. The key is that we have a system, and you have to remember that there are about 76 different joints available, which does not include all the combinations. There are loads of these floating out there trying to gain access to a very competitive market.

**Q5 Graham Stringer:** Are you saying that the metal-to-metal hip joints were allowed on the basis of an equivalence test alone?

**Dr Heneghan:** Nobody knows this. A notified body has looked at the data and approved it. Nobody knows the make-up of notified bodies or their skill base, and nobody knows their transparent process of approving. At least in the US, when somebody puts in a process, I can get hold of all the 510(k) information and the clinical PMA off their websites. If we were to do one thing the next time, it should be to provide a bit of transparency so that at least you could look at it and say, “I wonder what clinical data was submitted.” There will be manufacturers who are conscientious and do this really well, with an evidence-based system in place, but there will clearly be manufacturers who use up that. The answer is that I don’t know, and I very much doubt that anybody knows apart from the manufacturer and the notified body; the MHRA certainly does not know.

**Professor Westaby:** I have just one comment. For many years the top American companies, such as Medtronic, Edwards, and Boston Scientific, have routinely tested their products in Europe. I have been in a position on many occasions to have had the privilege to use excellent new American technology five or six years ahead of the Americans themselves and then gone across to the FDA to present our findings, which they then approve. There is no doubt that the US uses European patients to test their devices, but that is a two-edged sword. We get fantastic technology earlier. I am very positive about MHRA and how it works. I took a concern to it about the particular heart valve that I mentioned and how it was being washed and so on, and the fact that I had confidence in the valve but not in the way that it was being dealt with. Its response was very prompt and effective; it did a very good job in preventing the sort of scandal, which would have been completely inappropriate, that we saw in the PIP implants. In my view, MHRA is very much under-resourced. It does not have enough people. There are hundreds of thousands of medical implants, and it is simply not resourced to look at them all. PIP was very unfortunate.

**Q6 Stephen Metcalfe:** Do you believe that there is no role for equivalence, therefore, in assessing class III implants—that it is too risky?

**Dr Heneghan:** You have to get your head around it. Say that Stephen here makes a wonderful device and takes it to a clinical trial, and it is shown to be effective. The problem is that you don’t incentivise anybody to do that, because the problem is that manufacturers around the world will then use equivalence to start making devices that may be slightly cheaper and come to the market. The problem is that we have no system in place to incentivise people to produce evidence. The problem with the system is that it is expensive to do clinical trials, and most device manufacturers are not like drug companies with £20 million or £30 million floating around; they are in the innovation stage and don’t have the money to do the trials. We have to get our heads around equivalence. The FDA in America will be moving their high-risk devices to PMA and asking for clinical trials on all those devices. You might say that that is anti-innovative, but you should ask yourself where all the companies are located around the world for making devices. People should be aware of the framework of quality, if we
want to build high-quality products and not lots of tat and rubbish. I am sorry about that, but that is the problem that we are facing. We will build these systems and then have other companies with equivalence come on board.

**Professor Westaby:** I don’t think that equivalence works. My biggest research thrust is with miniaturised artificial hearts, which are rapidly becoming equivalent to cardiac transplantation. I believe that they are very important, because the heart failure issue is a global epidemic and we have an off-the-shelf solution to it. However, you cannot say if one device works in an animal for five years that it will work in a human. We have had some big surprises that way. The way we have to test devices in this country and in the States is with animal work. I have tested an American device; in fact, I did the first permanent implant here and got the world’s longest survival with any type of artificial heart. People like me have to do this work with animals in order to get class III devices implanted, but there is overt hostility in this country to animal work and we don’t feel protected, so I have had to go elsewhere to do it.

**Q7 Stephen Metcalfe:** For those particular types of device, do you think that there should be an explicit, specific requirement to have some clinical evidence before they are approved?

**Professor Westaby:** Yes.

**Q8 Stephen Metcalfe:** Does anyone disagree with that?

**Dr Heneghan:** The system in 1976, as it was brought around in the USA, was expected never to have equivalence for implantable devices, but they were in a bind for pre-existing devices. So it was said that there were some devices from before 1976 where you could use equivalence but any device from 1976 onwards should have clinical trials. The great thing about industry is that if they can get round anything they will do it, and they have got round that to such an extent that the majority, even in the US, is equivalence, and they are worried about that. Even the metal hip went into the US system for equivalence, passed through the FDA and got used in their market. That has been a real bind for them and a problem, so they are coming to what you are insinuating. They are calling it total product lifecycle evidence: you build pieces of equipment, and they may go wrong in 20 years, so you have to build with quality for the long term, and that requires trial data at the outset.

**Q9 Stephen Metcalfe:** If we move from the use of equivalence data to more clinical data for the higher-risk devices, will that delay their arrival into market? You commented on having the ability to use products perhaps five, six or seven years before they get approved by the FDA. Will there be less of a benefit to the patient by moving to an alternative system?

**Professor Westaby:** There could definitely be, but I sit on a Food and Drugs Administration committee relating to artificial hearts and it has recognised that things have got to change dramatically. Your artificial heart is an example of the epitome of implantable devices. If one stops, the patient dies, and I have had that in this country. To test one of these miniature artificial hearts costs a company $1 million per week—their clinical trials cost $1 million a week. If I have a device, and I want it to go into humans soon, but my little company cannot afford $1 million, full stop. The FDA recognises that it has radically got to change the way that it looks at devices and licenses them. The clinical trials have got to be made accessible and far cheaper than they are now, because right now it just does not work. Animal work, as I say, does not necessarily translate into what you find with a human; there have been big surprises in the translation of animal work to humans. It has to be clinical, but it has to cost less. In my view, the NHS has got to support it far better than it does.

**Dr Heneghan:** Can I give you a perspective? It will delay things, but that is not a bad thing actually. Let us take a simple device, such as a blood pressure machine, which is an important device. If that machine is not accurate, it could have profound implications for who gets treatment and who does not. Beyond the CE system, the British Hypertension Society and the European Society of Hypertension have worked out that they need clinical studies, kitemarks and protocols to stamp on these devices to say they are accurate. That is profoundly important if you are going to put a million people on treatment, because if the machines are not accurate we will have major problems. We do it better for simpler devices than we sometimes do for the high-end devices. Will it delay things? Yes. With a new drug on the market, would you expect to say, “Let’s just see how it goes on for a few years”, and after a few years you put it through trials and then get NICE to look at it? The perspective is that MHRA is a different body from what NICE is and does for you. NICE says, “Is this drug safe and does it have any benefit for society?” That body is not in place, so there is an argument that you could look at something like NICE and say, “What is NICE’s remit?” There is a medical technology committee, a device committee and a diagnostic guidelines committee. Its remit should be to put a stamp mark on products and say, “Yes, this will give us some benefit.”

**Q10 Hywel Williams:** I don’t want to go off on a tangent about NICE, but doesn’t NICE operate differently in Scotland from the way it operates in England and Wales? It is a quicker process in Scotland. I might be wrong about this. Is there anything to be learned by comparing and contrasting as far as this particular issue is concerned?

**Dr Heneghan:** Certainly, and there is a lot to be learned about international collaboration as well.

**Q11 Stephen Metcalfe:** Why do you think those two separate paths have been developed? Why do you think NICE went down the route that it did, with evidence-based clinical assessment, and we have not done the same kind of implantable studies? Perhaps you might argue could have an equal impact on the patient?

**Dr Heneghan:** Yes, you could say that. NICE was set up for a postcode lottery in drugs and medications. They said, “We’ve got people using drugs over here and they are not using it there, particularly in areas...
such as cancer; we need a perspective across the NHS.” It is an amazing innovation to say that that is what we do, but then people moan because they have to wait a bit longer—but you are better waiting.

**Professor Westaby:** May I just say that I am on the NICE Medical Technologies Advisory Committee? Its remit is only to look at devices that are submitted for assessment by companies, and there is a paucity of devices submitted to NICE to look at. The American companies will not go anywhere near NICE; they can market their products without being involved with NICE. There is an understanding that NICE is a lottery; it is based on cost containment, and most important devices never go anywhere near NICE.

**Dr Heneghan:** However, the flipside to that is in the US medical area in their purchasing activity. They do their own sort of technology assessments and work out the value for money and effectiveness before they decide to pay for it.

**Q12 Chair:** Before we move on, may I ask you, Dr Woodward, what you see as the patient perspective on this part of the debate, on delays versus the benefits? Dr Woodward: I think I slightly clarify the role of the National Patient Safety Agency? It is about looking at the whole system and trying to make it as safe as it possibly can be in a proactive and reactive way in the incident reporting system that we run. We run a national reporting system, and anything that could possibly go wrong in the NHS is usually reported to us. From our perspective, we look at what it feels like and how it is perceived by patients, but it is also very much related to staff and how staff feel when things go wrong.

From a patient’s perspective, you absolutely expect that when you are going to go in you are going to have the right thing put in the right place at the right time. That is what you should have, and that is also what you expect, so you don’t question it. If somebody says you need a replacement, you don’t question where the replacement is coming from, whether somebody has tested it in the right place or whether it is the right piece of equipment for you. If somebody tells you that you need a hip replacement, you sweetly say yes, sign the consent agreement, and go into surgery. When you come out, if things go right, that is fabulous, but if things go wrong, it is a very hard system to cope with. When things go wrong, you are rarely told that they have gone wrong, and you are rarely told why, and you don’t quite understand what can be put right for you as an individual. You also start to become very fearful of the system. You don’t come back into it because it doesn’t feel right; that frightens you, so you don’t want to have it happen again. It is a very confusing scenario for patients when things go wrong, and it is almost an ignorant system before they go wrong because you believe that everything is going to be right.

**Q13 Gareth Johnson:** Professor Westaby, I presume that decisions that you make about which particular implants to use for your patients are based on medical need and the available information that you have at the time about medical data. Do you suspect that any decisions you have made would have been different if you had had full access to the pre-market medical data?

**Professor Westaby:** No, I don’t believe that any clinician working in the NHS ever gets access to the pre-market data at all. At clinician level, you are provided with an evidence base to some degree, depending on experience, and this is where registries are very important. There are now registries for all types of implant, and registry data tends to be more instructive than clinical trial data, because a lot of what is published in terms of clinical trial is done by enthusiasts in the best units under ideal conditions. In contrast, registry data tells you how everybody has got on with the product and you can pick up variables from registry data.

**Q14 Gareth Johnson:** Professor Westaby, we have heard calls today for a far more transparent system than is currently the case. Presumably, one of the reasons those calls have come forward is because it would have an impact on patients.

**Professor Westaby:** Yes.

**Gareth Johnson:** In what way do you think it would change the medical decisions that you have made if we had a far more transparent system?

**Professor Westaby:** I have always been an academic to a degree, so I have always looked for an evidence base for products before I have used them. That comes from a massive amount of literature in journals. I have to say that most devices in clinical use are sold by enthusiastic representatives. It is not so long ago that trips to international conferences, pens, biros and everything else were given out by companies, and clinicians would make subjective assessments on which type of heart valve, pacemaker or stent to use depending on the representatives that they liked the best and the companies that looked after them the best. That is the way that the English market has worked for an awfully long time. I think there is regulation about that. In the United States the regulations about these things are very tight now, and I think it is similar in the UK now. You are not allowed to make judgments depending on which rep you like the best.

**Dr Heneghan:** In America, they have a thing called the Sunshine Act, which means that the companies have to post exactly how much they may or may not be paying the individual, so you will be able to look up and see if Dr Carl Heneghan has received any money from one of these companies or manufacturers. That does not occur in the UK.

**Again, that is a great transparency issue. A lot of it is about being able to trust your clinicians to make good decisions and them not having conflicts of interest, and having access to the information to make the best decisions—that is what we are here about. At the moment, that clearly is not happening and most problems arise because it is still going on and there is a potential for conflicts of interest to occur. I, and you, have no way of knowing who has such conflicts of interest, but I can tell you that I have not been paid any money by anybody.

**Dr Woodward:** May I talk about the transparency issue in relation to the work that we have done, which

---

*23 May 2012 Dr Carl Heneghan, Dr Thomas Joyce, Professor Stephen Westaby and Dr Suzette Woodward*
might give you some clues as to how to think about taking things forward?

We were very nervous in the early days of making our data as open as it could be. We collect 1 million incidents a year—around 3,000 a day. That, to a member of the public or a patient, could be a huge cause of concern—3,000 things are going wrong in the NHS every day. If you put it in the right context and look at the levels of harm associated with those incidents, only a very small minority lead to severe harm or death, but you also need to be open about that. That creates a feeling of trust between the public, the patient and the data that you have and, therefore, the system in itself. What you have to do is to back that up to show that the system wants to learn from that information, so we don’t just collect it and stick it out in statistical form; we collect it, send it out and say, “This is what we are doing about it.” I think that creates a different relationship.

That also leads to a much better informed patient. For example, with surgery we have something called a surgical checklist. When patients go through the system, lots of things are checked off as they go through. Many doctors are very reluctant to use that, surgeons in particular, because they felt that undermined their clinical expertise. “I know what I’m doing. Why do I need a checklist?” But, actually, it empowers surgeons, the teams and the patients. They then use that to go through the system, feeling as if they are part of that system and not just being done to. The transparency of the data is incredibly important in creating a different relationship between patients and the health service.

Q15 Gareth Johnson: May I follow up on that? In your particular role, if we had a greater degree of transparency in the system, would any data protection issues for patients or patient confidentiality issues arise because of having a far more transparent system?

Dr Woodward: We have to adhere to all of those things, obviously, and the things that we report go through a certain level of filter so that individual patients would not recognise themselves in something that was made public and so on unless they had consented to it. You would not issue incident data that was very much related, say, to one speciality that was dealt with in one hospital that probably only 10 patients had experienced over the last year, because that has the potential to identify those people. We are very careful about data protection and confidentiality. However, in presenting this data, you can be very creative in explaining the statistical data that you have in a way that does not mean that patients say, “That was me.” They could say, “That kind of scenario sort of happened to me”, but not, “That was me.”

Q16 Graham Stringer: There are obviously exceptions, but there are many different standards among the regulatory bodies in southern and eastern Europe comparable with northern Europe. Is there any sense that manufacturers can cherry-pick where they go for authorisation for devices?

Dr Heneghan: Is there any hard evidence? No. Is there anecdotal evidence—for instance, when you look at the minutes of meetings of the FDA or the MHRA—and they bring that out and say that there is an aspect that is a cultural issue that is known about? Some exists in the minutes of MHRA meetings, but nobody has any hard evidence of that at the moment.

Professor Westaby: There are very definitely tendencies to direct your research to areas where you are likely to get ethics permission early for certain things.

I have a lot of trainees in Greece in units. I support heart failure units there that are starting to use artificial hearts. I can do far more in Greece that is wholly ethical much faster than I can in the UK. As an example, I am using miniature blood pumps instead of cardiac transplantation and using stem-cell therapy to make the native heart better. Now, I can get ethics approval for that in Greece, where it would take me two years in Oxford. All clinicians do this; there are American companies that will go straight to South Africa to test devices first. It is very easy to selectively go to areas where it is easier to get ethics committee approval in order to make your advances more quickly. That is not a lack of integrity; it is a very practical aspect of getting medical devices and new techniques accepted. You have to target your patient population and get ethics committee approval for doing your clinical trials; and, naturally, companies will go where they can do that quickest.

Dr Heneghan: We did some work with the BMIJ on metal-to-metal hips, and one of the notified bodies in this country is BSI, which put the kitemarks on. We got into trouble because we did not realise this. We said that BSI must have looked at it and given it their stamp. It was interesting that they came back and said, “We don’t even look at the product, so you got it wrong,” whereas it will look at prams or toasters and put its BSI stamp on them. We made a mistake, and we held our hands up to it when they said that. That gives you a whole host of loopholes, if you don’t even see the product. It is a completely odd system that allows all these things to happen.

Q17 Graham Stringer: If it can be used to make the treatment or the medicine more efficacious, can it also be used to get round the system so that less good equipment can get into the market quicker? Do you know what the balance between those two things is? It is probably an impossible question to answer.

Dr Heneghan: You would need to have access to look at that. It is simple.

Q18 Graham Stringer: Going back to the metal-on-metal hips, was that a regulatory failure, inasmuch as they should never have been allowed on to the market, or was it a regulatory success, in that they were found to be dangerous in some way and were withdrawn from the market?

Dr Heneghan: That is two questions. There was a bit of both there.

Dr Joyce: It is a failure. We speak to many hundreds of people, and these lives have been absolutely ruined. I would like everyone to go away with that reality. We have been here before. With the 3M Capital hip in the 1990s there were questions in Parliament, and the Royal College of Surgeons set up a committee, which said that there is no such thing as a small
change. So we come back to the idea of substantial equivalence. I have this amazing sense of déjà vu. That was approximately 5,000 patients in the UK and Ireland. When the DePuy ASR hip was withdrawn in 2010, there were nearly 100,000 worldwide. We do not know the exact number of this group of devices, metal-on-metal hips, but somewhere between 500,000 and 1 million people worldwide have been fitted with these devices.

**Dr Heneghan:** It was a success of the registries, but it was a success of the Australian joint registry in 2007. We have a system, but there are problems with our registries and our regulators. No. 1 is that they are not independent enough, potentially. No. 2 is that they are not taking heed, and I don’t know whether they don’t have the skills or the framework to say, “We could have known this in 2007.” Interestingly, the Australians had a very comprehensive joint registry in place, and Tom would know more about this. It was telling the messages then but they were ignored. There is plenty of information that I could send to the Committee to show that they were systematically ignored because the make-up of some of these bodies, including our National Joint Registry, was not independent.

**Professor Westaby:** The important point here is that the public get access to a lot of medical science through the media, and they get hope related to medical advances. If you are dying of heart failure or cancer and something appears that you can see will clearly help you with your last couple of years of life, you want access to that treatment. With long-term medical implants such as hips and blood pumps—artificial lungs are on the way—and all sorts of exciting technology, you would have to embargo widespread use for something like 10 to 15 years before you got your outcome data. When the BBC and Fergus Walsh say that stem cells and blood pumps are the future for heart failure and so on, and it goes out on the BBC and Sky, the patients are on top of you, and you simply cannot say, “We have to wait 10 years for long-term trial data.”

We are up in the air with this, and there is no good answer. Registry data, as I intimated earlier, is important, and the MHRA does it well. You have to take a leap of faith with devices. You have to look at them carefully when they appear, but you have to give the public access to the technology, and you then have to watch it with registries and regular surveillance. That is the way that you will pick up problems, but you cannot deny technology to the patients.

**Dr Woodward:** One point that you made was that regulation was a success because it picked it up. One of the crucial things is the speed of picking it up and the speed of response. If you take the aviation industry as the gold standard and places such as Toyota, they have a system whereby, if something goes wrong with one airline or even one flight, it is known throughout the system within about 12 hours. That is what we need for the NHS—a system whereby, if you pick up really quickly that something is going wrong, rather than wait for months and months, you need to be able to spread it around really quickly. Toyota has a system called stopping the line. The moment you know that something is not quite right, you stop the line. What we would want to happen when somebody picks up that things are going wrong is that you stop any future surgery or implanting or whatever, until you know that it is safe to start again.

Q19 **Graham Stringer:** Collectively, your evidence is very interesting and getting increasingly scary. Who should be responsible for post-market surveillance? We have had some evidence that clinicians do not report failures and difficulties as quickly as they should. What are the barriers to clinicians reporting problems?

**Dr Woodward:** We have studied this to a great extent, because our work is not wholly dependent but largely dependent on having a very good reporting system. If you know about the ‘stuff’, you can actually start doing something about it. So we work very hard to identify those barriers and to address them. There are a large number of them: I shall give you some, but not necessarily in the right order, as it were.

There is the lack of feedback. If you report something and you hear nothing back, you say, “What was the point in me going and doing that?” There is the issue of immediacy. If something is going wrong, you deal with what is going wrong. You deal with the patient, the family and the issues. By the time you have done all that and ended your shift, you will want to go off and do not necessarily come back and fill out an incident report. Incident reporting systems are seen as highly bureaucratic. Performance management systems make you end up feeling that you as a person or your colleagues are being blamed, rather than the organisation, the group or team that you are in saying, “This has obviously gone wrong. Let’s see if we can learn from it.” We need a culture of learning rather than punishment.

All those issues to do with time, bureaucracy, immediacy of action and the lack of feedback lead to not reporting. There are a number of crucial things that you can do, which are obviously the opposite of all of those, to encourage people to report—make it feel worthwhile, give them lots of feedback, make it a learning system and make them feel supported when things have gone wrong. There are some fantastic lines about “The best people make the worst mistakes”. People don’t go into the health service wanting to make it go wrong; they go in wanting to do their absolute best. They are traumatised themselves when things go wrong, and they want to learn just as much as the system wants to learn. You need to create an environment within which they can do that.

Q20 **Graham Stringer:** What is the proposed market surveillance system?

**Dr Heneghan:** There are a couple of issues. First, we need to ensure that manufacturers do this, and this is coming back to the PIP implant, which is quite an interesting one. In America, if you make a change even to the industrial grade silicone, you have to tell the FDA—you don’t have to do that in Europe, by the way; we can change products in Europe. When they asked manufacturers to look into all breast implants at the time, they lost 80% of the follow-up because it is
Dr Heneghan: That is a great point. The first thing is, how many hips failed?

Dr Joyce: It depends on the data you look at, but it was about one in two DePuy ASRs or about 50%.

Dr Heneghan: How many was that in absolute numbers?

Dr Joyce: Somewhere up to 100,000.

Dr Heneghan: I am sorry, but I don’t see how that can be rare. This is one where I could give you a number of examples. Medtronic was mentioned earlier; its bone cement was used off-label. That has been all over the world, and they are looking at that. There are a number of devices, including breast implants, so it is not rare.

With the joint registry, there are two things we want to do with devices. No. 1 is to work out whether it is cost-effective and does it make a difference or at least whether it is equivalent to what we already know. You can do that with benchmarks as well, saying that after three years you should expect to see things in the context of a trial. The second thing is that, when you put it on the market, a registry is set up to be a quality assurance system. You don’t know, but in 10 years cancers could appear, or in 15 years devices may fail catastrophically. It should be a quality assurance system; it should not be designed to be about causation—“Oh, it went really well.” The argument now is that we have only had device registries since 2003, so we don’t know enough about the long-term consequences. We should expect devices to fail, but we should also see them as being complementary to sets. There is a three-year benchmark for hips with NICE to say that you should get 3% revision rates at least and if you are above this you are out of range.

Q22 Pamela Nash: Do you think that this can be made from the existing NJR or do you think that we need to rub it out and start again?

Dr Heneghan: No. I think it can be within the existing NJR, but you need to think about who is going to run that, and its nature, structure and independence. You should think about how it ensures quality and that it provides information really quickly when it finds out what is going on—not that it delays information. We could sit in a room and think, “Well, let’s wait a year,” but that is potentially damaging.

Q23 Pamela Nash: The key point of my question is whether we should expand this to include all medical implants and not just joints. Is that something that would be helpful?

Professor Westaby: There are thousands and thousands of medical devices that impact directly on the body, and many hundreds of implantable things, if you include fillings in the teeth and so on. There is a big difference between one device failing lots of times and a large proportion of devices failing. I will go back and say that the vast majority of devices have been proven to be safe. All devices will break down sooner or later. Clearly the hip issue is very serious, because it needs revision. If a blood pump packs up, the patient can die. One of my patients died when his blood pump stopped, but it was because he had not taken a spare battery out. It is as simple as that; it is about compliance. When
implants fail, there is a large amount of emotive stuff around it, but I personally have confidence in what I said previously and that surveillance right now by MHRA is good. What you have to do is to persuade the clinicians to provide you with the data.

Q24 Pamela Nash: You also said that you did not think that it had the resources to do the job properly. Do you think that we now need to set up a registry of all implants that are used within the UK?

Professor Westaby: Registries are very good, and it is worth all class III implants having registries. Many companies have their own registries. The valve companies and the pacemaker companies want feedback. They are very keen to know if any of their devices go wrong. The current level of integrity in the device market in my view is very high and the regulation of the device companies in the States is very good, and—let’s face it—most of the devices that we use come from the States.

Q25 Pamela Nash: The fact is that most of that information is not centralised anywhere if it is registered by the company.

Professor Westaby: Yes.

Pamela Nash: And the next part of my question is whether we should be publishing data from the registry as it stands at the moment and if we were to expand it, which we cannot do if we have different registries.

Professor Westaby: Cardiac surgeons a long time ago set up a heart valve registry, a registry for mechanical assist devices and so on and so forth. You will find that the medical profession in many areas sets up its own registry, and this is happening more and more often. We feed information to the Department of Health and MHRA, and, if all branches of the profession did the same as the cardiac surgeons, then you would have the information that you want.

Dr Heneghan: You can take a perspective that is cynical or of being on the sidelines, but let us go back to the analogy of Toyota. If you own a Toyota car and there is a brake failure in one car, they know how to alert and get hold of everybody and draw them back. If you have a failure in your joint, or in your x, y or z, we have no system in place for saying, “Let’s use this to alert the 8,000 people who now have the implant.” That does not happen, and that is absurd. Your car is in a much safer position than the stuff that we put inside your body. That is what we are talking about.

Q26 Pamela Nash: Given my understanding of this, which you are expanding rapidly, would that not be a function of MHRA rather than a registry?

Dr Heneghan: No. The MHRA’s job is just to respond to manufacturer alerts and/or clinicians who alert them to x, y or z. Given how it is set up and its role in the system, it is in a bind. It can only impact on what it can do. All that it is saying is that it responds. It could take a more neutral viewpoint and say it could have more clinical data and so on, but it says it only responds. You could argue, in the case of the hips, that it could have responded earlier and taken a more uncertain viewpoint as opposed to this certainty viewpoint.

Dr Woodward: The MHRA sends out some alerts that alert the service to certain concerns on the use of devices or medicines. There is something about the timeliness of that which could definitely be speeded up. Actually, it is similar to the system that we have when we produce things called patient safety alerts or rapid response reports, as they are currently known. Lots of national bodies can send out as many alerts as they like and as much guidance as they like, but the crucial thing is implementation and compliance. There is a big gap between what we tell them should be happening and what they actually do. The key question is how we manage that bit. Is that the role of regulation, or is it the role of the local provider to police or monitor that, and how do we monitor it? We currently have a system called the central alerting system, or CAS for short, and people self-report their compliance with an alert. If we send an alert in January 2012, we expect it to be implemented in full—we usually give them a year—by January 2013. Over a certain period we expect them to report back to say, “Nearly compliant”, “Nearly compliant”, and “Compliant”. That is self-reported, and you can only spot check some organisations to see whether they truly are compliant or not, and we expect the Care Quality Commission in our respect to do that. At the moment, we have 99% compliance. Lots of people say that that is fantastic, but I disagree. I think that 1% non-compliance is really poor. You would not expect to go on an aeroplane or take a train journey and think that 1% of the things that they are supposed to be doing have not been implemented. You would be scared from point A to point B on your journey. Why should it not be the same in the NHS? If you are issuing an alert and it is because there is a problem—you have really good evidence that there is a problem and you can tell people that they should be doing something about it—people should be compliant with that, and that is a big issue.

Dr Heneghan: There is a real problem with timeliness here. The MHRA committee on safety of devices said in 2006 that there is growing concern over the biological risk of metal wear debris, yet it was March 2012 before we came to a decision. Going back to your other industries, I cannot imagine getting on a plane and saying, “We have a problem with wear debris.” How does that get communicated? People need to say, “Hey, we need to draw back now. We need to stop and think about patient safety.” There is an issue here that we should not be sitting here doing this now; we should have been sitting here four years ago.

Q27 Pamela Nash: Before we move on, Dr Joyce, you mentioned in your evidence that you thought it would be helpful to conserve explanted joints. First, would you address the earlier points I made? Do you think that we should have a registry of all medical implants, and should it be published? Secondly, on the final point, if you are able to give us any examples of when that has been of advantage it would be really helpful.

Dr Joyce: It is one of those things where you could argue it could have more clinical data and so on, but it says it only responds. You could argue, in the case of the hips, that it could have responded earlier and taken
Dr Joyce: I think that the registry should be expanded to all artificial joints. On implants, I am not sure because it depends on the implants. One thing that we need to point out, which was alluded to earlier, is that, if you are going to have a heart valve put into a patient, they are probably in a life-threatening situation. That might be one situation, but with a hip with osteoarthritis it is not the same.

The other thing is that pre-market testing is crucial. It is certainly my experience, in the case of the DePuy ASR, that there was no need for one of them to go into a patient. That could have been identified by pre-market testing. They had the machines and the equipment, and those tests could have been done.

To answer your other question on explants, again I mention Toyota. If there is a problem, what do you do? One of the things we do is to go into a workshop and say, “That is all that I am suggesting. Similarly, with plane or train crashes, you look at the bits and pieces afterwards. At the moment, it is just not done with hips or knees. Most of them are just thrown away. To be honest, without the work that we did I am not sure whether ASR might still be on the market now. We want to get it done that you are not just sharing that information, saying, “We think there is a problem,” and having scientific publications produced which share this information.

Q28 Hywel Williams: We have already talked about public perception and public understanding of this entire issue and how important that might or might not be. I have a feeling that you are in a situation where you need a lot of help and support, you are in a lot of pain and you are very vulnerable, Dr X or nurse Y will say, “You need to have this. Please consent.” It is a bit like looking at the terms and conditions to some of the things that you sign up to on the internet. You just tick “I agree” and get on with it. It is only when it has gone wrong that you start to rationalise why you said yes to this.

Professor Westaby: After 40 years in the medical profession and at least 35 at the sharp end, I can tell you that very few patients actively take an interest in their treatment. They want to know that they can trust their doctor and that the doctor will give them the best advice. I am sure that this resounds with you. No one has heard of MHRA or at least until the recent issues. There are many bodies involved in safety now, and it is bewildering for the patients. But, because of the internet, let us say 5% of patients are avidly interested in what is going to happen to them. They tend to be the academics and people who are obsessed with healthcare. For the sake of those 5% of patients, I think that we are absolutely going to have to make information like this available on the internet. We are going to have to publish registries for different types of implant. We are going to have to publish mortality rates for different procedures. It is already happening in cardiac surgery. Many surgeons are having to drop out because their mortality rates are already perceived to be too big. I shall shut up now, Mr Chairman, because I know that you don’t want to divert into another area.

Q29 Chair: Having listened to Dr Woodward’s last response, I think that some of your colleagues are going to have to learn how to communicate to patients in English. Issues of probability are not easy concepts to put across to patients, especially when they are ill.

Professor Westaby: Absolutely.

Chair: There is a serious challenge to the medical profession about how to do that better.

Professor Westaby: Absolutely.

Dr Joyce: We sit down with patient groups and let them talk together. We have focus groups, and they produce minutes like this; I shall pass these round. They say things like, “Why does a GP ignore tests?”; “My GP does not understand the information and cured if at all possible, or helped and so on. It is usually when things have gone wrong that they start to try to find people in the system to help them figure that out. On the issue of consent, a lot of people compare the system in the US with that in the UK. In the US you are told about absolutely every single possible thing that can go wrong in major, major detail. In the UK we are veering towards that, but what you have got to do is to explain that in a way that is genuinely understood, because risk is a really hard thing to understand. If you say that you have a one in 10 chance of this happening to you, what does that really mean? Do you think that you are the one, or do you think that you are one of the nine? If you happen to be the one, will you think that the nine people behind are okay? I know that I am being simplistic, but it is a really hard concept to get across to patients.

The other aspect is choice. If you are in a situation where you need a lot of help and support, you are in a lot of pain and you are very vulnerable, Dr X or nurse Y will say, “You need to have this. Please consent.” It is a bit like looking at the terms and conditions to some of the things that you sign up to on the internet. You just tick “I agree” and get on with it. It is only when it has gone wrong that you start to rationalise why you said yes to this.

Professor Woodard: I am not sure as a patient that they really want to know about the role of the MHRA or what the NPSA or NICE do. They just want to have their problems addressed and to be pain-free and
Dr Heneghan: May I come in on this issue? In my experience as a GP—perhaps this is a reflective—I think that people do want to know what is going on. Increasingly with the internet age, they are becoming more sophisticated and more knowledgeable. Boy, every time they walk in I say to them, “What have you looked up? What do you think is going on?”, and they know what is going on. People do want to be informed and they do want to know. They take an interest in what we do, and we should particularly explain the decisions that we make better, why we do not have access to certain treatments and why we need to do this. We do it really poorly, and we need to take a perspective on that.

Q30 Hywel Williams: How could notified bodies and manufacturers be more publicly accountable for their role in certifying products? Should the work of the notified bodies be conducted by public organisations such as MHRA?

Dr Heneghan: You are in a bind there, and the Americans find this. If you try to do it with a public organisation, you will need a massive organisation and it will become very costly very quickly. Whichever way, the manufacturer will have to pay for it. The US FDA does this. The solution is to make it transparent. It is to say, if it is a notified body, we are in the UK and we need the information to be made available. Let’s try to do it one; let’s look at it online. They will argue that there is commercial confidentiality in those documents, but the clinical data should never be commercially confidential. There may be design aspects that they cannot give, and I am happy with that, but let us publish the clinical data. If you did that tomorrow, I would be on the case working out what is going on. I have been trying to do it for three years, and I cannot do it.

Dr Joyce: I agree with that need for transparency. With artificial hips or knees, they should tell us how they have been tested and what the results are, and share it with everyone. If there is nothing to hide, why not?

Dr Heneghan: There is another route as well. You should never have a situation where someone suffers because of a problem?

Q31 Hywel Williams: I move on to my final question. Who should bear the costs of corrective surgery and public health messages when an implant is found to be unsafe? For example, with PIP we have a difference between Wales and England.

Dr Heneghan: If you wanted to fund independent registries, they are very cheap. When I was in Australia, it worked out at about 20 Australian dollars per patient entered; that is one. The first is registries from a manufacturer.

The second is what is wrong with an insurance-based system? Here is another analogy. If your plane crashes or your plane company goes bust and you are in Spain, they have to get you back. They will fly you back. What is wrong with having an insurance-based system equivalent to the level of evidence? It should go down as you promote it. If the device has 20 years and not many problems, you won’t need much insurance; but in the early days it is going to cost a lot of money for some of these devices.

Q32 Stephen Mosley: Dr Woodward, you talked about risk in your previous answer. When we were talking to the MHRA, it gave the quite simplistic case of bed rails, saying that patients had been trapped by a bed rail and injured. They looked at it and thought that it was bad news, but when they actually looked at the data they found that you were at much greater risk of falling out of bed and injuring yourself in that way than you were from a bed rail. You therefore have to take a risk-based approach.

You can see, with some of these implants, that if someone is going for a hip replacement they need the replacement, but if problems occur two or three years down the line where does the ratio of risk apply? Are you trying to suggest, between you, that if you have a situation you should be upfront and honest about it and say, “Look, if you have this operation there is a 50% chance that it might go wrong in a few years”? Are you saying that that is okay if you are upfront and honest about it so that professionals such as yourselves can make the right decision, or are you saying that that should never happen and that you should never have a situation where someone suffers because of a problem?

Dr Heneghan: Let me clear about it so that you understand. There are three classes of device—class I, class II and class III. The bed rails are a class I device and you get a CE marking, rather like you get for a teddy. It is a bed rail, it is to standard and you hold that documentation. Yes, they will fail, but that is okay. Actually, there is a system in place that probably deals better with class I devices because there will be slight problems—boils fail and all these sorts of things. That will happen regularly. For that, the current system is okay because they are low-risk devices, and you hope that somebody would put up a better system for patients and the public, probably like the Yellow Card system, so that you can communicate that better.
However, let me be clear that when you are talking about class III the capacity to do harm to a number of patients is so great. It is like with a drug: if there is a problem with a drug tomorrow, we can stop you taking it. You can have hundreds of thousands of patients with a hip inside them, who are saying, “What do we do? Can you take it out tomorrow?” You can get rid of the bed rail tomorrow; you can change it; but you cannot change something that is inside somebody. So you want to know really quickly what is going on if it is going badly.

**Dr Joyce:** On the point about being upfront, most hips are excellent. It is just some of the modern designs that have failed. However, when we talk to patients, they tell us that when they went to see the surgeon, he said, “This will last 30 years. You will be horse riding and skiing.” The patient will say, “I have never skied in my life or ridden a horse.” The patient is left in a situation where they are expecting some brilliant device that will last for 30 years, and then suddenly they have pain and they are ignored. Eventually, they find out that there is a major problem with the hip. They are not alone. Then there are the long-term concerns about the potential cancer risk, with these metal particles travelling around the body, and we still don’t know the long-term implications of that. I think that no one was upfront about that with the patients that we speak to.

**Dr Woodward:** People underestimate the actual skill required to do a really good risk assessment. You obviously need to understand the risk of doing something versus the risk of not doing something. Then you need to show the risks in the short term, the long term and the medium term. You need evidence behind all of that if you are going to do it really well, so it is not about gut feelings or intuition but about history and evidence over time. That would cover your clinical patients and your clinical outcomes, the research, the audit, the patient safety and incident data and the case note review methods that people use. There are also fancy tools that you can use, such as failure modes and effects analysis and hazards analysis and all sorts. You need some skills in order to do that.

Once you have made the probability assessment, you need to use those skills to turn it into something incredibly simple in order to communicate it. It is not as simple as saying, “This could happen to you tomorrow and you need to be aware of that.” It is a balance of probabilities, as they always talk about, and that is a really hard thing for clinicians to do and a very hard thing for patients to take on board. Then we have to weigh all that as a matter of judgment, asking ourselves whether or not we do it and what are the options.

**Dr Heneghan:** In the current situation, it is impossible to do that because nobody has any data on the effectiveness of devices. In lots of situations you will say, “We will tell you how it should perform at some point in the future.” It does not matter how much we discuss the ins and outs; the key for lots of devices is that we cannot generate the information to inform patients in the first place—until perhaps at some point in the future.

Q33 **Stephen Mosley:** Do the MHRA and the other notifiable bodies—the regulators—have the expertise and the skills to do that?

**Dr Heneghan:** It is interesting when you look at the make-up. In terms of organising a regulatory body and what it should look like, the answer is yes. In terms of how they look at the data and how they communicate that data, it is no. The Americans have realised this and set up a network to support them from epidemiology and statistics-based centres and made them independent. The key is that you want people who will look at the data and be able to unblind it and produce that data in an independent and transparent fashion, in a meaningful way. We already do this with drugs. In clinical trials you have stopping rules that are built by smart people, and if things are going wrong they can unblind it and say that it is not working. There is a nature problem in the make-up there. It is the same with the joint registries. You have to think about who you want, particularly for understanding the data and the independence.

**Professor Westaby:** I sense that we are getting down the line with this. Right now, I would make one caution. It is that the NHS is becoming so stiff in bureaucracy that it can hardly move. If we are not very careful, it will just grind to a halt. I will tell you frankly that the amount of scrutiny that was levelled at heart surgeons after Bristol has put people off in this country from going into the profession. We have to do the right thing for the patient, but virtually the whole conversation this morning has revolved around one breast implant, one hip and one valve that was not really faulty but which was not used properly. We would take a long time to make a list of 20 devices that had gone wrong in this country. I would reiterate that, if we are not careful, we will make the whole system so bureaucratic that it will not move at all.

I shall finish by saying that, when we contacted MHRA about the anxieties about that one heart valve that was not being washed properly, an alert went out about it within one week to every single cardiac unit. In two weeks the MHRA knew everything about how many valves had been used and in what centres, and everything else. I thought that was a very fine response and they did the right thing. They cannot do that for absolutely everything because there are not enough people and, in my view, they are under-resourced—like the whole of the NHS. You will not be surprised to hear that several eminent members of MHRA are going to leave imminently. Quite simply, you can only put so much attention and flak in one direction before people do not want to be involved.

**Dr Heneghan:** The key here is combining innovation with patient safety. That is what we want. We want to be global leaders in industry and to bring work here, but when you look at where all the companies are located most of the device companies are located in America; most of the drug trials are done in America; and two thirds of the regulatory trials are done in America. They have a tougher, tighter regulatory framework and they are about to make it tighter, which will incentivise their companies to build higher-quality products. In the end, you will acquire quality
and you will win. In the short term there will be lower-quality products; yes, you will have lots of little industries making a lot of little bits of devices here and there, but we want to be the Formula 1 of the industry. That is what America has realised. So the argument does not wash when people go, “We’ll not have a business if we become more regulatory.”

Professor Westaby: There is a perspective here. You may say for very high-risk devices that the MHRA should at least take a sample of them and say, “Let’s audit a sample of these”—perhaps 10% or 20%. You have to start somewhere. We cannot suddenly say tomorrow that we are going to put a load of work on here; you will need to increase the work load. You would start with some perspective and say, “Let’s start towards it with a sample and then move forward.” If you find problems you will have to expand that, but if you don’t find problems you can carry on with the audit.

That is exactly what the FDA is doing. The FDA even go out and visit manufacturing plants—surprise, surprise. Do we do that in Europe? No. Will we be able to effect the EU regulatory framework to do anything? Probably not, but we can effect our regulator.

Professor Westaby: You would have to disassemble and chemically analyse every implant that was presented to you. The number of independent experts needed to do that, even before you started the clinical assessment of a device, would be massive. You are pushing us towards a situation where the whole thing will be so stiff with bureaucracy that it will not move. On cardiac transplantation, I can tell you that if we applied the stringent criteria that we are suggesting for donor organs and donor hearts you can forget it. That would be transplantation gone right now.

Chair: Let me assure you, Professor Westaby, that we are not pushing you anywhere. We are simply seeking evidence.

Professor Westaby: No; I know that.

Dr Heneghan: May I come in here? In the USA, Steve Nissen looked at the American system and the number of devices that had failed. For cardiovascular devices, there were 76; that was the highest, so there is a lot going on. What Steve Nissen found, which was a really interesting issue for the FDA, was that 90% of them had gone through the 510(k) route. Of the ones that had gone through the pre-market approval process, very few failed. Some manufacturers are incentivised to produce evidence in clinical trials, but those who build a wonderful piece of kit have not got a system in place to stop somebody six months later using a 510(k) equivalent to bring the same piece of kit to the market. With global expansion, the number of equivalent devices is going to get worse.

Q34 Stephen Mosley: Turning to the PIP breast implants, I think it was you, Professor Westaby, who said that it was not a problem with the regulations as such. It was more that the application was in effect fraudulent. They were claiming that there were different things in them, basically. Should the regulators just be looking at the data that manufacturers supply, or should they be looking to see whether they are doing as they say? Should they be looking beyond the data? I know that you can do that in the long term if you have a registry and look at how effective things are, but when someone comes upfront to get approval, should you just be looking at what they are telling you or should you be trying to get behind it?

Dr Heneghan: There is a perspective here. You may say for very high-risk devices that the MHRA should at least take a sample of them and say, “Let’s audit a sample of these”—perhaps 10% or 20%. You have to start somewhere. We cannot suddenly say tomorrow that we are going to put a load of work on here; you will need to increase the work load. You would start with some perspective and say, “Let’s start towards it with a sample and then move forward.” If you find problems you will have to expand that, but if you don’t find problems you can carry on with the audit.

That is exactly what the FDA is doing. The FDA even go out and visit manufacturing plants—surprise, surprise. Do we do that in Europe? No. Will we be able to effect the EU regulatory framework to do anything? Probably not, but we can effect our regulator.

Professor Westaby: You would have to disassemble and chemically analyse every implant that was presented to you. The number of independent experts needed to do that, even before you started the clinical assessment of a device, would be massive. You are pushing us towards a situation where the whole thing will be so stiff with bureaucracy that it will not move. On cardiac transplantation, I can tell you that if we applied the stringent criteria that we are suggesting for devices to donor organs and donor hearts you can forget it. That would be transplantation gone right now.

Q35 Chair: Let me assure you, Professor Westaby, that we are not pushing you anywhere. We are simply seeking evidence.

Professor Westaby: No; I know that.

Dr Heneghan: May I come in here? In the USA, Steve Nissen looked at the American system and the number of devices that had failed. For cardiovascular devices, there were 76; that was the highest, so there is a lot going on. What Steve Nissen found, which was a really interesting issue for the FDA, was that 90% of them had gone through the 510(k) route. Of the ones that had gone through the pre-market approval process, very few failed. Some manufacturers are incentivised to produce evidence in clinical trials, but those who build a wonderful piece of kit have not got a system in place to stop somebody six months later using a 510(k) equivalent to bring the same piece of kit to the market. With global expansion, the number of equivalent devices is going to get worse.

Q36 Stephen Mosley: How important is the MHRA’s committee on the safety of devices? How effective is it at giving expert opinion? Should it operate more transparently that it currently does?

Dr Heneghan: I have been looking at this for three years, so I know quite a lot about it. First, there is an issue about declaring and thinking through the conflict of interest issue, what it should be, what the make-up of that should be and what is the best perspective to do that. At the moment you have a mixture of people from industry and non-industry on it. At the end of the day there will be conflicts of interest. I have conflicts of interest; everybody does.

The second issue is that we should start to expand it, because it is not big enough to deal with the numbers, the size and the amount of work load going on. You have just one device safety committee meeting every few months, and it is not big enough. The complexity of the issues is important and difficult, and I don’t think it is currently equipped for that role.

Q37 Chair: I have one final question. One of the things that is happening in the world of medicine is this extraordinary convergence of technologies—for instance, the way in which engineering is now so fundamental to medicine. Are we heading towards a regulatory problem in some respects? For example, Professor Westaby, some of the stents that some of your colleagues put in will release chemicals.

Professor Westaby: Yes.

Chair: And there are other devices that are designed to release medication into the patient. Is a point arriving when the convergence of pharmaceutical and engineering technologies and surgical skills will require a different approach to the regulatory structure?

Professor Westaby: It is there already. For instance, I use plastic tubing that is coated with heparin. I am working on a total artificial heart with a professor of bioengineering, who is going to line the device with stem cells so that the propensity for clotting within the device is much less. Yes, the complexity of artificial organs is moving on at a great pace.

One very interesting thing that has not been mentioned is cost containment in devices. Every one of the small artificial hearts that we can use instead of transplants these days costs the same as a Porsche car. It is a tiny thing, so why does it cost the same as a Porsche? It is not that it is more complex. It is because of all the regulatory issues and risks associated with an implantable device. To get around that and to make this sort of thing accessible to British patients on the NHS, we put together a company to make a far less expensive device that is probably even better, but it is here in the UK. We are doing that, and there is a lot of
interesting work going on in the UK that will combine biology with mechanical technology. It is becoming very interesting, and it is going to be very good for patients. For enormous groups of patients, like heart failure patients, there is an enormous imperative to get this technology available quickly. If we make regulation more bureaucratic, there will be another whole generation that we cannot treat in the way we should, according to current medical science. That is why I am kind of worried about anything that will put the brakes on more than we have already.

Dr Heneghan: That is a very good question. What you have described is a device with a drug in—heparin or stem cells. That means that it has to go through the drug regulatory pathway and through the usual clinical trials. It will require two randomised trials to be implemented, and it will then be submitted to NICE guidance. Take the heparin out of the stent and you don’t need any of that—you can use equivalence to bring it to the market.

The key of what you allude to is whether we are going to look back in time and think that it is ridiculous. Yes, it is a bit like 50 years ago with drugs, when we had a situation with Thalidomide, and look what happened then. Under the current system, if we don’t do something different, at some point a device will come on the market that will cause something catastrophic that will make people stand up. Currently, we have not got that yet.

Dr Woodward: This may be a very simplistic answer, but my simple approach is this. As the system gets more complex there should still be the same principles, no matter how complex it becomes, or how innovative or technical it becomes, or how much more technology there is. The simple principles are: is it safe, is it effective, does it meet patient needs, does it pose the least risk and all those things? There are some key principles that will apply no matter how complex the health service becomes.

Chair: May I thank the panel for a very informative session this morning? If you have any additional thoughts, we would welcome a note from you because this is clearly an issue that is considerably more complicated than most people realise. Thank you very much indeed.
Members present:
Andrew Miller (Chair)
Gareth Johnson
Stephen Metcalfe
Stephen Mosley
Pamela Nash
Sarah Newton
Graham Stringer
Roger Williams

Examination of Witnesses
Witnesses: John Howlett, Head of Notified Body, British Standards Institute (Healthcare) (BSI), Peter Ellingworth, Chief Executive, Association of British Healthcare Industries (ABHI), and Mike Kreuzer, Technical and Regulatory Executive Director (ABHI), gave evidence.

Q38 Chair: Gentlemen, I welcome you to this morning’s hearing. For the record, I would be grateful if the three of you would formally introduce yourselves.
John Howlett: I am John Howlett from BSI, a UK-notified body.
Peter Ellingworth: I am Peter Ellingworth, chief executive of the Association of British Healthcare Industries. We represent the medical technology industry.
Mike Kreuzer: I am Mike Kreuzer, the director in charge of regulatory affairs for ABHI.

Q39 Chair: Perhaps I may start with you, Mr Ellingworth. Tell us a little about whom you represent in the field of implants and why it appears that none of the businesses was prepared to come and give evidence this morning.
Peter Ellingworth: We represent the medical technology industry in its broadest sense. That is everything from simple syringes and dressings all the way through to active implantable devices. The industry itself employs about 64,000 people; it is comprised of many small and medium-size enterprises in the UK. We probably represent about 75% of that industry, and we have in the order of 250 members. We operate with a mandatory code of practice for our membership as well. Our job is to represent that industry and to provide a broad industry perspective on major issues. Essentially, our role is to ensure that we create a positive environment for the uptake and diffusion of technologies that are safe and effective for patients.

Q40 Chair: And the second part of my question? Peter Ellingworth: Indeed. As far as we were concerned, it was our role to represent the industry, and the decision by companies is entirely up to them. We do not have any particular authority over those companies.

Q41 Chair: You are not particularly surprised that none of them wanted to be here and explain to us how good their products are? Peter Ellingworth: Indeed. We are more than happy to be here and to do that representation for them, but there are no particular issues from our perspective. Often they would expect us to take that role, and certainly we will speak openly and frankly about any issues you wish to raise.

Q42 Stephen Metcalfe: Did any of the companies who had been approached ask you to represent them here?
Peter Ellingworth: No one has particularly asked us to represent them. We get involved with the Department of Health, BIS and many other Government Departments. It is normal business for us to represent those who are our members rather than any individual company. We will not talk for an individual company. If you ask me a particular question about a company, I would not answer that simply from an equity perspective, but, broadly, I am very happy to discuss anything that you wish today.

Q43 Chair: I want to move on to you, Mr Howlett, and ask some questions about equivalence data. If the other panel members have comments they want to make, please feel free. Are you content to rely on equivalence data when certifying new implants?
John Howlett: Our role as a notified body is to ensure that the manufacturer meets the essential requirements for clinical data established in Annex X of the directive, supported by guidance in MEDDEVs, and the clinical data are established through literature or literature and a clinical investigation. If the clinical data are established in Annex X of the directive, supported by guidance in MEDDEVs, and the clinical data are established through literature or literature and a clinical investigation. If the manufacturer goes down the “literature” route, which is essentially the equivalence route, the guidance is well established, and as a notified body we follow that guidance. We do not make the rules; we implement them. The system is different from the one in the FDA with their equivalence. We do not work with the term “equivalence”. The data have to be sufficient in literature or literature and trial form to meet the essential requirements of the directive.

Q44 Chair: Is that because there are difficulties in conducting clinical trials in some cases? John Howlett: The decision on a trial has to be made in the first instance by the manufacturer. Trials are by nature costly for the manufacturer to set up, but we challenge the manufacturer on the availability of the data. In the FDA, the equivalence aspect is based on a predicate device; our measures are really against the essential requirements of the directive.
Q45 Chair: If I were a customer for an implant, I would want to know what data were being relied on to give me some confidence in the product that was going to be put inside me. Would it be better if that information was available to the patient and the doctors?

John Howlett: I think transparency of the data to support compliance would be beneficial. That is a role for the regulators. The notified bodies cannot make that information public, but, in the interests of transparency, I would support that. I think it would be better, yes, to have a clear indication so that the public, in the interests of patient safety, can visibly see the route and compliance either through clinical literature or trials.

Q46 Chair: I noticed that Mr Ellingworth was nodding at that point. Transparency of data is a simple thing, but would more stringent regulations risk losing some of the industry to overseas manufacturers?

Peter Ellingworth: Of course we would have to take a look at what was required, and “proportionate” is always a good approach. Safety comes first. The industry is going to support anything that improves safety. We are supportive of improving transparency. The devices directives have been around for 20 years now and have been through a number of improvements. With any process, we are supportive of continually improving it. There might be some requirements that could be an issue for smaller businesses because they have more limited resources. Essentially, the UK is made up of 2,500 small businesses in this sector, but, of course, every problem has a solution. We would be very positive about anything that improves patient safety.

Q47 Chair: Your understanding would be that we could mandate the issue of transparency to British companies, but as to things that have been approved in other member states, could we mandate it to them?

Mike Kreuzer: No. It is a pan-European system and works in the same way right across Europe. Transparency is an extremely important topic. Greater transparency will be introduced in the revision that is currently taking place. There are plans for that, which I am sure you will be hearing about later from the European Commission, and it is something we completely support. There is definitely a need for greater transparency.

Q48 Stephen Mosley: Mr Howlett, could you briefly explain the resources and expertise that the BSI have in order to assess implants?

John Howlett: I am sure you have read the guides we have put through. A conformity assessment essentially is made up of two parts. Most manufacturers would go through an Annex II route, which would require a quality system assessment. We have in excess of 200 assessors around the world doing medical and conformity assessments. Then it is based on the technical documentation and on classification. As to an implant, generally we are talking of IIB, which is high to medium risk; if we are talking about any of the up-classified items, like hips, knees, shoulders and breast implants, we are talking about class III. As to our expertise, we have highly qualified reviewers from industry and the universities where they have been involved in the design and development of those particular products.

Q49 Stephen Mosley: Moving on to the faulty metal-on-metal hip replacements, in particular the degree of recall, do you think a breakdown in regulation allowed these faulty metal-on-metal hip implants to be used in the EU market for so long?

John Howlett: We have talked about transparency. With any device there needs to be a strong post-market surveillance system. Much work has been done, and all of us as notified bodies are looking at that in greater detail against current expectations. Post-market, it is all about having early warning systems, gathering of data and registries, and that information would give an early warning about the medium and long-term events that would happen with a device.

Going back to the equivalence or clinical trials, we have to realise that the metal-on-metal device has been around for decades. What we have seen recently is not an indication of a failure in all those devices. The devices have performed against their essential requirements—the test methods—and we and the manufacturers would have tested against those standards. Short-term compliance on wear and fatigue is all carried out in the design phase. The medium and long-term effects have to be coming from post-market. It is unreasonable to think that we can predict 10-year performance if we are looking at hip joints and, say, 90% success after 10 years. It is not reasonable to think that you can do that through a clinical trial. It is a combination of test data and doing all you can to demonstrate patient safety in the short term, and then monitoring for any further medium to long-term effects through the post-marketing phase.

Q50 Stephen Mosley: You have said what needs to be done and you have given a good idea of what should be done. What was actually done in this specific case? Was all of that done or not?

John Howlett: I cannot answer on specific cases. As a notified body we work with a number of clients. I can talk in general terms. The notified body would assess the manufacturer’s data—bench testing—because, obviously, you do not want to put any patients at risk initially. You do all that you can through bench testing, literature and clinical trials as best you can, but you will not get trials that will continue for 10 years. Patients have to be considered in this, to bring innovative and good technology to patients’ use, and to follow up the medium and long-term effects is not reasonable. In any situation where we have a manufacturer, we would assess the company’s system, design dossiers and technical files against those essential requirements.

Q51 Stephen Mosley: I can understand you not wanting to talk about particular things, but can I specifically ask about the impact on BSI? Do you think that BSI has suffered reputationally because of the recall?
John Howlett: I would hope not. We are in a high-risk business. The products that go to the market have to show benefit over risk, and that is a judgment the manufacturer has to make. It is a judgment that the notified body has to challenge and agree with if it is to certify that product. We are assessed in doing our duties as a notified body by the MHRA. We are rigorously audited both in the office and on site for the audits. I believe that our application of those duties is in compliance.

As to reputation, I could not really answer that. I hope people would see that, as a leading notified body in this industry, that would be recognised, and recognise that, although we get small numbers of devices that may show some fault, in the main, the system is generating devices for patients to ensure patient safety across many hundreds of thousands of patients in the EU, which are performing perfectly satisfactorily.

Q52 Stephen Mosley: Could I just ask the other witnesses, and also add this: what do you think the public accountability should be of the notified bodies? Peter Ellingworth: Public accountability is taken care of in the Medical Devices Directive. One thing I would like to comment on is the National Joint Registry, which is a fantastic aspect of what we have in this country. Clinical registries, led by the cardiac one several years ago, are a great way of ensuring patient safety and continuing to ensure it. Again, they can be built on. The National Joint Registry is now mandatory, and it looks at revision data. We are now engaged in discussions to see how that can be improved further to continue to try to pick up aspects. Mr Howlett is correct in saying that the real challenge is about doing a 10-year clinical trial, but the National Joint Registry is there and is a real asset for us in this country, and we can continue to work on improving it with clinical professionals as well.

Mike Kreuzer: It was the NJR—the National Joint Registry—that picked up the metal-on-metal issue in this country.

Q53 Roger Williams: I was fitted with a metal-on-metal hip about four years ago. It seems to be working very well, but last year I was recalled to the hospital where it was fitted and I had an x-ray and blood samples were taken. At the same time, I received a letter from somebody volunteering to represent me in any legal case I could take against the firm. Can you tell me from where that information was likely to come, and should my medical history be in the public domain? John Howlett: I personally could not answer that. Peter Ellingworth: No, I do not understand where that information would come from. Mike Kreuzer: I have no idea.

Peter Ellingworth: I believe that in the case Mr Mosley mentioned, they are taking great pains to make sure that patients are looked after, but they would not be sharing any information about patient names. That really is quite strange. I do not know where that would come from.

Roger Williams: Thank you. I will continue my inquiries.

Q54 Sarah Newton: I would like to pick up where my colleague left off on auditing and particularly ask John Howlett about how the MHRA audits BSI and, in turn, how you audit manufacturers. John Howlett: I believe the MHRA is one of the strongest and most recognised of the competent authorities in Europe. It audits us regularly with auditors who understand the quality systems side and with product experts to assess what we are doing in terms of a review of the dossiers. It would also send in its clinical experts to look at our review of clinical data that we talked about earlier. I believe that is a very robust system. Representatives from other member states have joined those audits by the MHRA. We are one of the few where there has been a common playing field and even, consistent application, with people coming from other competent authorities in Europe. In addition, it audits us on all the medical directives. We are talking here mainly about MDD 93/42 for implants. It would observe us carrying out audits of manufacturers during our surveillance cycle. Our audits of the manufacturers follow all the guidance in terms of the harmonised standards that support the directives. We are auditing the manufacturer against the requirements of the directives and all the MEDDEV guidance that goes behind that. We are involved in improving the guidance. We work with the Commission at NB-Med and Team-NB meetings in pushing for and getting better guidance in that area. Obviously, we are not the authors of that; we help and inform, but we operate against that guidance. As a notified body that is all we can do, and we lobby for improvements in the areas that we do.

I think BSI has been very strong and instrumental in doing that. You have probably seen from the papers we have provided that on NB5 we have a code of conduct that is generated by the notified bodies to improve the regulation, so it has come from within the notified bodies. In the absence of greater control from outside, we have helped generate that with a number of the other leading European notified bodies to the point where the Commission are looking very favourably at that initiative to improve the consistent application of our work against the directives.

Q55 Sarah Newton: How many of the BSI members you have approved through the audit process have you subsequently found to be wanting in some way and not meeting your high standards? John Howlett: That happens. I could not give the numbers offhand, but that does happen with any robust auditing process. It has to be recognised that the majority of manufacturers wish to take a product to the market that is going to be in the patient’s interest; they do not want to have problems with their products. Taking on that aspect and the fact that the notified body is doing all that it can to do that leads, hopefully, to an improvement in patient safety.

Q56 Sarah Newton: It would be helpful if perhaps subsequent to this meeting you could provide that information. John Howlett: I could give more information on that. When we are looking at situations where a
John Howlett: I think we have already covered some of that, as you will appreciate. We go regularly to the NB-Med meetings in Brussels. I represent BSI on that committee. We are members of a voluntary organisation called Team-MB also, which is there to benefit and improve the guidance we give to notified bodies. In addition, I mentioned the NBS where, as an initiative, we have tried to define the requirements for reviewers and auditors and achieve a common playing field and consistency in those audits. I think we have a good relationship with the other leading notified bodies. It is perhaps not too clear whether all are operating at the same level. It is a perception that many have that it is not a level playing field. I think our relationship with the other leading notified bodies is to try to achieve a transparency that will give greater awareness of the designation of those bodies in order to achieve consistency in their delivery.

Q60 Gareth Johnson: You mentioned the weaknesses of the notified bodies, but is your opinion that, if you did have a central body in Europe, for example, that would give an overall better performance? Would you support having a central body in Europe?

John Howlett: Whatever process is put in place—I am sure a more robust system will come in—it is not really for BSI or the notified bodies to judge what that should be. How it is achieved is not too important, but there is a need for transparency and for the competent authorities to be accountable for the designations that they give within their own member states. In the legal or regulatory framework each member state is responsible for designating its own notified bodies, and they are the ones that are designating and monitoring. In my view or in the view of BSI, there is not sufficient oversight of that activity. Who should do it, I suppose, would be open to discussion.

Q61 Gareth Johnson: What if we moved to a situation where we retain the notified bodies but also have the check and balance of a central body?

John Howlett: I was talking of having a central body or accountability for the decisions on designation. What you are touching on is perhaps a central designation or another step in the licensing or approval for the high-risk devices. That would be a different discussion.

Q62 Gareth Johnson: If you had a situation where you still had those notified bodies but a central body, too, what impact do you think that would have on the notified bodies in terms of their accountability, responsibility and so on? Do you think that would diminish or increase?

John Howlett: I think the current system is robust. We must not lose sight of the fact that the process has been in place for 15 years plus. You have to look at the successes that it has achieved and perhaps not necessarily get drawn into the unfortunate performances of one or two devices. Widespread non-compliance is not there; the vast majority have been compliant. We have to take that into account first. If there was another step—if you like, a central review—
we would not be against that. If you look at the current system, that process is already in place.

For a device that has a medicinal substance in it, we have to do a medicines consultation with the Medicines Agency; if it has animal tissue or human blood derivatives, then again we have to involve another authority. I can see a situation where, if you have new technologies and specialist areas, you would draw in another authority to aid that decision. I do not think it is for us to judge what should be the regulatory framework, other than saying that we should work with what we have got and at ways of improving it in some of the ways we have put in our papers to the Commission and yourselves in preparation for this meeting.

Q63 Chair: Mr Howlett, you are a very experienced engineer with a lot of time under your belt working in high-level quality assurance, including your work in BSI. You are sort of implying but not saying that somewhere in those 78 there are notified bodies that do not meet your rigorous standards.

John Howlett: Yes, I am. That is certainly an implication, and it is a perception in the whole industry. I think my colleagues here may well wish to comment on that. The only evidence we could have for it is that, where manufacturers have sought CE certification and perhaps have been going through the equivalence route, as we have called it, or the clinical literature review without clinical trial data, and we have felt that is necessary to meet the requirements of the directive, it has perhaps led to manufacturers going elsewhere and for the product to appear on the market some two or three months later perhaps with a CE mark from another body, without any further clinical trial data. The only conclusion we can draw from that as a notified body is that the other notified body that has picked up that manufacturer has accepted data that in our view are not supportive of compliance with Annex X of the directive.

Q64 Chair: And greater transparency would aid that process.

John Howlett: Greater transparency would help enormously in making that visible to people.

Peter Ellingworth: The companies we represent take the statements about improving the overall quality. Patient safety is of paramount importance here. It is not just about bringing technology on to the market; it has to be safe. Anything that is done to improve the quality of the notified bodies is a step in the right direction. In the work we are doing within Europe at the moment in Brussels—my colleague Mr Kreuzer will comment as well—is about reducing the number of notified bodies, which is something we will support, and about increasing quality. It is an iterative process, as we said earlier on. Everything we can do as we get examples of how to do things better we shall continue to pursue.

Mike Kreuzer: Coming back to the point about a central body, we do not believe that is needed. What is needed is better co-ordination. The system as it is set up at the moment is actually pretty good. What is needed is better co-ordination between the competent authorities and how they designate the notified bodies. That is my first point here.

That will lead to fewer notified bodies because, as you get stricter designation, there will be a process of attrition and a lot of them will fall out of that. Although I would not want to be quoted on this, I have picked up rumours that at least two or three notified bodies have got out of the medical business in recent weeks because they can see which way the wind is blowing. We would support that. We think that in absolute terms there are too many to run the system properly, and there are too many in the sense that many of them are not doing the job they should be doing.

Q65 Graham Stringer: This is very worrying because people’s health is at risk. In this Committee you are speaking with full parliamentary privilege. Can you tell us which notified bodies do not think they are hitting the right quality standards?

Mike Kreuzer: No, I cannot tell you that precisely, but certainly none of the ones in this country are involved.

Q66 Graham Stringer: Can you tell us about ones in other countries? The issue is that people are going to these bodies in other countries and that enables their products to be used in this country, does it not?

Peter Ellingworth: The companies we represent take patient safety incredibly seriously, and finding a quick or easier route is not in their interests and not in their long-term interests because it is not going to be an aid to patient safety. Your point, Mr Stringer, is absolutely right. This is about making sure that everything can be done to make devices as safe as possible. That is no intent on the part of the companies we talk to and deal with to do anything to circumvent that process, but in the European Union there are 27 member states. We do not have sight of those. We have comments from people as we meet them in Brussels, and we are expressing our general concern. There is not a great body of evidence that says that body A and body B are more or less qualified, but because we have a concern we are raising it. If we had the examples, we would certainly share them with you.

John Howlett: The only thing I can add—it has been expressed in Brussels—is that, if a leading notified body loses a manufacturer to another notified body, it knows that it has lost the manufacturing part, but it is not sure where they go. That is a very clear statement that the transparency is not there. From that perspective in the UK, perhaps that question would be best put to MHRA, who would be co-ordinating with the other member states on that particular issue. I do not think we could give you any more information on that.

Peter Ellingworth: Moving notified bodies is not necessarily that easy. We talked to one large manufacturer recently and had a very comprehensive discussion on these matters. They said they wanted to work with a strong notified body. They are involved in the process and development of a product, which may take seven years. The regulatory process here is not just a question of developing the device, getting to the end and going through a tick-box exercise. This is a very complex and involved process. They said that to change a notified body would probably take them six months or more and would involve
considerable expense, as they understood the new requirements were too stringent and it was easier to get it approved somewhere else?

**John Howlett:** It has certainly happened, and more than once. We are required to give information to the competent authorities on certificates granted, suspended, withdrawn and refused. There is a mechanism in place to share that information, but it is not strong enough in the eyes of many people.

**Q70 Stephen Metcalfe:** In light of that and the fact that you can see quite a wide range of quality thresholds that some of the notified bodies might apply, post-market surveillance is even more important. I am sure we all agree with that. Presumably, that is how we ensure that the product once into market is performing in the way it was predicted to perform. Can you take us through what that process of post-market surveillance is, please?

**John Howlett:** Yes, I can go through that. With regard to the guidance for post-market surveillance and particularly post-market clinical follow-up where we are talking about a plan for a specific product, if we are looking at post-market surveillance in the wider sense, it is gathering all information. Post-market clinical follow-up is a requirement where we have a plan post-market for a new product going to the market. All of that can come forward in terms of gathering that information. How do we cover that? We do it in many ways. There are requirements on the manufacturer in regard to post-market surveillance. Obviously, the complaint has to be recorded in the hospitals and authorities; otherwise, it does not get to the notified bodies or manufacturers. That is the first area. A lot of people would have a view on that—that not enough incidents are being recorded at the point of the incident.

**Q71 Stephen Metcalfe:** On that very specific point, is that a passive or proactive process?

**John Howlett:** The complaint, obviously, is not proactive, but there are other mechanisms to gather that information from surgeons, groups and whatever. That is what I would describe as gathering post-market production experiences. If you are looking at specific product-related follow-up, then you have to use. You cannot have a clinical trial; you cannot deny a patient a product for 10 years while you go through a trial. It has to be a combination of clinical data plus follow-up. We would be looking for the manufacturer to give us a robust plan where they will gather that information, probably from a range of patients, almost a type of trial that is going to do it in many ways. Our audits from the quality system side will be looking at the complaints and vigilance reporting of those incidents that gets through to the competent authority. The MHRA as our competent authority requires us to be copied in on all those incidents. That is not a mandatory requirement in the regulations, but it is a requirement on all UK notified bodies. We monitor that through our surveillance, so that information comes in on the complaints.

On the other post-market gathering of information, again you follow that through on the audits but on a product-related basis. If you are looking at a product-related certificate—the class IIIIs, where you have a design examination certificate—there is a periodic review of those certificates. The maximum period is five years, and that is what we adopt. In those five years the company can make changes and extensions to ranges or changes to the design. At each one of
those events or prompts, there will be a review of the performance of that particular product. It is very much proactive in gathering that information and for us as a notified body to monitor it.

Q72 Stephen Metcalfe: Is that information then made available to clinicians, or even the public, in a centralised form so that they know they are getting the best possible product and have the best possible opportunity to choose?

John Howlett: What we are talking about is the visibility or lack of visibility of that information outside the notified body and manufacturer’s area.

Q73 Stephen Metcalfe: But can a clinician access that information easily or not? I understand what you are saying.

John Howlett: No. There is no framework for them to require or gain that. They could go to a manufacturer and ask for that information. I can’t answer for what success they would have in those requests.

Mike Kreuzer: As partners. The original device will be a specific clause in the revision to require devices to carry a unique identifier machine-readable code. The revision will take up to four or five years to come.

Q74 Stephen Metcalfe: I accept that, but what we are trying to do is work out what happens when it goes wrong or there is something at the margins.

Peter Ellingworth: And that is where we have to be continually vigilant. I completely agree with you.

Q75 Stephen Metcalfe: Therefore, I am sure that for the vast majority, the relationship with the registries will be a positive experience. How do the manufacturers and registries see their relationship? Is it as partners working for the benefit of the patient or as regulator and regulated?

Peter Ellingworth: As partners. The original device was the size of a car battery, but there is a unique relationship here, unlike many other industries, where clinicians and companies are focused on the patient at the centre of this exercise and how they work together. Nothing is developed purely on a bench; it is a combination of that professional relationship between the healthcare physician and the company, and it is a very intricate relationship.

Q76 Stephen Metcalfe: If they are working as partners, and the registries are collecting data about how products are performing, whose responsibility is it to analyse that data? Is that through the registries or is that then returned to the manufacturer to do that?

Peter Ellingworth: It depends on whose data it is. The registries clearly are owned by the clinicians, and the manufacturers will analyse their own data but will be continually sharing it as there are elements of it from which to learn. The improvements that are coming or we hope are coming will certainly be part of that. Going back to the points that have been made, we will support the transparency.

Q77 Stephen Metcalfe: Do you think there needs to be a mandatory element to that? Do you think clinicians should have to report?

Peter Ellingworth: The National Joint Registry is now mandatory.

Q78 Stephen Metcalfe: For manufacturers?

Peter Ellingworth: No; for clinicians.

Q79 Stephen Metcalfe: They have to report? There is no one who is not—

Peter Ellingworth: For hospitals. That was changed very recently.

Q80 Stephen Metcalfe: As I understand it, across the whole industry there is no formal system for that; there are good and bad examples, and this is a way of identifying presumably what is effective?

Peter Ellingworth: Yes, and they need to be proportionate. If you are dealing with a simple cotton swab, you would not go through the same process that you would with respect to a complex implantable device, but, as ever, there are ways to improve. How we have got to the great state of the industry with its high safety record for patients today is by continually reviewing and looking back to see how we can do this differently. Any negative incident is, of course, incredibly regrettable, but you have to balance that against the number of people who are benefitting and are pain-free. We talked about hips at the beginning of this. It has made a significant difference to people’s lives.

Q81 Graham Stringer: Should there be a central European registry for all medical devices? Would it be helpful to have a unique device identification on all those devices with that information held centrally in Europe?

Peter Ellingworth: UDI is coming, and we are actively engaged in that. There are many positive aspects to that. Mike in fact works in Europe.

Q82 Graham Stringer: What is the schedule for that?

Mike Kreuzer: Incidentally, I chair a European industry group that is driving this at the moment. The schedule for unique device identification is that it will now be part of the revision; in other words, there will be a specific clause in the revision to require devices to carry a unique identifier machine-readable code. The revision will take up to four or five years to come.
fully into force, but a lot of work is being done at the present time to drive this ahead. I believe it will be of enormous benefit—it is not the complete answer—in setting up new registries. To follow on from the previous point, this is a fairly uncharted area at the moment and we do need registries. To come back to your point about a pan-European one, that would be an ideal, but it is probably something that would not be easily achievable. What might or should be achievable is to have registries that are interoperable.

Q83 Graham Stringer: To follow up on Stephen’s question, who should have access to that information? Peter Ellingworth: Registries today are available and are transparent.

Mike Kreuzer: Manufacturers, clinicians and regulators. This is something that needs some advancement and new design, if you like. We are just moving into that period now.

Peter Ellingworth: It is certainly a question, again, for the healthcare professionals. There is a lot of information in there. To make it available to the public, there may be some questions about educating people to understand that information. I suggest that you talk to them.

Chair: Gentlemen, that has been a very helpful session. Thank you very much indeed for your evidence. If you have any other thoughts about some of the issues that have been raised, including some of the sensitive questions we asked, we would be grateful if you would follow that up in writing.

Examination of Witness
Witness: Jacqueline Minor, Director of Consumer Affairs, Directorate-General for Health & Consumers, European Commission, gave evidence.

Q84 Chair: I welcome you to our session and invite you to introduce yourself.

Jacqueline Minor: My name is Jacqueline Minor. I am the director in the Directorate-General for Health & Consumers of the European Commission with responsibility for medical devices.

Q85 Chair: Will you start off by giving us a brief summary of what is happening to the Medical Devices Directive, and in what time frame you envisage this matter being resolved?

Jacqueline Minor: As you have probably heard from a number of previous witnesses, the medical device regulatory framework in Europe consists of three directives, the oldest of which was adopted in 1990, so these directives have been in place for about 20 years. They have been amended fairly consistently on specific points, but we believe the time has now come for a more far-reaching revision. We started consulting broadly on this in 2008. We carried out a further consultation in 2010, and we have also had ongoing discussions with stakeholders throughout the last four to five years about what changes are needed. We have now got to the point where we are about to make our proposal. It should be tabled by the Commission in late September of this year, and then it will go to the co-legislators, the European Parliament and Council of Ministers. In the best of all possible worlds, we would hope for adoption by the end of 2013. There will be a period of implementation, so the new regulatory framework will probably not be in full force until the end of 2014–2015.

Q86 Chair: Our understanding of the original directive is that it was all about providing unhindered access to the European market. Is the balance shifting from that towards public health in the debates that are going on?

Jacqueline Minor: The directives have always had twin objectives: securing the safety of devices and meeting public health objectives but also securing the free movement of the product in question—the medical device—in Europe’s internal market. That will remain the case in the new regulatory framework. However, over time, there has perhaps been a shift in the perception of the importance of medical devices to public safety and health, and a greater awareness of the need to ensure that public health, and the safety of patients and other users, are the paramount concerns in putting together the regulatory framework. Experience and recent events in particular have shown us that we can do better, and we want to address a number of weaknesses.

Q87 Chair: You heard some of the concerns expressed by previous witnesses. Do you share those concerns?

Jacqueline Minor: Yes, absolutely.

Q88 Chair: You would want to see issues like transparency and better controls over some of the 78 notified bodies being incorporated in a directive that is enforced rigorously across Europe?

Jacqueline Minor: Indeed. The diagnosis, if I may call it that, of the weaknesses is fairly broadly shared. Everybody involved in the industry and in regulating it—competent authorities across Europe—shares a view as to what needs to be addressed in the revision. We intend to propose two regulations, so we are going to move from directives to regulations. That has the effect of meaning that no national legislation is required to translate the rules into the legal systems of the member states, which will eliminate to some degree differences of interpretation or of application. We want to address particularly oversight of notified bodies and their initial designation by competent authorities in member states, and the way in which they carry out their conformity assessments. We want to address transparency, which I noticed was a recurring theme as I listened to the previous witnesses, and post-market follow-up and surveillance.
Q89 Chair: I have just done some work outside this Committee on health and safety. I am serving on a panel that the Government established to review some of the health and safety legislation in the country. We were looking at pan-European experience in that respect. There appear to be differences between member states in what the law says and its enforcement. Is this your underlying worry in the case of medical implants?

Jacqueline Minor: One has to acknowledge that the rigour of the system always depends upon the resources, stringency and effort with which national supervisory authorities in the end exercise their responsibilities. There is always that issue with internal market legislation.

Q90 Chair: You are implying that there is a spectrum.

Jacqueline Minor: There is a spectrum of resource, competence and size of market, but what we hope to do in the revision is create greater commonality of view and shared resource management but also shared oversight of the system.

Q91 Stephen Metcalfe: In the previous session, I was concerned about post-market surveillance in light of some of those inconsistencies. To iron out those inconsistencies, we need a more standardised approach. It is a pan-European market and therefore I imagine we all want the same level of quality assurance across the whole market. I think you accept there is a role in that for a central body. Do you see a role for member countries to help register and judge each another’s competent authorities and notified bodies to try to get a level of consistency?

Jacqueline Minor: Certainly, for notified bodies, we envisage a system where responsibility for designating a notified body remains with the competent member state, but prior to that designation there would be a joint inspection. Whereas currently, as you heard from the gentleman from BSI, it is the British authorities who carry out the inspection of BSI before designating, or confirming its designation, we would have a system whereby there would be a joint team. You would have a team from the member state concerned but that would also include people from another member state, probably people drawn from a European list. The team would draw up an inspection report. That would be submitted to a group of European experts, who would issue a favourable or unfavourable opinion, or an opinion with reservations. That would go back to the competent member state, which would make a final decision on designation. One imagines that if there were reservations, or the report was negative, they would not go ahead with the designation, and the report would be public, so that would bring some pressure to bear upon them.

Q92 Stephen Metcalfe: Do you envisage a central EU committee overseeing that process?

Jacqueline Minor: We are proposing something called the medical devices expert group, which would be composed of representatives appointed by member states, but in their personal capacity—either one or two from each member state.

Q93 Stephen Metcalfe: Do you see that leading to a lower number of notified bodies?

Jacqueline Minor: To lower the number of notified bodies is not an objective in itself, but it might well be a consequence.

Q94 Stephen Metcalfe: But, if there were a smaller number, presumably it would make it easier continually to assess whether those standards are being maintained?

Jacqueline Minor: Yes, indeed. What we would also expect to see is that, even if there is not a reduction in the absolute number of bodies, there might well be a restriction on their areas of competence, so some of them would be designated only for a more limited range of devices.

Q95 Stephen Metcalfe: Presumably, this would add some additional cost to bringing a product to market?

Jacqueline Minor: Yes.

Q96 Stephen Metcalfe: How do you envisage that cost being paid for?

Jacqueline Minor: Manufacturers currently pay notified bodies a fee for the work carried out, and obviously notified bodies have to cover their overheads when they charge that fee. Presumably, that fee would increase as a result. Having talked to the industry, they feel this is a cost which the industry must bear—would be willing to bear—in order to improve confidence in the system and restore trust.

Q97 Stephen Metcalfe: You do not see it being such a prohibitive high cost that it would put off even the smallest of specialist manufacturers from bringing a product to market in Europe?

Jacqueline Minor: I honestly do not think so, because we are talking about a notified body, as you have heard, which is designated for a number of years. A number of manufacturers go to them for certificates, so when it is spread across all the certificates and all the manufacturers, I do not think it would amount to a substantial increase.

Q98 Pamela Nash: Do you think that the revisions to the directives that are going through at the moment will address co-ordination of post-market surveillance throughout the UK?

Jacqueline Minor: I hope so. We want to change the current system from one where incidents are reported to national authorities and national authorities report them at a European level, so we have a kind of two-stage process, to one where we create a single portal so every serious incident would be reported directly at European level. I hope that would enable us to pick up more quickly any emerging trend that gave concern in relation to a device. We also hope to make some funds available to have some central trend analysis, so that we would have scientists working in our joint research centre looking at the data coming in and being able to check it and sound the alarm more quickly than has been the case in the past.

Q99 Chair: This would be a portal to which clinicians themselves would have access?
Jacqueline Minor: Clinicians, even patients, but mainly manufacturers.

Q100 Pamela Nash: If you had to create that single portal, can you expand a bit on what you see as the practicalities? Who would set this up? How long would it take? What would be the costs involved?

Jacqueline Minor: We would set it up. I cannot remember the exact cost at which we have assessed it, but we would plan to set it up in the period between the final adoption of the legislation and its coming into effect so it would be available when the new regulatory framework goes live.

Q101 Pamela Nash: Is that information that you could send us? Could you share that with us?

Jacqueline Minor: Yes.

Q102 Pamela Nash: If an implant is found to be faulty, in your experience so far, is its withdrawal from the market consistent across member states at the moment? How would the new registry be able to help fix those problems that have been found so far?

Jacqueline Minor: Under the current framework, both risk assessment and risk management are left in the hands of member states. A member state determines what it believes is the risk from a particular product post-market incident report. It also decides how to address that risk. Initially, the onus is on the manufacturer to determine whether they need to modify or recall their own product, but with a large-scale incident, such as the PIP, it was up to each member state to determine the advice it would give to the women concerned. What we hope or plan to do under the new system is move risk analysis to a more central position: that is, the trend analysis. We will also make provision for a common risk management, so in certain cases involving large-scale incidents such as the PIP—maybe metal on metal—we may also have a European recommendation as to how that should be addressed by clinicians, so we will not have the situation where patients in different countries—

Q103 Pamela Nash: Could you explain that a bit more? Does that mean that individual countries would still have the power to take a decision based on information given them from the central registry, or would rules be implemented that meant that you would have to have a uniform approach?

Jacqueline Minor: The proposed regulation will give rise to the possibility of a uniform approach. It will depend on the nature of the incident, but I would imagine that for a widespread incident such as the PIP, we would try to aim at a common European recommendation as to how it should be addressed.

Q104 Pamela Nash: But the power would still lie with individual countries to take that decision. Jacqueline Minor: There would be a recommendation, and I think it would then be difficult for individual member states to ignore it.

Q105 Pamela Nash: On the question of co-ordination throughout the EU, do you think there should also be a policy on healthcare professionals having to report if they find a fault in the devices they are using?

Jacqueline Minor: Yes. Currently, the rule is that manufacturers must report serious incidents. What we want to do is open up the possibility of healthcare professionals and patients themselves reporting incidents. That is not without its difficulties, because a patient often cannot tell whether the problem is with the device itself or the care they receive from the health system. It is difficult to make that obligatory because of the legal basis on which we work, but we would certainly encourage a co-ordinated approach.

Q106 Pamela Nash: Is that covered in the directive, and is it being looked at in the revision?

Jacqueline Minor: It is being looked at. We will try to have a permissive provision in the regulation, and when we set up the single portal, we will also try to ensure that it enables reporting by patients and healthcare professionals as well as manufacturers. For healthcare professionals it is easy enough to do; for patients it is a little more difficult.

Q107 Graham Stringer: Perhaps I may read you a quote from the Royal College of Physicians: “Despite the lack of hard evidence that the current system of approving implanted devices for marketing within the EU, there is concern that the current system of competent authorities being involved at the clinical trial approval stage and with post-market vigilance, but not directly with product approvals, is unsatisfactory.” That leads to the obvious question: should the expertise of those competent authorities be used in the initial approval stage?

Jacqueline Minor: This is something that we are considering in the revision. There are several ways in which we will address that. The first is that we will make available to producers, and to notified bodies early scientific advice. We will have a scientific panel, and anyone developing a novel technology will be able to go to that scientific panel to ask about the kinds of evidence they will need to bring forward to support its safety when the time comes for conformity assessment and placing it on the market. The second and perhaps more significant strand that we are developing is that in future anyone who brings a new class III device to market—that is the highest risk for us—will have to notify their intention centrally. At that point, competent authorities in all the member states would learn of something that is approaching the point at which it will be placed on the market. Currently, a competent authority does not know what is coming on to the market until the goods are there. When that notification is made, it will be examined by our scientific experts. It could be called in for something we are labelling the scrutiny procedure. The file presented by the manufacturer—the design dossier and the clinical evidence—could be called in and looked at by a central body and our scientific experts. The scientific opinion would go to the central committee, the medical device expert group, and they would offer an opinion as to the evidence presented, which would then go back to the notified body. The notified body would have to take that into account in its final conformity assessment.
and its decision as to whether or not to issue a certificate.

Q108 Graham Stringer: Would it be fair to characterise it—tell me if it is not fair—as that, in the future, you are going to rely on better communications between the different bodies with the knowledge rather than actually involving the competent authority in the approval process itself? Is that a fair way of putting it?

Jacqueline Minor: No. I think there would be an involvement of the competent authorities. First, they would get this prior warning, which they currently do not. Secondly, the medical device expert group that we are creating would have an upstream view and offer an upstream opinion on a device which was coming new to market before it received its certificate and was allowed to circulate in the internal market. What we are not envisaging, which other jurisdictions apply, is pre-market approval, which is where a central body has to grant authorisation to a medical device before it is allowed to go on the market, as happens, for example, in the US.

Q109 Chair: Are there any other aspects of the proposed revised directives that we have not discussed this morning that are relevant?

Jacqueline Minor: You have discussed it, but I would like to emphasise transparency, which is very important. It is very difficult, as I think a number of your earlier questions pointed out, for anyone to know what devices are on the market; what evidence was used to support their safety; and what information is available about the associated risks and the incidents they might have provoked. We are planning to have a central registry in which all manufacturers and all devices will have to be listed. For each device, there will be some standard information, such as the name of the notified bodies, the class of risk, and the unique device identifier, when we have that. There will also be a summary of performance and clinical data. For the first time, for example, clinicians will be able to have access to the clinical data which supported the certificate granted to the device.

Q110 Chair: You have no doubt in your mind that that information ought to be available to both the clinician and patient?

Jacqueline Minor: It is a summary; it is not the full technical file, but we believe it should be made available.

Q111 Roger Williams: I was going to ask whether the information was made available to the patient. Some clinicians will use only specific products. How does that leave the patient if they have made up their mind that a particular product is the one that will give them the best relief and the particular doctor does not supply it, or does not do it?

Jacqueline Minor: To some extent, that goes beyond the ambit of the regulation of the product. That is a question about the healthcare system offering the patient choices and informed consent, of the doctor in trying to explain to the patient why they are using a particular device—in the same way as why they recommend a particular drug—but we know from our broader discussions with stakeholders that the role of the patient is changing. There is a belief and expectation that they have a far greater role in the management of their condition and a far greater say in the therapy applied to it. In line with that trend, I would expect this data to be useful, maybe not so much to individual patients, but you could imagine that associations of patients with a particular condition would offer guidance about the choice between different devices.

Q112 Stephen Metcalfe: You said that this register would hold information on all medical devices. For clarity, you do not mean just class IIB and III; you mean all of them?

Jacqueline Minor: Yes, although the details for all classes would differ of course.

Q113 Stephen Metcalfe: That means there will be many thousands of items on it?

Jacqueline Minor: Yes.

Q114 Stephen Metcalfe: Would the cost of that be covered by the industry itself?

Jacqueline Minor: There would probably be a fee for registration, but what industry is looking at at present is the possibility of having to register 27 times, because a number of member states have set up registries. They are perfectly entitled to do that under existing legislation. Either they charge a fee or, if they do not, there is the administrative burden of having to go through the registration process in each member state.

Q115 Stephen Metcalfe: For a product that is available across the whole of Europe, it could reduce costs?

Jacqueline Minor: It could certainly reduce burden and, one hopes, consequently costs.

Q116 Stephen Metcalfe: We are talking about covering things like sticky tape, bandages, rubber gloves and plasters.

Jacqueline Minor: Yes.

Q117 Chair: A final question: I recognise issues to do with protocols in the Brussels machine, but I suspect we are the only group of parliamentarians across the whole of Europe looking in such detail at this.

Jacqueline Minor: The French Senate is doing so.

Q118 Chair: Excellent. It would be extremely helpful, if you are able to do it, if you would provide us in confidence with a draft of the thinking, with obvious caveats that we would respect the necessary protocols. I think it would mutually help the thinking in this very important area.

Jacqueline Minor: I cannot give you a positive “yes” to that now; it is something I would have to refer to higher authorities.

Q119 Chair: Even if it was a summary. You have given us a summary already, in a sense.
**Examination of Witnesses**

**Witnesses:** Sir Kent Woods, Chief Executive, Medicines and Healthcare products Regulatory Agency (MHRA), and Earl Howe, Parliamentary Under-Secretary of State, Department of Health, gave evidence.

**Q122 Chair:** Minister, welcome to you and thank you for agreeing to come to see us today. Sir Kent, I would be grateful if you would formally introduce yourself to the Committee.

**Sir Kent Woods:** I am Kent Woods, chief executive of the Medicines and Healthcare products Regulatory Agency.

**Q123 Chair:** We have heard some fascinating evidence on this issue. Minister, in what areas of the revised directive have the Department and, to you, Sir Kent, the MHRA been most heavily involved, and what are your priorities?

**Earl Howe:** Sir Kent can probably fill out the detail, but the Commission have already given us an indication of where they think the focus should lie in terms of revising the directives. Undoubtedly, there needs to be greater focus on ensuring that notified bodies are fit for purpose. There is a perception of a variation in the performance of notified bodies across the European Union. I am glad to say we do not have any worries about the ones in the UK, but there is a need to ensure that notified bodies are performing as they should and have the right expertise to address the areas with which they are concerned.

Subsequent post-market surveillance undertaken by manufacturers is an area to be looked at. We want to ensure that EU competent authorities co-operate and co-ordinate their post-market surveillance activities. Sir Kent can probably flesh out some of that usefully.

**Sir Kent Woods:** Our starting point when we were thinking as an agency about the revision of the directives was to reflect that pharmaceuticals and medical devices are fundamentally different, and the way they are regulated needs properly to reflect those differences. As regards medical devices, the areas in which they differ are, first, the way they are innovated. They are innovated in a rather iterative way with progressive, relatively small changes in technology and refinement, perhaps as frequently as every year or two, which is quite unlike the situation with pharmaceuticals.

The second point is about their sheer multiplicity. When we look at pharmaceuticals we are talking about the low thousands; when we look at medical devices we are looking at hundreds of thousands in the EU. Therefore, the regulatory system has to be able to cope with that. The third and perhaps most important difference is the way in which they fail when they give rise to problems. In contrast to pharmaceuticals, the areas where medical devices give us problems are, first, in relation to sporadic manufacturing problems, which are not easily picked up at the market authorisation step; and, secondly, particularly in terms of implantable devices, the way they wear over time, and all of them will over time. Again, that is on a time scale that is not easy to pick up in pre-clinical studies.

The other aspect of the failure pattern of medical devices is the much greater involvement of the operator factor—in other words, the way they are used and the way patients are selected for particular devices.

The regulatory system we wish to see for medical devices has to accommodate these rather distinctive characteristics. Our view has been that, in principle, the Medical Devices Directives under the new approach are appropriate, but in detail, as you have heard from the Minister, there are areas where we would wish to see a greater degree of consistency of application and rigour across the piece in certain areas. At the centre of this has to be the designation and the performance of the notified bodies because of the fact that in Europe we are essentially working on a mutual recognition system. A notified body can award a CE mark in any country of Europe—there are 70 or 80 notified bodies—and that gives access to the entire European market. Clearly, the performance of notified bodies is central to the integrity of the system.

Going back to what I said earlier about the distinctive features of medical devices, the balance has to be right between the pre-market assessment of the device—what one can learn before it goes into use—and the post-market evaluation, which requires a high degree of vigilance, market surveillance and the best possible means of monitoring outcomes under conditions of use, and feeding that back both to clinicians and manufacturers.

**Q124 Chair:** I take it you would agree that, if one saw a product being questioned or refused by BSI, for example, and it went off and got approval from
another notified body, that is a pretty unsatisfactory situation?

Sir Kent Woods: Indeed.

Q125 Chair: That process at the very least ought to be totally transparent.

Sir Kent Woods: Indeed. You have touched on an issue we take very seriously for the revision, which is this question of transparency. Criticism has rightly been made that under the existing arrangements, and it is in the Medical Devices Directives, there are obligations of confidentiality on those who run the system. We find this frustrating and unhelpful, and I think the general public and health professions would wish to be able to see more of the evidence underpinning, for instance, the award of a CE mark, and evidence emerging from post-market surveillance, and all this can be incorporated into the revision of the directives.

Q126 Stephen Metcalfe: Are there any proposed changes that you do not agree with and are not in step with the way we do things at the moment?

Sir Kent Woods: We have not yet seen in detail the proposals. I have been in close contact with the Commission as these ideas have been developed. For me, one of the most important issues was to avoid going in a direction that placed a very large additional burden on the pre-market authorisation step. My reason for saying that is partly because there is this iterative process of product development, which is difficult to evaluate in depth pre-market, and also because we know, from the experience of the United States, that going down that route very much increases the time delay of giving patients access to new technologies. There is a balance to be struck clearly between speed of access to new technologies and the degree of protection of patients, but we would wish to see—I think the revisions will address this—a greater strengthening of the post-market surveillance process, but also in detail an improvement in the way the notified bodies confer CE marks.

Q127 Stephen Metcalfe: From what you understand, you think the balance is probably about right.

Sir Kent Woods: I think that is right.

Q128 Chair: I want to pursue this a little more. Last night Mr Mosley and I heard a very interesting presentation about the work going on by our colleagues in the Home Office to bring up to date the directive covering experiments on animals. These discussions and debates are tortuously difficult, and making sure that we end up not harmonising down to a lower common denominator than the public would expect us to do is very difficult. We recognise in this case that the evidence we have had suggests that some of the notified bodies are not as rigorous and effective as our own. Earl Howe, if the outcome was the right level of regulation but it was more centralised within the European machinery, would that create problems for you?

Earl Howe: It would be likely to result in a more costly system, because you would have to populate whatever European body was charged with this job with the right experts. We would prefer to see a model involving much more efficient co-operation between member states. To come back to what Sir Kent said on transparency, this was a point that ran through my own report on PIP implants. If there was one expression that summarised my recommendations on that, it was “greater transparency”. If we can get greater sharing of data between member states, maybe even have an EU portal where data can be fed in when there is an adverse report on a device so that it is clearly on view to all member states, that would be much more efficient and effective and much less cumbersome.

Q129 Chair: A portal that included good as well as adverse information?

Earl Howe: Yes. Why not?

Q130 Chair: You would prefer that kind of European co-ordination rather than a new body?

Earl Howe: Yes, I would. Reading the opinion and talking to medical devices companies, that is what they would say they would prefer, largely because they fear that a centralised European mechanism could act as a brake on innovation and add to costs unnecessarily.

Q131 Chair: Has your thinking on this been affected by your experience of dealing with the metal-on-metal hip joints and PIP?

Earl Howe: Yes, undoubtedly. One of the lessons of the metal-on-metal hip joints can be drawn by making a comparison between the situation in this country and in the United States. What we have in this country is a regulator—a competent authority in the shape of the MHRA—that has very close, active links with the professions, royal colleges and experts of all kinds so that early intelligence is available on any problems in medical devices. We have seen with metal-on-metal hip joints a dramatic drop in their use of ever since it was first suspected that there might be a problem with them. That is not the case in the United States. I think the latest figures in my brief are that in this country 60,000 or 70,000 joint replacement operations go on in a year, of which 2% are metal-on-metal at the moment, and dwindling. In America it is 35%, because in the United States their post-market surveillance is much weaker than in this country. It is a case of being able to react swiftly, as Sir Kent has said, in the face of any problems while also ensuring that new technology is available swiftly to patients, and that many of our medtech companies, SMEs mainly, are able to start up and get going in a way that does not present them with unreasonable regulatory burdens at the outset.

Q132 Gareth Johnson: Perhaps I can ask you some more general questions about the MHRA. In particular, where does the MHRA get its expertise from? I understand that you have a Committee on the Safety of Devices. How important is that in providing the MHRA with the expertise it needs?

Sir Kent Woods: Thank you for the question. We have in-house 104 staff working on medical devices regulation at the moment, and of those about 60 are...
specialists; they are scientists, engineers, technical in their background. Because of the enormous scope of medical devices technology we must draw extensively on external expertise, not only to provide us with scientific and technical knowledge about the devices themselves but to provide that sort of clinical interface so that we are aware of issues arising in clinical practice.

We have several ways of doing this. As you mention, we have a Committee on the Safety of Devices which has been in existence for nearly 10 years. This is a group of 25 external experts from clinical and scientific disciplines, who meet regularly. We take to them issues of general principle, and where we have a concern about a specific area of technology usually there will be somebody on that committee who can lead us in to the relevant expertise externally.

We have a wider panel of experts whom we consult on an ad hoc basis, depending on the nature of the problem, and we also have very strong links with the professional bodies. If we take the metal-on-metal hip incident and the investigations we have done on it, we have worked very closely with the British Orthopaedic Association and British Hip Society, and the guidance we have put out has been jointly between the clinical professional bodies and the regulator, drawing on the expertise of both. That interface with experts and clinicians in the field makes a huge difference to the way we do our business.

Q133 Gareth Johnson: I get the impression that you are quite a private organisation, if I may put it that way. You publicly state that the work of the committee must remain confidential at all times. Is that purely for commercial reasons, or is there any other reason why that is the case? Is it possible that that committee could be a little more open?

Sir Kent Woods: It goes back to what I said earlier about the obligations placed on us by the Medical Devices Directives. I think article 20 of the main directive requires that information obtained by regulators is confidential. I would like to see that changed. In the revised legislation I would like to see that the default assumption is transparency rather than confidentiality. That has really somewhat set the tone for the way in which we regulate medical devices. To an extent the same thing has happened in our pharmaceutical regulation. The Medicines Act 1968 again imposed a legal obligation of confidentiality, which has changed. I think we are seeing that process happening also on the medical devices front.

Q134 Gareth Johnson: That is quite interesting. If there was a change, what aspects of the work that you do at the moment that you currently keep confidential do you think you could put in the public domain?

Sir Kent Woods: For instance, with pharmaceuticals we put into the public domain routinely tabled analyses of the adverse drug reaction reports we have received on all the medicines we regulate. That data is there; you can look at it on our website. Although we have to hedge it around with cautions about how it can be interpreted, none the less the information is there.

On the medical devices side, to be able to give greater public visibility to accumulating experience would be valuable. Going back to the metal-on-metal case—this is a really instructive issue—in the UK we have the National Joint Registry. It is not within the MHRA, but we are closely involved in it and have representation on it. The National Joint Registry is the biggest in the world now. It has over a million hip, knee and ankle replacements in its register, and it produces an annual report, which sets out in very great detail the follow-up results of those procedures by type of operation, type of device and manufacturer of device. That is a valuable resource for changing clinical practice. That is the way in which accumulating information on outcome is fed back to improving care and, therefore, improving outcomes. Fundamentally, that is what regulation is about. Regulation is not about standing as policeman over the industry; our motivation is to make sure that the end results in terms of clinical care are the optimum. So the transparency that now exists around the outcomes of joint replacement surgery through the National Joint Registry is a model of what might be achieved in other areas were there to be better follow-up data presented in a more coherent and consistent way.

Q135 Gareth Johnson: Do you ever privately share information with any other competent authorities?

Sir Kent Woods: Yes, indeed.

Q136 Gareth Johnson: Can you give any examples of that?

Sir Kent Woods: We have an obligation to notify competent authorities if we hear of serious adverse incidents that might affect products on the market in the other countries of Europe. There is that communication. I do not think in practice it is as regular and detailed as it could be. One of the aspects of the legislative review has been how to improve the interaction between the national competent authorities across the 27 member states. As you might expect, some of the national competent authorities are larger; they have better resources and more data, but we are dealing in a European system and it is important that we draw on experience from the whole population of 500 million and share our resources. We have been exploring among ourselves as heads of the national competent authorities how best to do this. I am sure there will be progress within the next months and years in further formalising the interactions between the national authorities.

Q137 Sarah Newton: I would like to pick up the very welcome comments you made that the key way forward is improved transparency. This has come out very strongly from all our witnesses, but I would like to move on to transparency in the process of how you go about selecting the notified bodies and the notified bodies themselves. We have heard a lot of criticism, especially from clinicians and the royal colleges, about the lack of transparency in the pre-approval process. Why is there not more transparency in the process?
Sir Kent Woods: There are probably two subsets to that question. One is transparency about how notified bodies are designated and how we audit their capabilities over time. The other bit is about how the notified bodies assess products that are brought to them, how they evaluate the design dossiers and how they evaluate the company quality systems with which they are faced. As I touched on earlier, the relative lack of transparency dates from the original legislation, which has seen much of this as being commercially confidential information, but expectations change and this is information that will influence the way clinicians do their jobs; it will influence the way patients make decisions about healthcare. I think we have seen a shift in social expectations over the years, which means that we must explore every opportunity to get that information into the public domain, with some protections remaining for what is genuinely commercial in confidence and for data protection purposes down to the level of individual patient outcomes. Those clearly are the red line areas that we have to protect, but the definition of what constitutes commercial in confidence is something that exercises us constantly.

Q138 Sarah Newton: We have—citizens, I should say—now developed a level of individual patients/customers and their expectations over the years, which means that we have to explore every opportunity to get that information into the public domain, with some protections remaining for what is genuinely commercial in confidence and for data protection purposes down to the level of individual patient outcomes.

Earl Howe: I am aware—Sir Kent can perhaps confirm this—that the Commission are equally concerned that there should be a levelling up in the quality of notified bodies, and that the process of designation and audit should not be up to just one competent authority but it should involve joint assessment teams comprised of experts from more than one member state and, indeed, the Commission, this being overseen by a central EU committee. Those are the kinds of noises we are getting at the moment.

I think we should be reassured by that. Whether that is the precise formula we arrive at eventually we do not know, but clearly there is an awareness at Commission level that the point you make is a very valid one.

Sir Kent Woods: The distinction between directive and regulation has two sides to it. On the one hand, I think the motivation is to achieve consistency across Europe, and the theory would be that a regulation would do that more reliably than a directive, on the grounds that a directive has a transposition step where there may be variations that allow excellence to flourish in one part of Europe but may allow the opposite to happen. It is even more important, therefore, that, if there is to be a regulation, the input from the more active member states is very forceful in making clear what the essential requirements of that regulation should be.

As far as transparency goes, everything I hear suggests that there will be a fundamental shift to a more permissive approach to the use of data, whereas what we have at the moment in the directives is a very restrictive legal basis around the use of data. Provided we have that permissive framework, I think member states have the ability to use their best judgment as to how that is done.

Q139 Chair: You regard that point as non-negotiable; it is a top priority.

Sir Kent Woods: The issue of transparency—absolutely.

Q140 Chair: Minister, do you confirm that on behalf of the Government?

Earl Howe: I am absolutely behind this. All the lessons of history tell us that we need to make a fundamental shift in the direction of transparency and away from unnecessary confidentiality. There may be some confidentiality that needs to remain, but the presumption is far too heavily weighted in the wrong direction at the moment.

Q141 Sarah Newton: I want to put one question that came up a few times in the evidence of our witnesses this morning. If a notified body rejected an applicant, they would go to another notified body and somehow get approval. What do you do when you find that has occurred? I understand it is quite rare, but the fact it is going on causes us a lot of concern. What do you do with that information when you receive it?

Sir Kent Woods: We have had anecdotal accounts of this, but it is terribly difficult to get the data, partly because we have a system of 70 or 80 notified bodies across the EU. There is no reliable way of detecting that to the extent that one can say it is not happening. The anecdotes have certainly circulated. I think that is a potential weakness. Whether it is a real weakness I am not sure. I think the solution comes back to the future arrangements for designating and auditing notified bodies. If we genuinely are able to achieve on a multinational basis a consistent standard of designation and audit, the incentives for forum shopping will not be there. It may be that we end up with fewer notified bodies, but we must have a consistency of performance of notified bodies. If we have that, the problem of forum shopping is not a worry.

Earl Howe: There is also a case for specifying in greater detail how notified bodies should undertake conformity assessments and ongoing monitoring of manufacturers, and the use of unannounced inspections and audits, perhaps requiring physical checks of devices. I know this takes us into the territory of greater prescription, but perhaps there is a case for looking at that more closely if we really want...
to see greater consistency of performance across Europe.

Q142 Graham Stringer: Patients and politicians always want the best of both worlds. Patients want medical devices to be 100% safe. If they are going to save lives or improve the quality of life, they also want them now rather than in two years. How do you balance those competing demands, Sir Kent? We heard evidence from Professor Westerby a few weeks ago that people were moving to Greece because they could use devices to help with heart problems because they could use devices to help with heart problems there now that we cannot not use in this country. How do you balance those issues?

Sir Kent Woods: You are absolutely right. There is always a balance to be struck. As a regulatory agency, we are firmly of the view that innovation is a positive contributor to public health, and therefore to the extent we can do so without endangering clinical outcomes we should enable it. That is one of the reasons why I think the existing broad approach to medical devices is right, because the innovation happens in small incremental steps. But the corollary of that to protect the interests of the patients who receive implants is the obligation to make sure there is real, accurate and timely monitoring of outcomes. We are moving quite quickly to a situation where that is technically much easier to achieve. The introduction of IT systems into healthcare and the ability to capture and process large amounts of data gives us huge potential to make sure that outcome monitoring, and indeed traceability if necessary, is achieved much more consistently. But it requires partnership working between the active participants—the regulator working with the industry, the notified bodies and the clinical community to make this happen. The capture of event and outcome data fundamentally rests with the clinicians and to some extent with patients. We all depend on that happening, which is why these good working relations that we have with the clinical community are so important to us.

Earl Howe: Sir Kent said earlier that it was less a case of amending the structure of the legislation than making sure that the regulations work as intended and as they should. What that implies in the context of your question is looking at the legal underpinning of all this in relation to the relative risk of different types of medical device. What we have is an intent at least to ensure that the pre-market data that a regulator or a notified body receives is commensurate with the risk associated with the innovation or change.

We can take that only so far, because, as Sir Kent said at the beginning, it would be lovely to be able to predict the likelihood of failure of a device in pre-market studies, but it is totally impracticable to do that. Even if one were to try to do it, it would be so onerous that the product would probably be unable to complete the development process. It is important to achieve that balance between pre-market and post-market processes so that innovation can proceed so as to benefit patients while maximising the ability to act quickly if any problems materialise.

Q143 Graham Stringer: I realise this is a difficult question to answer because we are dealing with averages and very different devices. Is pre-market approval likely to get more expensive and take a longer or shorter time as you try to balance those two things? In which direction are we moving? Is it going to get more expensive and burdensome in a regulatory way, or can we do it more quickly?

Sir Kent Woods: We can certainly continue to do it quite quickly, but it is likely that for the more high-risk devices, particularly implanted ones, there will be an increased cost of doing more clinical studies pre-market authorisation, but, as I was suggesting earlier, we should not allow that to become so burdensome that it shuts off the innovation process. There are equally important—in fact more important—ways of learning more about the overall effect of devices in terms of benefit and harm from the more systematic interrogation of what happens after it goes on the market. We can learn a great deal at relatively low cost by using the information systems we have in a joined-up way, whereas, if you were to focus the effort on insisting, for instance, that there were randomised clinical trials of every device going out to the pre-market approval process, first, it would become unworkable; secondly, it would become impossibly expensive; and, thirdly, there would not be a flow of innovative devices because it just could not be made to function. In terms of a trade-off between a system that is expensive and one that protects patients and is optimal for patient benefit, I think the right direction to travel is to strengthen the system as it is but particularly in relation to the use of registry-type data for longer-term outcome. Of course, that ought to be part of good practice anyway. If you are studying the outcomes of a procedure, you want to know it anyway. The fact that there is a device integral to that procedure is just a special case.

Q144 Graham Stringer: The problems about authorising devices do not stop at the boundaries of the European Union. The equivalent European Union institution that deals with drugs has come to agreements with European countries on the immediate boundaries of Europe. Tell us what is happening because I do not know. Is it possible to come to agreements with the Norways, Switzerlands and Ukraines of this world so that regulation applies to more than just the EU?

Sir Kent Woods: I think there are two parts to that. One is the formal arrangements. For instance, Turkey, although not in the European Union, does have notified bodies. That is an exceptional situation and is driven by considerations of the single market. But there is a wider question about products being manufactured outside the EU and coming into the EU. How do we achieve a consistent standard of conformity? The requirement is that they have to get a CE mark and do that by the same process as if they are manufactured in the UK or anywhere else. A deeper layer to that is that we are looking at an increasingly globalised world. We have seen very strongly on the pharmaceutical side that manufacture, research and development are global activities, and to think even in terms of the European Union as if it was a completely self-contained system is no longer
appropriate. As an agency, we have been very active in the last four or five years in developing good relationships with the regulatory authorities in China, Singapore, north America and Australasia. Our international strategy is driven by two considerations. First, where are our major lines of supply starting from? Therefore, we have to be concerned about the quality of manufacture in those places. I am thinking particularly of pharmaceuticals. Secondly, globally regulators need to work together to think through these problems because they are the same problems round the world. If we are regulating globalised industries, regulators have to think globally, and that is a trend I have seen very strongly in the last few years.

Q145 Stephen Mosley: Following on from that, one thing that interested me a few weeks ago when Professor Westerby was here was that he said that NHS rationed life-saving technology in a way that many more lives are lost through that than by devices going down. Do you have any guidelines as to the acceptable failure rate? If you have a device that is going to improve someone’s life but is not going to be 100% perfect over a period of time, do you have any criteria you use by which you say, “It’s better to save someone’s life now than run the risk of it going wrong in five years”? Are there any guidelines or figures on that?

Sir Kent Woods: There is a general principle that we use throughout the agency around risk-based regulation. In other words, rather than having arbitrary rules that we apply across the piece, in every case you have to consider the risks and the potential benefits of alternative approaches: this medicine against that medicine; this medicine against no medicine; a medical device against no medical device. Depending on the underlying condition in the population you are treating, that judgment has to be made every time. It is striking that, if we look at the totality of adverse incident reports that come in every year—we get about 10,000 or 12,000 reports, which we analyse in various ways—a consistent feature is the significance of operator factors. The way devices are being used will be a determinant of the outcome in about a third, we reckon, of these adverse incidents. It raises a question as to our responsibility not just in informing the world outside about the risks and benefits of medical devices but how to use medical devices. We have put out training materials in relation to infusion pumps and a whole range of commonly used devices; we have put out information to patients who are considering breast implants and all that sort of thing. These are essentially educational activities that do not fall within our legal remit, but we think that in terms of improving health outcomes they are important for us to do, and we feel that we are quite well sighted to do it.

Q146 Stephen Mosley: We have heard some very positive comments this morning about the National Joint Registry. Aside from joints, in the other areas that you cover, we have been led to believe there is less of a formal reporting system. Do you think this leads to under-reporting of problems with implants?

Sir Kent Woods: Yes. I think under-reporting runs across all areas of regulated medical products. In many ways the National Joint Registry teaches us lessons that we can roll out to other areas. First, the component parts of a good registry are that it has strong professional leadership. This is not something that the regulator imposes on an unwilling world; this is professionally driven, as indeed the NJR has been from the outset. Secondly, you need to achieve consistently high data input and make sure that procedures and the details of devices are routinely and accurately captured. That may seem a terribly simple thing, but the whole system depends on it. Thirdly, you have to think about how the database is to be interrogated, by whom and how often. Those are the standard questions you ask whenever you are trying to set up a registry. I personally believe that registries have huge potential. We tried, as you may know, in the 1990s to set up a breast implant registry and it failed. It had Government funding, and after a dozen years it had to be discontinued because, first, the completeness of registration was totally inadequate, and, secondly, the willingness of patients—the women concerned—to follow-up information was far too low to allow conclusions to be drawn. That is a contrast, if you like. It was a registry that failed compared with the joint registry that succeeded. Going forward we have to learn those lessons. I think the key issue for me, certainly within the NHS, is to make sure that the data are captured at the time the procedure is done. The key to that would be to have a unique device identifier so that there is a recognised code that describes a device. That is something that is very much in the Commission’s thinking for the revision of the directives.

Earl Howe: That is very important. I would only add to what Sir Kent has said that the experience of the National Joint Registry clearly shows the benefits that registries can bring to post-market surveillance. We talked about the issue of metal-on-metal hips, and the problems in that area were first identified and acted on because of the data emerging from the National Joint Registry. Before we start to get too enthusiastic about extending registries to all implantable devices, there is a lesson to be learned from the breast implant example, but we also need to bear in mind that these registries are not cheap to maintain. The National Joint Registry costs about £3 million a year. One could compare that with the £10 million spent on the whole of the MHRA’s devices-related work. That is why I have asked Sir Bruce Keogh in his review of the regulation of cosmetic interventions to consider the pros and cons of registries for all implantable devices. I think there are a number of complex issues at play here.

Q147 Stephen Mosley: A slightly different approach might be to look at the yellow card system that is used for pharmaceutical products. Do you think that might work with implants?

Sir Kent Woods: We have done two things to make it easier to report adverse incidents related to medical devices. We have created an IT system that makes it easier for manufacturers to deliver the reports to us which they hear about, but, for patient and clinician
reporting, if you go to the MHRA website, in the middle of the home page there is a button about medical device adverse incident reports. That will take you into an electronic reporting system that can be used by clinicians, patients or whoever, and will go straight into our database and be analysed. We also have electronic yellow card reporting now, too. In terms of opening up the accessibility of reporting to patients and healthcare professionals, we have done both of those, but they are still spontaneous reporting systems. They complement but do not replace the need for systematic analysis of outcomes.

Q148 Stephen Mosley: After PIP and metal-on-metal hip replacements, do you think the systems are now in place to prevent another faulty implant being used so many times after problems have been detected?

Earl Howe: On the PIP implant issue, we must always remember that we are dealing there with a clear case of fraud. It was clear from my investigation that no amount of regulation could have prevented deliberate fraud of that kind. There is no criticism of the notified body in relation to the PIP manufacturer; they did their job as far as we can see perfectly adequately, but the manufacturer was out to hoodwink everybody. Prior to that finding becoming public, the MHRA's focus was very much on trying to find out whether there was a higher than expected rupture rate in PIP implants. There is a catalogue at the back of my report of what was done when, and there is no doubt they followed up rigorously and very conscientiously every report they got in an endeavour to get to the bottom of this. I have no criticism on that front.

In the metal-on-metal example, it is probably a good news story for the reasons that I gave earlier. In this country we were able to react very swiftly with the medical community to influence clinical practice when concerns became apparent.

Sir Kent Woods: It will inevitably be the case as you improve post-market vigilance systems that you will find that some products perform below average and some above. The way the clinical community and, if necessary, the regulator responds to that is very important, but we cannot get round the fact that the systems are there to detect the less well-performing devices and to take action accordingly. There are some really interesting lessons we can draw from PIP and metal-on-metal hips, but they are totally different ones. As you have heard from the Minister, with PIPs there is no regulatory framework that is immune to being subverted. In relation to metal-on-metal, if you have a good registration and monitoring system, you will find there are some that are outliers in the wrong direction, and the speed with which you pick that up and practice and regulation respond to that is the hallmark of the quality of the regulatory system.

Chair: Minister and Sir Kent, thank you very much for an informative session. We look forward to seeing you batting in the debate over the directive. We are confident that there is a strong body of opinion inside the UK, including from patients, that, first, we want to see more transparency; secondly, we want to see British industry succeed in this field because we have some incredibly good businesses in the UK; and, thirdly, as a corollary to that, we want a regulatory system that is not so burdensome that it squeezes them out, especially in those small, very specialist areas. At the same time, there is a very difficult balance to achieve, and we wish you well in your negotiations. Thank you for coming today.
Written evidence submitted by the Medicines and Healthcare products Regulatory Agency

SUMMARY
1. The Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for the oversight of medical devices regulation in the UK, the framework for which is set by European legislation. The regulatory system for medical devices, of which medical implants are a subset, has operated effectively for the period that it has been in place and the MHRA does not believe that fundamental change is required. However, there are aspects of the system that could be strengthened and the forthcoming revision of the Medical Devices Directives provides an opportunity to address these.

CONTEXT—REGULATION OF MEDICAL DEVICES
2. Medical implants are regulated in the UK under a broader framework of regulation covering medical devices. Legislation in the UK (in the form of the Medical Devices Regulations 2002) stems from three main European Directives:
   (a) Directive 90/385/EEC on active implantable medical devices (AIMDD);
   (b) Directive 93/42/EEC on medical devices (MDD); and
3. The Directives have a dual objective: firstly, to provide manufacturers with a single set of regulatory requirements that, once met, provide free and unhindered access to the EU market and secondly, to provide users of medical devices and patients a high level of confidence that devices, when used in accordance with the manufacturer’s instructions, are acceptably safe and perform as claimed.
4. The Directives set out a list of essential requirements which all devices must meet before being placed on the market, as well as imposing various other regulatory requirements upon the manufacturer. The essential requirements concern matters such as the safety and performance of the device and the amount and type of information given to the user of the device by way of the label and instructions for use.
5. Under the MDD, devices are placed into four categories according to risk—classes I, IIa, IIb and III—where class I is the lowest and class III the highest risk. A manufacturer of class I devices can self-certify conformity with the essential requirements, whereas all other devices will require assessment by an independent third-party organisation, known as a Notified Body, of which there are around 80 across Europe. A manufacturer can select any Notified Body across Europe irrespective of location, provided that their field of expertise covers the device being considered.
6. There are various options set out within the Directives which a manufacturer may choose to demonstrate compliance with the essential requirements to a Notified Body, termed conformity assessment. These will involve, broadly, an assessment of the manufacturer’s quality control systems, manufacturing processes, or individual testing of each device type. The aim is to match the level of control of the device—and thus the depth and challenge of the conformity assessment procedure adopted—to the perceived risk associated with the product.
7. Once a device has been demonstrated to meet the essential requirements, a manufacturer places a CE mark on the device and is free to place the device on the market in all EU countries without further controls.
8. The overarching legislative framework for medical devices is part of the EU’s “New Legislative Framework” (formerly known as the “New Approach”), which is concerned with facilitating operation of the single market in various areas of product legislation. The principles of CE marking are common across a number of sectors; they are used, for example, in relation to the safety of toys and personal protective equipment, although the standards involved vary substantially from sector to sector.
9. The Directives are implemented and overseen by a competent authority in each EU Member State; in the UK this is the MHRA. Broadly speaking, the role of the competent authority is to implement the provisions of the Directives, to appoint and control Notified Bodies, to assess and authorise clinical investigations of non-CE marked devices and to monitor and investigate adverse events and field safety corrective actions (including recalls) occurring in their country.
10. These general principles are explored in further detail in relation to medical implants in the following sections.

3 http://ec.europa.eu/enterprise/newapproach/index_cfm?focaction=directive.main
5 http://www.mhra.gov.uk/Howweregulate/Documents/index.htm
Regulation of Medical Implants

11. Medical implants are regulated under the MDD, which classifies them in the two highest risk categories, classes IIb and III, and the AIMDD, where all devices fall de facto into class III. As set out previously, the risk category that a device is placed in determines how a manufacturer is able to demonstrate conformity with the relevant Directive and the level of scrutiny required by a Notified Body.

12. Examples of class IIb implantable medical devices are bone plates and screws, gastric bands and intraocular lenses; class III implantable medical devices are heart valves, total hip replacements and breast implants; and active implantable medical devices are pacemakers, implantable defibrillators and cochlear implants. Appendix A sets out in further detail the relevant definitions from the MDD and AIMDD relating to implantable and active implantable medical devices.

13. When undertaking conformity assessment for class IIb implants a Notified Body typically carries out a detailed assessment of the manufacturing facility to look into design, manufacturing and inspection of the devices concerned. They also cover other general requirements such as staff training and the handling of complaints. They will also sample technical documentation for compliance from the range of products being manufactured. These assessments normally take place annually to ensure ongoing compliance with the requirements of the legislation.

14. For class III implants, as well as the assessments at the facilities as outlined for the class IIb products, there is also a requirement for the Notified Body to review the technical documentation of each product to ensure that it is in compliance with the essential requirements. Dependent upon the product this will cover such areas as safety, performance, biological properties, sterilisation, software and labelling.

15. For medical implants, clinical data is required to demonstrate compliance with the relevant essential requirements. Before placing a medical implant on the market a manufacturer must have undertaken a clinical evaluation. This process involves an analysis of clinical data that can come from a number of sources including clinical experience of the medical device or a similar device, published clinical investigations or other studies of similar devices in the scientific literature, or from the results of a specifically designed clinical investigation of the device. Clinical investigations will typically be required where a medical implant has new design features or uses new materials.

16. Clinical data for implants will typically not include an evaluation of medium- and long-term clinical performance since it is not feasible to run pre-market clinical investigations for the expected lifetime of an implant, nor is it usually possible or appropriate to carry out randomised clinical trials such as is done with pharmaceuticals. A critical aspect of ensuring the safety of implants is therefore a manufacturer’s responsibility to ensure that adequate post-market surveillance is in place once an implant has met the relevant requirements for CE marking. For implants, this should include properly structured post-market clinical follow-up (PMCF) studies designed to confirm the medium- and long-term safety and performance of the implant. This applies equally to implants that are the subject of pre-market clinical investigations prior to CE marking and to those that are introduced to the market on the basis of existing clinical data. The results of post-market surveillance programmes should be fed back into the risk assessment and clinical evaluation of a device by a manufacturer and should be assessed by the Notified Body.6

17. The role of the MHRA in relation to the regulation of medical implants falls into three main areas—the oversight and designation of Notified Bodies, assessment of clinical investigations and investigation of adverse incidents.

18. Oversight and designation of Notified Bodies—there are currently six Notified Bodies in the UK that are designated to undertake conformity assessment for some or all of the devices covered by the MDD and AIMDD.7 A key role of the MHRA is to ensure that the Notified Bodies have the appropriate technical competence to be able to cover the product scope for which they have been designated. Routine monitoring of Notified Bodies by the MHRA involves two processes—office audits and witnessed assessments.

19. Office audits generally focus on specific client files, reviewing the complete process from receipt of application, assignment of assessors, reports and issue of certificates. For high-risk devices such as implants, the audit team will include technical and clinical experts to support the assessment. In witnessed assessments the focus is in ensuring that the assessor has the right level of competence and fully addresses all the issues found during their assessment. Any issues in either audit process are highlighted, with the Notified Body required to provide acceptable corrective action plans which are monitored by the MHRA.

20. Assessment of clinical investigations—as set out previously, clinical investigations are generally likely to be required for medical implants. A clinical investigation of a non-CE marked implant must be designed to establish that the performance claimed by the manufacturer can be adequately demonstrated, and that the device is judged to be safe to use on patients taking into account any risks associated with the use of the device when weighed against the expected benefits. The role of the MHRA is to assess the technical and clinical evidence provided by the manufacturer to ensure that there are no public health or public policy reasons whereby the

6 MEDDEV guidelines 2.7/1 and 2.7/4 explain the principles of clinical evaluation and investigation in further detail—see http://ec.europa.eu/health/medical-devices/documents/guidelines/index_en.htm
7 http://www.mhra.gov.uk/Howweregulate/Devices/NotifiedBodies/UKNotifiedBodiesundertheMedicalDevicesDirectives/index.htm
proposed clinical investigation should not proceed. Examples of instances where the MHRA might object include where there are reasonable grounds to suspect that a device does not satisfy relevant essential requirements, or where there is inadequate pre-clinical data in order to make it reasonable for clinical testing to commence.

21. **Investigation of adverse incidents**—the MHRA investigates both mandatory serious adverse event reports from manufacturers and adverse events reported voluntarily by healthcare professionals and members of the public. As a result of these investigations the MHRA will take further action as appropriate, including recalling faulty products and offering advice to the health service, primarily through Medical Device Alerts, but also through safety pamphlets, posters, and bulletins. This illustrates the fact that many of the issues that arise in relation to devices regulation are concerned not simply with the characteristics of the products themselves but also through the interface between the product and the manner in which they are used. The MHRA therefore has an important role in working with professionals and the public, not only to inform but also to influence their behaviour.

22. Appendix B provides an example of how the MHRA has fulfilled this role in the past in relation to a medical implant, and Appendix C sets out further information and statistics in relation to the MHRA’s role in medical device vigilance.8

### Improving the Regulation of Medical Implants

23. This written evidence has, to this point, provided a factual account of the regulation of medical devices, with a particular focus on how this applies to medical implants. Further important context is provided in the number of reports and initiatives that have, are, or will be looking at issues relating to the regulation of medical implants as well as this inquiry; these are as follows:

(a) the review of the actions of the MHRA and Department of Health (DH) in relation to Poly Implant Prothèse (PIP) silicone breast implants, expected to be published in May 2012;

(b) the forthcoming review by Sir Bruce Keogh of the regulation of cosmetic surgery, which will include examination of the feasibility of a register of medical implants;9

(c) the Health Select Committee report on PIP breast implants and regulation of cosmetic interventions, published on 28 March 2012;10

(d) the proposal from the European Commission on 9 February 2012 for a “joint plan of immediate action” by Member States in response to issues raised by PIP silicone breast implants;11 and

(e) the forthcoming revision of the Medical Devices Directives.12

24. This section goes on to consider how the existing regulatory framework could be strengthened, considering first the general principles and going on to examine particular aspects in relation to medical implants. The revision of the Medical Devices Directives is a focus for many of the potential improvements, although there are some aspects that fall outside of the scope of this exercise.

25. **The principles of the European regulatory system**—recent events involving PIP silicone breast implants and metal-on-metal hip replacements have exposed a general lack of understanding of how the European regulatory system for medical devices is structured and, perhaps more importantly, why it is structured in this way. In particular, the difference to how pharmaceuticals are regulated is often used as a point of comparison.

26. One of the main differences between the regulatory systems is the differing requirements prior to a device being placed on the market. Medical devices are unlike pharmaceuticals, in that their development is generally based on principles of engineering, rather than of chemistry and pharmacology and, as such, greater reliance can be placed on laboratory tests rather than clinical studies in patients. Furthermore, relatively minor design and manufacturing improvements are frequent, and medical devices tend to evolve over time in a manner similar to other engineering-based products; the development of the pacemaker over the past fifty years, for example, is as a result of dozens of small design improvements made over that time.

27. Equally, it is relatively straightforward to demonstrate the short-term safety and performance of a device which is not intended to be implanted for an extended period of time using a short-term clinical investigation in a relatively small group of patients. The particular challenge for medical implants comes in that, unlike pharmaceuticals and non-implantable medical devices, an implant is intended to have many years of use inside the human body and there are limitations to what can be studied pre-market, for example in animal models. Adverse incidents with implanted devices differ from adverse reactions to drugs in several ways: sporadic manufacturing defects in components, operator-dependent variations in implantation, and long-term failure related to mechanical or chemical processes in the human body. It is not feasible to adequately study the absolute long-term safety and performance of implants in patient groups of sufficient size and diversity prior to their being placed on the market, which is why the ongoing post-market surveillance of implants is a...
particularly critical aspect of the regulatory system for these devices. It is the joint responsibility of manufacturers, Notified Bodies, clinicians and regulatory authorities to ensure that this happens.

28. In addition, pre-market assessment for pharmaceuticals is undertaken by the MHRA, whereas for medical devices this role is fulfilled by Notified Bodies. Aside from the responsibility for designation and audit of Notified Bodies in the UK, the MHRA’s only other responsibility in pre-market assessment of devices is in assessing clinical investigations submitted by manufacturers.

29. The question is posed why this crucial role for assessing the safety of devices is delegated to Notified Bodies and not undertaken by publicly employed experts. The rationale for employing such a system is largely down to the size and breadth of the market for medical devices—a typical estimate is that there are in excess of 400,000 different medical devices on the market in the EU. The medical devices sector is constantly innovating, and new technologies appear at far greater rates than they do in pharmaceuticals. Individual Notified Bodies are able to specialise in certain areas and react to market demand, adding expertise and capacity where required in a way that would not be possible for public sector bodies. The result is a system that is efficient and able to rapidly undertake pre-market assessment; the EU is widely recognised as being an innovation-friendly environment largely due to this regulatory structure, and the Notified Body model of third-party involvement is increasingly being adopted in various forms by regulatory authorities outside Europe.

30. Taking the above considerations into account, the Government’s departure point for considering how the regulatory framework for implants can be improved is concerned with strengthening the current system, rather than advocating fundamental change where there is no evidence that this would improve patient safety, and so delay the availability of novel treatments to patients.

31. **Notified Bodies**—Notified Bodies play a critical role in the regulatory system for ensuring the safety of medical devices: this is heightened by the fact that the EU operates a system of mutual recognition, and so a CE mark awarded in any Notified Body in any EU country allows free movement of that device across the EU.

32. There is general concern about the variability in performance of Notified Bodies and as such one of the MHRA’s priorities for the revision of the Medical Devices Directives has been to strengthen the criteria for designation of Notified Bodies, and to ensure a consistent application of these criteria and monitoring of performance of Notified Bodies across the EU.

33. The MHRA has advocated the involvement of experts from more than one Member State to be involved in the designation and audit process, and for this process to have oversight by a central EU committee comprised of experts from Member States. The aim of these changes would be to drive a consistently high level of oversight of Notified Bodies, ensuring that they are designated on the basis of proven competence for the devices that they will be assessing. This is of particular importance for higher risk devices such as medical implants where significantly greater specialist technical and clinical input is required to adequately assess the safety and performance of the device.

34. In advance of the revision exercise, the MHRA has been involved in a programme of peer review of Notified Bodies, which has been a voluntary programme amongst some Member States to attempt to drive greater consistency in the designation and audit process. The MHRA was also heavily involved in drafting best practice guidance for designating authorities, which is increasingly used by Member States and provides a solid base for the actions needed to improve this area.

35. Addressing the performance of Notified Bodies has also been an area highlighted for action in the Commission’s “joint plan for immediate action”—which is a recognition that there is a need for this area to be addressed in advance of the revision exercise, where changes are unlikely to take effect for a number of years. In particular, this focuses on designation and audit of Notified Bodies by designating authorities, but also highlights the requirements of Notified Bodies when they audit manufacturers, with a particular focus on ensuring that Notified Bodies undertake unannounced inspections of manufacturers. The MHRA supports the measures outlined in this plan and has been working with the Commission and UK Notified Bodies to address practical implementation of the areas highlighted.

36. **Clinical evaluation**—as outlined previously, clinical evaluation of a device is required when demonstrating conformity with relevant essential requirements to verify the clinical safety and performance of a device. For medical implants, this process is particularly important, as the technical and biological characteristics of a device when implanted in the body need to be understood and documented.

37. An area that we have identified for improvement is that the Medical Devices Directives are permissive when setting out when manufacturers need to undertake clinical investigations, or to what extent they are able to rely on existing scientific literature and claiming equivalence with an existing device. The MHRA was key to making changes in the last revision of the Directives such that implantable devices covered by the MDD and devices covered by the AIMDD now require specific justification for not undertaking a clinical investigation, but it is still the case that a large number of implants placed on the market do not have any new clinical investigations undertaken. Furthermore, manufacturers should also be gathering clinical data on devices

---

14 http://www.nbog.eu/ has details on peer review and best practice guidance
in use not only to ensure the safety of those devices but also to inform the development and clinical evaluation of future devices.

38. As Notified Bodies are responsible for assessing clinical evaluation by manufacturers as part of conformity assessment, ensuring that appropriate clinical investigations have taken place falls to them. We consider that many of the areas for improvement outlined in relation to the oversight and designation of Notified Bodies in the revision of the Medical Devices Directives will result in greater scrutiny in this area—in particular ensuring that appropriate clinical expertise is in place to be able to assess clinical evaluations—but we also consider that reducing the extent to which manufacturers are able to rely on equivalence to be critical. This can be addressed through both further strengthening the legislation and ensuring that Notified Bodies place appropriate scrutiny on the use of equivalence.

39. Additional scrutiny on high-risk devices—a key question that is being posed as part of the exercise to revise the Medical Devices Directives is whether additional pre-market scrutiny by public authorities is required in some cases in addition to that undertaken by Notified Bodies. This concept was first raised in the 2008 consultation paper issued by the Commission, which proposed a role for the European Medicines Agency (EMA) in the assessment of the highest risk devices. Whilst the idea for using the EMA has since been disregarded, it seems likely that the Commission will include a proposal for some sort of central EU scrutiny of new class III devices in addition to assessment by a Notified Body before they are placed on the market.

40. Whilst this idea does, at face value, appear to have some merit in providing additional assurance for the highest risk devices, we have concerns about such a proposal. The principal concern relates to the resourcing implications of duplicating the work of Notified Bodies—there is a considerable amount of work undertaken by specialist staff in Notified Bodies in conformity assessment of class III devices and it is unclear to what extent a central EU resource will be able to scrutinise this in any meaningful way, without requiring a substantial investment in staff. The expertise required is compounded by the breadth and complexity of class III devices; an estimate is in excess of a thousand new class III devices are placed on the market in the EU every year. An additional concern we have is that introducing this additional step could serve to muddy the water in relation to where responsibility lies for pre-market scrutiny, and risks reducing the onus on a Notified Body to undertake their activities properly.

41. The MHRA's view is that addressing concerns with clinical evaluation and Notified Bodies—particularly ensuring that those Notified Bodies designated to assess the highest risk devices are competent to do so—should drive improvements in assessing the highest risk devices, without introducing a system that will drive up costs and delays with questionable benefits.

42. Post-market surveillance—the Medical Devices Directives require manufacturers to undertake post-market surveillance but in rather general and imprecise terms and, as such, it is undertaken with variable rigour. We have therefore identified this as a key area that needs to be addressed in the revision of the Directives, and expect that there will be provisions included that more clearly set out the responsibility of manufacturers to put in place adequate and proportionate systems to systematically collect information on the performance of their devices in the post-production phase. We would also expect Notified Bodies to be required to assess the appropriateness of a manufacturer's post-market surveillance system as part of their assessment.

38. Sir Bruce Keogh’s forthcoming review will examine the feasibility of a wider register for medical implants, such a register would have the aim of gaining the benefits seen by the orthopaedic community from the NJR across a much broader range of medical implants. In the context of this review, the MHRA is currently examining how the current use of barcoding in the NHS17 and likely proposals in the revision of the Medical

15 Based on information provided by the French competent authority, AFSSAPS; “new” covers both novel devices as well as developments of existing devices on the market
17 http://www.dh.gov.uk/health/2012/01/it-systems-coding/
Devices Directives to mandate a system of Unique Device Identification (UDI) across the EU could be used to facilitate better traceability of devices and linkage with outcomes. Such an approach would support manufacturers’ responsibilities to undertake appropriate PMCF studies in a co-ordinated and cost-effective manner.

47. We expect the Commission to include proposals for a system of UDI to be included in the revision, although it seems very likely the precise details of any EU system would be specified in delegated or implementing acts, rather than on the face of the revised legislation. The Commission recognise that different Member States are currently addressing the issue of UDI and traceability individually, and so plan to issue a Recommendation before the end of 2012 that will set out the principles that a UDI system should follow. At the same time, the International Medical Device Regulators’ Forum (IMDRF), a collaboration between international regulators that is replacing the Global Harmonisation Task Force (GHTF), are also addressing this issue to support a consistent approach globally.18

48. A further initiative that the MHRA intends to explore is the feasibility of including in the revised legislation the requirement for all implantable devices to include with them an implant card that would be given to a patient following a procedure. Such a card would include basic details about the patient and implant, including implant date, name of implant and batch/lot/serial number. It has become clear following media attention on breast implants and metal-on-metal hip replacements that most patients do not know what sort of implant they have had, and an implant card would help to support post-market surveillance, as well as providing patients with valuable information about their implant.

49. Co-ordination and co-operation—one of the key benefits from being regulated under a single EU framework is that manufacturers of medical devices do not have to undertake a large number of costly, time consuming assessment processes in every country in which they wish to market their device. However, there is currently no way to systematically use the breadth of information available to individual Notified Bodies and competent authorities across the EU to inform regulatory actions. Improving co-ordination, both within the EU and globally is an aspect of the Commission’s “joint plan for immediate action” and will also feature in the revision of the Medical Devices Directives.

50. The MHRA has been encouraging the Commission to address this weakness in a number of ways. One aspect is to require registration of all devices placed on the EU market, and the economic operators19 that do so, on a central EU portal; this is currently the responsibility of individual Member States. A further, critical aspect is in the development on an effective and efficient electronic communication and information support tool to support co-ordinated post-market surveillance across the EU. Such a system would allow:

   (a) centralised post-market surveillance and vigilance reporting by manufacturers, with automated notifications to relevant Competent Authorities;

   (b) access to a comprehensive EU database of post-market surveillance plans, incidents and field safety corrective actions (FSCAs); and

   (c) support for co-ordination of competent authority communications and actions.

51. We are expecting proposals from the Commission to address the areas outlined above; this will very clearly support better co-operation and communication between Member States, but also has the added benefit of simplifying and streamlining reporting structures for manufacturers of devices. We are also anticipating proposals that will address the wider need to improve co-ordination and oversight of the regulatory system—covering areas such as the central scrutiny process for designation and audit of Notified Bodies and ensuring swifter determination of issues relating to the borderline between legislation for medical devices and other, related, areas such as pharmaceuticals, cosmetics and biocides.

52. Transparency—the revision of the Medical Devices Directives provides an opportunity for a substantial change in the availability of information about medical devices and the regulatory system. Currently, very little information is available about a medical device throughout its lifetime—clinical evaluations, conformity assessment, adverse incidents and post-market surveillance plans, for example, are generally not published. Such opaqueness undoubtedly contributes to a degree of unease about the regulatory system, and a lack of feedback to those submitting information to the MHRA through the voluntary reporting system does not help encourage its use amongst clinicians. A key aim for the UK in the revision is therefore to drive far greater publication of information in a format that is useful for the public, as well as regulators and manufacturers; this is currently generally prohibited by explicit confidentiality requirements within the MDD and AIMDD that we wish to see removed.20

Conclusion—Supporting Innovation Through Regulation

53. One of the widely recognised benefits that the regulatory system in the EU brings is rapid access to the market for new and innovative devices. Studies have suggested that new devices come to market in the EU typically between one and two years sooner than the US, without any evidence that this comes at a higher risk

---

19 An “economic operator” is a manufacturer, distributor, importer or authorised representative
20 Article 15 of the AIMDD and Article 20 of the MDD refer
to patients and the public.\textsuperscript{21} One of the underlying objectives for the MHRA in the revision of Medical Devices Directives is to continue to strike this appropriate balance between supporting innovation and providing adequate safeguards to patients. Recent events involving PIP silicone breast implants and metal-on-metal hip replacements will make this objective more challenging, as we see the immediate reaction to problems being identified of assuming regulatory failure and calling for increased regulatory scrutiny—essentially moving from a system that balances risks against benefits to one which takes a more precautionary approach.

54. A common response to events involving PIP silicone breast implants has been to identify the US system as an improved model that the EU should be following,\textsuperscript{22} owing largely to the fact that pre-market assessment is undertaken by a governmental body. It is difficult to speculate whether the US Food and Drugs Administration (FDA) would have picked up problems with PIP silicone breast implants since PIP did not place them on the market in the US, but no regulatory system is set up to anticipate deliberate fraud. A more relevant comparison would be to consider metal-on-metal replacements—the DePuy ASR hip was placed on the market in both the US and the EU, having satisfied the pre-market requirements of both regulatory frameworks and yet, as outlined previously, problems with the implant were first identified in the UK.

55. Issues with PIP silicone breast implants and metal-on-metal hips stem from very different root causes—the first from deliberate subversion of the regulatory system and the second from unanticipated wear over a long time-period. However, this illustrates that picking isolated examples and attributing them to regulatory failure should not be the basis on which to advocate widespread changes to a system. Nonetheless, any regulatory framework has room for improvement and it is important for lessons to be learned from all instances where devices cause harm to patients. Equally, the regulatory system for medical devices does need to evolve to reflect the increasing complexity of devices. These include new and emerging technologies that involve novel materials and increasingly incorporate and interact with pharmaceuticals and information technologies.

56. The areas outlined in this evidence—which generally result from considered analysis of the current system over the course of a number of years—will bring about significant improvement to the devices regulatory system in the EU, whilst, at the same time, ensuring that the benefits that the EU system currently offers, by way of proportionate, efficient and effective regulation, are not lost.

\textit{April 2012}

\textbf{Appendix A}

\textbf{DEFINITIONS RELATING TO MEDICAL IMPLANTS}

A1. In order to explain fully how medical implants are regulated, it is helpful to consider the definitions relating to medical implants.

A2. The definition of a medical device in the MDD is:

\textit{“medical device” means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:}

\begin{itemize}
  \item diagnosis, prevention, monitoring, treatment or alleviation of disease,
  \item diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
  \item investigation, replacement or modification of the anatomy or of a physiological process,
  \item control of conception,
  \item and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.
\end{itemize}

A3. The definition of an implantable device within the MDD is:

\textit{Any device which is intended:}

\begin{itemize}
  \item to be totally introduced into the human body or,
  \item to replace an epithelial surface or the surface of the eye, by surgical intervention which is intended to remain in place after the procedure.
\end{itemize}

\textit{Any device intended to be partially introduced into the human body through surgical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implantable device.}

A4. The definition of an active and active implantable device within the AIMDD is:

\textit{“active medical device” means any medical device relying for its functioning on a source of electrical energy or any source of power other than that directly generated by the human body or gravity; and}

\begin{itemize}
  \item http://www.eucomed.org/newsroom/13/19/European-patients-have-access-to-new-medical-technology-sooner-than-American-patients/ \\
  \item http://www.eucomed.org/newsroom/8/19/EU-regulatory-system-brings-Europeans-fasted-access-to-medical-technology-without-compromising-safety/ \\
  \item Eg. http://in.reuters.com/article/2012/02/03/breast-implants-regulation-idINDEE81208U20120203
\end{itemize}
“active implantable medical device” means any active medical device which is intended to be totally or partially introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain after the procedure.

A5. The classification rules within the MDD relevant for implantable devices are contained within Rule 8 of the classification criteria:

All implantable devices and long-term surgically invasive devices are in Class IIb unless they are intended:

— to be placed in the teeth, in which case they are in Class IIa,
— to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are in Class III,
— to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class III,
— or to undergo chemical change in the body, except if the devices are laced in the teeth, or to administer medicines, in which case they are in Class III.

Appendix B

CASE STUDY OF THE MHRA’S ROLE IN INVESTIGATING ADVERSE INCIDENTS

B1. The MHRA was contacted by a surgeon at an Oxford hospital who was concerned about the rate of failure of a particular Labcor Heart Valve. A team was immediately sent up to the hospital which included clinical input, the technical expert in heart valves and experts in sterilisation and toxicology. An investigation was launched to understand the cause of the problems; this involved interviewing relevant clinical staff, assessing practices in theatre, liaising with the manufacturer to find out whether there had been some change in the manufacturing process, in the sterilisation process or in the fluid used to contain valve for transport, and contacting the FDA which had carried out a recent site visit.

B2. As a result of this extensive investigation, it became apparent that the Labcor Heart Valves require a longer washing period prior to insertion into the patient. This was not being adequately carried out by the theatre staff because they were used to the shorter washing periods for other heart valves. This action halted the further unexpected failure at the hospital; at the same time the MHRA also issued a generic Medical Device Alert bringing this issue to the attention of all cardiothoracic surgeons and cardiothoracic theatre staff.

Appendix C

THE MHRA’S MEDICAL DEVICE VIGILANCE SYSTEM

Adverse Incident Investigations

C1. The MHRA operates a medical device vigilance system in the UK which encourages and provides guidance on adverse incident reporting by:

— manufacturers and their various economic operators in compliance with the Medical Devices Directives and EU vigilance guidance;
— healthcare professionals; and
— members of the public, including medical device users and carers.

C2. The MHRA’s system meets all EU requirements and guidance including the need to centrally record and evaluate all information received, to inform manufacturers of all incidents received from healthcare professionals and to warn other Member States of any corrective action or enforcement measures being taken to address serious safety concerns.

C3. The numbers of adverse incident reports received by the MHRA has increased substantially over the past five years:

<table>
<thead>
<tr>
<th>Year</th>
<th>Adverse Incident reports received</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>8,634</td>
</tr>
<tr>
<td>2008</td>
<td>8,910</td>
</tr>
<tr>
<td>2009</td>
<td>9,096</td>
</tr>
<tr>
<td>2010</td>
<td>10,282</td>
</tr>
<tr>
<td>2011</td>
<td>10,967 (a 27% increase since 2007)</td>
</tr>
</tbody>
</table>

C4. In addition, data from the first quarter of 2012 show a dramatic increase in reporting—a 38% increase over the first quarter of 2011.

C5. In order to handle this increasing number of incident reports effectively, two new processes were introduced during 2011. The introduction of a triage process in April 2011 has ensured that medical device specialists are able to focus their efforts on the most serious adverse events that require their immediate attention and intervention, whereas more routine problems are investigated by device manufacturers in
accordance with their post-market surveillance obligations. The reports submitted by manufacturers following their investigations are reviewed by medical device specialists and further action is taken as necessary before transferring the adverse incident report to a trending and surveillance database.

C6. At the same time as the introduction of the triage process, a systematic trending system was established. This trending analysis reviews adverse incident numbers by device type and manufacturer on an ongoing periodic basis. The effective use of trending enables signals relating to incipient problems to be picked up earlier and more consistently. Further work to develop these trending systems is planned.

C7. Outcomes of adverse investigations can include:
- a Field Safety Corrective Action (FSCA) such as product recall, design change, software upgrades, amended instructions for use, including patient management for implants;
- quality assurance improvements;
- device repair;
- additional post-market studies;
- further monitoring and trending;
- local training of users or improvements in device storage; and
- supplementary safety advice from MHRA including One-Liners, Device Bulletins (see below), posters and pamphlets.

**Medical Device Alerts and the Central Alerting System**

C8. Medical Device Alerts are the MHRA's primary means of providing important safety advice. They can be issued for a variety of reasons:
- to provide an MHRA view or endorsement;
- to inform a wider user-base;
- to clarify and/or supplement information provided by a manufacturer;
- to speed up user response to manufacturers Field Safety Notices; and
- to provide advice on generic safety issues.

C9. In line with the increasing number of adverse incident reports received there has been a corresponding increase in the number of Medical Device Alerts issued. The figures for the past five years are shown in the table below:

<table>
<thead>
<tr>
<th>Year</th>
<th>Medical Device Alerts issued</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>100</td>
</tr>
<tr>
<td>2008</td>
<td>88</td>
</tr>
<tr>
<td>2009</td>
<td>85</td>
</tr>
<tr>
<td>2010</td>
<td>98</td>
</tr>
<tr>
<td>2011</td>
<td>113</td>
</tr>
</tbody>
</table>

C10. Medical Device Alerts are distributed via the Central Alerting System (CAS), a function that was transferred from the central Department of Health to the MHRA in January 2012. CAS distributes safety warnings to all hospital trusts and Primary Care Trusts in England. A monitoring system provides feedback on the receipt, analysis of the need for action and completion of the required action by the addressees.

C11. An analysis of this feedback data is conducted on a regular basis to ensure that the important messages contained within Medical Device Alerts are being received and acted upon by the recipients.

C12. In addition to the publication of Medical Device Alerts, the MHRA also publishes monthly editions of One-Liners and Device Bulletins to address specific topics of relevance to healthcare professionals.

**Liaison with Healthcare Professionals**

C13. The MHRA maintains regular dialogue with a range of external stakeholders: professional bodies, trade associations, patient user groups and external clinical experts through its expert advisory group and the Committee on the Safety of Devices (CSD).

C14. In the past year the MHRA has made extensive use of these liaisons to cover major issues related to PIP breast implants, metal-on-metal hip implants, and vaginal tapes for stress urinary incontinence. In addition, consultations have occurred on a wide range of clinical issues and input has aided the assessment of clinical investigations.
Written evidence submitted by the Association of British Healthcare Industries

About ABHI

The Association of British Healthcare Industries (ABHI) is the industry association for the medical technology sector in the UK. ABHI’s mission is to champion the benefits and use of safe and effective medical technologies to deliver high quality patient outcomes. With over 240 members, ABHI leads the advocacy of the industry in order to advance access to medical technology. Its membership includes many UK small and medium sized enterprises (SMEs) and some of the leading multinational businesses in the sector.

Executive Summary

— Implantable medical devices provide benefits to millions of people in the UK.
— Medical devices are regulated under the Medical Device Directives. It is important that the legal frameworks governing their introduction to the market maintain the highest standards of patient safety.
— The current system has been in place for twenty years, and like any regulatory regime dealing with innovative products it needs regular revision. This process is currently underway.
— The medical device industry supports the process of revision and has suggested a number of amendments to the system around the following areas:
  — Notified Bodies.
  — Vigilance and post market surveillance.
  — Clinical Evaluation.
  — Mechanisms for consistent implementation.
  — Unique Device Identification.
  — Confidentiality.
  — Coordination and management.
— The medical device industry firmly believe that if the changes outlined below, in particular those around Notified Bodies, vigilance and consistency, are enacted and implemented Europe will have a system which continues to support the development and introduction of innovative medical devices that will continue to improve the lives of people across the UK whilst improving patient safety.

Introduction and Overview

1. Millions of people in the UK benefit from implantable devices. For example, each year over 150,000 people in the UK receive artificial knee and hip joints (National Joint Registry, 2011). Implants enable patients to continue to live fulfilling working and family lives, and prevent their premature withdrawal from the labour market. In 2009 it was estimated that 11,000 people were able to return to work following a total hip or knee replacement, saving the welfare system £37.2 million (Bevan et al., 2011).

2. The term “implant” covers products ranging from active (ie powered) implants such as pacemakers to non-active implants such as joint replacements. These products are regulated in the UK under the Medical Device Regulations 2002 which transpose three main European Directives:
   (a) Directive 90/385/EEC on active implantable medical devices (AIMDD).
   (b) Directive 93/42/EEC on medical devices (MDD).

3. The term medical device covers a vast range of products ranging from syringes to scanners. Only a small proportion of these products are implants. Medical devices are central to the operation of all health systems. They enable clinicians to carry out procedures, facilitate the effective operation of the hospital infrastructure and are often used in the home by patients themselves.

How the Current Legislation Delivers Innovation to Patients

4. Medical devices are regulated under the Medical Device Directives. The products regulated by these directives play a crucial role in keeping the UK population healthy and productive by supporting innovation in healthcare, while also contributing to the UK knowledge-based economy. The UK medical device sector employs 64,000 people in the UK and is a key part of the UK life science industry that was described by the Prime Minister as the “jewel in the crown of our economy” (Department of Business, Innovation and Skills, 2011). The medical technology sector’s contribution to safe, efficient and life-enhancing products and services is based on its capacity to innovate.

5. The Medical Device Directives ensure that patients receive treatment from safe products which have undergone a thorough compliance process. At the same time, they enable the free movement of product between EU member states.
6. The Directives were first developed in the 1990s under the framework of Europe’s “New Approach” (today replaced by the New Legislative Framework) in response to the threat of proliferation of different regulatory systems around Europe and the need to protect public health.

7. As with any regulatory regime that deals with a large range of products the Medical Device Directives use a classification system. This system classifies devices by risk with the lowest risk devices being in category I and the highest risk devices falling into category III. Implantable products are subject to the most rigorous controls and therefore attract the most stringent compliance rules. However any consideration of the regulations covering implants must also address the entire framework of device regulation.

8. Following extensive consultation with all stakeholders the European Union issued a Council Conclusion in June 2011 which reaffirmed European Member States commitment to the current legal framework. This capacity is in turn dependent on an effective and efficient EU-wide regulatory framework.

9. This framework needs to provide for patient access to safe, high quality healthcare products while allowing for the timely introduction of innovation. Indeed good regulation should be supportive of innovation which can deliver safer more effective products; to stifle innovation would stifle this cycle of improvement and delay patient access to potentially lifesaving innovations.

10. We therefore believe the current regulations have been instrumental in safeguarding patients whilst bringing them medical benefits. Like any system it is important that there is a regular review to identify potential improvements. There have been very few instances of product failure when one takes account of the many millions of products used annually—it is estimated 38 million people come into contact with a medical device every day (SEHTA, 2011).

11. The system is currently under review and the resulting Revision will be the subject of an EU Commission “Formal Proposal” in mid 2012. ABHI and the medical technology industry fully support the need for changes to the system.

The Role of the MHRA

12. We believe that the MHRA does a very effective job in implementing the Directives. It is indeed often considered to be the pre-eminent Device authority in the EU and is well respected throughout Europe and beyond among those concerned with efforts to achieve global harmonization in device regulation.

How can the Legislation and Regulations be Improved?

13. The system is currently under review. During wide consultation by the EU Commission a number of potential improvements were identified. The UK medical device industry believes the system should:

— be robust and comprehensive;
— protect public health and enable efficient healthcare delivery;
— enhance public confidence whilst avoiding unnecessary bureaucracy;
— be consistent and transparent; and
— effectively foster and support innovation.

14. The following points will explore this, addressing the areas where we believe reform is necessary.

Notified Bodies

15. Notified Bodies are independent third parties nominated and monitored by Member State Competent Authorities, such as the MHRA. Therefore, they act on behalf of the member state authority that has designated them. They carry out pre- and post-market scrutiny and certification of medical devices. The operation and coordination of Notified Bodies is an area that industry would like to see improved as part of the Revision. As structured today, the control and oversight by National Competent Authorities of their Notified Bodies depends largely on voluntary and national approaches rather than on consistent, mandatory EU level rules and standards.

16. We therefore believe that Notified Bodies which are central to the New Approach system have not been designated or controlled with sufficient rigour and that this aspect of the device regulatory system must be improved. Steps are already being taken by the EU Commission as part of a series of short term measures requiring Competent Authorities to review the designation of Notified Bodies. This, together with the development of better control mechanisms, must feature in the Revision. Policy makers should focus on oversight of notified bodies’ performance, rather than introduce further steps in the regulatory process. There are currently c.80 Notified Bodies across Europe and we believe that a more robust approach to designation should result in a significant reduction.

Vigilance and Post Market Surveillance

17. These are key features of the system and are central to its improvement in the future. The sharing of data between Member States is crucial for patient safety; there must be a cross border communication system that facilitates the efficient transfer of information between national Competent Authorities. The current...
regulatory framework for medical devices requires vigilance and market surveillance systems to be put in place by manufacturers and national Competent Authorities. This is intended to allow for rapid identification and response in case of incidents which may put patient or user safety at risk or create doubt about the product performance. At present however, there is a lack of coordinated exchange of information on reported incidents as well as considerable variation in how different EU Member States respond to incidents. This has resulted in both duplication of effort and inconsistencies.

18. A better defined legal framework on vigilance and greater harmonisation of Member States’ market surveillance activities are therefore needed to ensure rapid and consistent EU-wide risk identification and response. This would deliver significant benefits for overall patient safety allowing centralised reporting and surveillance, using an EU portal for reporting.

**CLINICAL EVALUATION**

19. Clinical evaluation of a device is required when demonstrating conformity with relevant essential requirements. For medical implants, this process is particularly important, as the characteristics of a device when implanted in the body need to be understood and documented. ABHI believes the revision of the MDDs should see the system become more prescriptive in setting out when manufacturers need to undertake clinical investigations, or to what extent they are able to rely on existing scientific literature claiming equivalence with an existing device.

20. Notified Bodies are responsible for assessing clinical evaluation by manufacturers as part of conformity assessment, ensuring that appropriate clinical investigations have taken place. ABHI therefore believes that by improving the coordination of Notified Bodies, the scrutiny of clinical evaluation will be greatly improved.

**MECHANISMS FOR CONSISTENT IMPLEMENTATION**

21. Currently, the European Commission, in consultation with Member States and affected stakeholders, issues guidelines aimed at supporting consistent implementation and interpretation of the Medical Devices Directives. However, the process leading to development or revision of these guidelines lacks pace and legal certainty. In addition, when the guidelines are finalised and agreed, evidence shows that there are severe disparities in the way and extent to which they are implemented in the Member States. This has led to significant cross-border variations in terms of quality of conformity assessment procedures, lack of process clarity and predictability for manufacturers and national responses to vigilance.

22. These cross-border disparities must be addressed in the Revision by changing the current procedure for development of guidelines. This needs full commitment from Member States in order to use clearly defined and transparent drafting procedures, including timelines. This must involve all stakeholders including the European Commission to ensure coherence with European law.

**CONFIDENTIALITY**

23. The confidentiality requirements under the current Medical Devices Directives are seen by some stakeholders as being too restrictive (eg in terms of access to information about products on the market, or the functioning and decision-making of Notified Bodies).

24. The Revision of the EU legislative framework for medical devices must result in greater overall transparency and access to information for patients, consumers, healthcare professionals and manufacturers as well as for Notified Bodies, national Competent Authorities and the European Commission.

**UNIQUE DEVICE IDENTIFICATION**

25. Unique Device Identification (UDI) is a requirement for all devices to carry a machine readable identifier (today probably a bar code but this may change as other technology becomes available). This requirement will be included in the Revision and will be a significant step in the quest to improve patient safety. UDI will enable a particular implant to be linked to the patient who receives it and will greatly assist in the setting up of databases and registries. UDI will be based on internationally accepted standards and will eventually become a global requirement for devices as it is also the subject of legislation in North America, Australia and other regions.

**COORDINATION AND MANAGEMENT**

26. Today the EU oversight of medical devices is decentralised and this European approach makes it possible to manage what is a highly innovative and diverse industrial sector in terms of products, technologies and services. The decentralised approach is best placed to provide the capacity to efficiently deal with the many applications related to over 400,000 products on the market from over 22,000 medical technology businesses, 80% of which are SMEs.
27. The decentralised approach, which is the essence of the current system, should remain a basic principle of the future legislative framework for medical devices in order to preserve safety, flexibility and pace. However, the current system does suffer from disparate national approaches. It needs improved coordination at EU level to ensure uniform application by Member States, especially in the areas of Notified Bodies and vigilance.

*How could the European Commission ensure that potential changes to the Medical Devices Directive do not hinder the introduction of innovations in medical implants to the market?*

28. As stated above the medical device directives have been instrumental in safeguarding patient safety whilst bringing them medical benefits. The current system allows patients to access innovation at the appropriate time.

29. We firmly believe that if the changes outlined above, specifically those around Notified Bodies, vigilance and consistency, are enacted and implemented Europe will have a system which continues to support the development and introduction of innovative medical devices that will continue to improve the lives of people across the UK whilst maintaining patient safety.

**Bibliography**


April 2012

**Joint written evidence submitted by Dr Thomas Joyce and Dr Pauline McCormack**

**Respondents**

Tom Joyce is a biomedical engineer with almost 20 years of experience specialising in the design, testing, analysis and evaluation of artificial joints including hips, knees, shoulders and fingers. He works extensively with industry and clinicians in order to inform and improve future designs of artificial joints. He currently supervises a number of projects around hip joint failure including: ex vivo analysis of failed resurfacing hip prostheses; improving the metal-on-metal hip prosthesis—a study of failures and wear mechanisms; investigation of failed lower limb arthroplasties; and “when technology fails patients”: engaging with stakeholders on metal-on-metal hip joint failures. He has taken part in recent investigative media programmes highlighting problems with metal-on-metal hip failure, these include Dispatches and Newsnight in the UK, Primetime in Ireland, Four Corners in Australia and Kontant in Denmark.

Pauline McCormack is a medical sociologist who researches social and ethical aspects of treatment, care and research in health. She has interests in disability, notions of power, the patient voice, and how policy serves individuals. As part of the project “when technology fails patients”: engaging with stakeholders on metal-on-metal hip joint failures, she is collecting data from patients and their families about their experiences with a failed hip implant.

**Scope**

Our submission to the Committee focuses on an area of recent controversy, that of failed metal hip implants, which intersects with our areas of expertise. We will concentrate on:

1. Engineering analysis of failed metal-on-metal hips. We have examined components from almost 400 failed hips and published much of our data. We are the only independent centre in the UK, and probably the world, undertaking such extensive research. We were the only research group in the world to publish critical data on the DePuy ASR metal-on-metal hip prior to its worldwide recall in August 2010.
2. Qualitative data from patients about their lived experiences. We believe we are the only people in the world undertaking specific, sociological research into current patient experiences with failed metal-on-metal hip implants, gathering data on their daily lives and the impact on their work, families and social activities. We are in the midst of data collection and, while the findings presented here are very preliminary and are unpublished, we are prepared to make them available to the committee as we feel strongly that the patient voice should be audible in these deliberations.

**Responses to the Consultation Questions**

1. Are current legislation and regulations on safety and efficacy of medical implants fit for purpose?

   No. In the case of hip joint replacements we believe that this has been shown in various scientific publications (Langton, Jameson et al., 2008; Joyce, Langton et al., 2009; Langton, Sprowson et al., 2009; Langton, Jameson et al., 2010). To give the Committee a summary idea of the problems, we cite the example of the DePuy ASR hip which was implanted into almost 100,000 patients worldwide (around 10,000 UK) and which is responsible for causing widespread health problems in patients. This has been described as perhaps the biggest disaster in the history of orthopaedics. As international experts in implant design and analysis we have no idea whether this device was tested before it was implanted in patients, as there is no regulatory requirement for such tests. If it were tested in house, we have no idea what the results were as there is no legislative or regulatory requirement for companies to publish data.

   For a detailed discussion of the general problems, particularly those of substantial equivalence, we would refer the committee to the work of colleagues who are experts in regulatory affairs (Heneghan, Thompson et al., 2011; Matthew, Carl et al., 2011; Heneghan, Langton et al., 2012).

   In engineering terms we believe that the international standard ISO14242, “Implants for surgery—Wear of total hip-joint prostheses” is not detailed enough and should be amended to include specific guidance on the testing of acetabular cups at various angles of inclination and anteversion. In addition, it should require the smallest and largest sizes of artificial hips to be tested. Had such pre-clinical tests been undertaken on the ASR then the current disaster might have been averted.

   Data from patients with failed metal-on-metal hip implants shows they are perplexed, confused and often angry as to why, in their opinion, the regulatory system has not protected them. They query how effective the system is, which allowed hip joints which are failing so disastrously, onto the market in the first place.

   “...the medical regulatory bodies, they’ve really got to protect us better and they’re not being bold enough in doing that, they’re passing the buck”. (Focus Group patient)

2. How effectively does the MHRA implement the Directive in the UK?

   This question does not draw attention to the fact that, if the Directive is not fit for purpose, then the effectiveness of its implementation is largely academic.

   In our patient focus groups people consistently interrogated the responsibilities of the MHRA and concluded the MHRA do not have a clear remit and lacked sufficient authority to take responsibility over, and act decisively on implant failure. The patients saw the gap in responsibilities as ethically and morally wrong.

   [We] “we’re really annoyed that the regulatory body, we felt that they shirked their responsibility and, what is the regulatory body? Has it not got enough teeth”? (Focus Group patient)

   Worryingly, they interpreted the lack of action as evidence that the regulator could not be impartial or independent.

3. How could the legislation and regulations be improved?

   We outline a number of areas where we believe legislation and regulation should be improved, points (i) and (ii) should be treated as urgent:

   (i) Testing

   “The reality is, you cannot test the wear patterns of human joint replacement in any animal species”.23

   “I cannot believe in this advanced technological age that no-one could design a machine that would replicate the movement of variously fitted hip joints”. (Patient panel participant)

23 Professor Sir Kent Woods, Chief Executive, MHRA http://www.bbc.co.uk/news/health-17200330
Observations about testing human joints in other species are spurious and the apparent lack of understanding by the regulator on this point is disturbing. Fortunately, machines do exist to wear-test human joint replacements. They originated in the UK in the 1960s (Duff-Barclay and Spillman 1966) and are validated to international standards (ISO 14242:2000). They have been further developed since then and are now commercially available. It is our view that stringent, mechanical, pre-implantation, testing should be mandatory for all joint replacement implants and that test data should be publicly available. Ideally such testing should be undertaken independently by not-for-profit organisations, as designers and engineers working for companies could be subject to commercial pressure which can lead to publication of favourable results (Schott, Pachl et al, 2010). At the very least, if testing is allowed by commercial companies for their own products, test data should be open to scrutiny by independent experts and the public.

We believe that the international standard ISO14242, “Implants for surgery—Wear of total hip-joint prostheses” is not detailed enough and should be amended to include guidance on the testing of acetabular cups at various angles of inclination and anteversion. In addition, the smallest and largest sizes of artificial hips should be tested.

(ii) Explant retrieval and analysis

Examination of explanted joints that have failed or caused problems in the body is one of the most valuable sources of data about how and why implants fail—they can be thought of as the “black box”. Revision operations, which remove such problem implants have to be reported to the National Joint Registry (NJR) but conservation of the failed joint itself is not required and many are simply thrown away. We have some evidence of surgeons and hospitals disposing of joints even when patients have requested that the joint be kept to be sent for analysis.

We call for the conservation and analysis of explanted joints to be made mandatory as part of the NJR reporting procedure. This analysis should be undertaken by independent, not-for-profit experts. Such a move might be facilitated by the establishment of a national explant retrieval centre and the committee should consider putting in place consultations for how such a centre could be managed and funded. One option might be a universal tariff on all new joints, as currently funds the NJR. Another option would be that a charge is made to the manufacturer for each joint examined—in this way manufacturers would be additionally encouraged to design and produce joints with the greatest longevity.

(iii) Symptom reporting

We have repeated reports from patients that their concerns over symptoms from their hip implants were dismissed and/or ignored by medical professionals. We believe that the Yellow Card System, whereby a user of medication can report side effects directly to the MHRA, could be usefully expanded to include users of medical devices.

(iv) Data transparency and results publication

We join the ever-growing body of professionals who are calling for greater transparency of the results of experiments, particularly in medical trials and testing where the results can have profound implications for patients (Groves 2010; Alsheikh-Ali, Qureshi et al, 2011; Ross, Lehman et al, 2012; Wellcome Trust 2012). Research and innovation moves more quickly in a positive direction when data and findings are shared between investigators, meaning they can build on colleague’s work. The practice of pharmaceutical companies publishing mainly favourable data means that investigators do not get to learn from the mistakes of others and may waste valuable time repeating failed experiments (Schott, Pachl et al, 2010; Lundh, Krogsbøll et al, 2011).

The NJR is something that this country should be proud of. It is the largest such registry in the world, but we should consider whether the raw data contained in it could be made more readily available. We also suggest that the NJR should be expanded to cover all artificial joints.

The NJR could also provide a publicly available, adverse event reporting website along the lines of the MAUDE (Manufacturer and User facility Device Experience) database offered by the FDA in the USA, so that all interested parties can view this important data.24

We believe surgeons should be required to disclose payments received from orthopaedic companies and that such data should be made publicly available as is the practice in the USA. This would free medical professionals from accusations that their choice of treatment or device for their patient is not based on the patient’s welfare. Such an observation was made in our focus groups and in a patient panel:

“If you can’t trust the surgeon who is the expert, to give you the best advice and a device that is suitable for you, not one that has been “sold” to them, who can you trust? Are patients just pound signs at the end of the day”? (Patient panel participant)

24 http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm
4. How could the European Commission ensure that potential changes to the Medical Devices Directive do not hinder the introduction of innovations in medical implants to the market?

It is a misconception that more regulation hinders innovation. As President Obama said in his 2012 State of the Nation address “rules to prevent ... faulty medical devices don’t destroy the free market. They make the free market work better”. As noted above, regulation can aid collaboration and mutual education through transparency and openness, which only helps innovation. In addition, regulating medical devices to ensure that better products reach the market means that devices sold will be more efficient and successful, which will result in better uptake from surgeons and greater trust from patients. Evidence shows that devices in the USA, which follow a longer, stricter regulation route are more successful and have fewer recalls (Heneghan, Thompson et al, 2011).

This said, we caution against a constant focus on innovation rather than on patient safety and precautionary measures. Innovation should result in improvement or enhancement—not for their own sake but in order to pass on improved treatments to the patient. The current situation around medical devices is such that not only does the system not guarantee improvements for patients, it hampers them.

The last word in our submission goes to the patients, who are astute in summarising what action they would like to see taken:

“We are just saying that the MHRA need to learn and listen to the experts, take action without fear of being sued and the government need to step in and sort out the seeming corrupt practices and hidden and unacknowledged evidence”. (Focus Group patient)

“We here on the shop floor are suffering, so everybody should be responsible for bringing this out into the open and making sure it doesn’t happen again”. (Focus Group patient)

REFERENCES


April 2012
Written evidence submitted by Professor Stephen Westaby

The breast implant and metal hip joint issues have diverted attention away from other serious problems. I would like to reiterate that more patients die from limits in access to medical technology than from faulty equipment. In some cases restrictions based on cost containment contravene NICE and GMC guidelines and may infringe human rights (please see enclosures). If the UK is to meet the aspirations of “world class healthcare outcomes” proposed in the recent White Paper, Equity and Excellence: Liberating the NHS, then systems of care must keep pace with advances in technology. The single most important issue is timely access to new life saving drugs and equipment. This is an area where the NHS in some cases remains well behind the rest of Europe and North America. We need access to modern imaging for early diagnosis, to telemedicine, to technology based cancer and cardiac care and many other advances which remain restricted for cost containment reasons. It is unreasonable to publish outcomes for hospitals and medical professionals based on simple Hospital Episode Statistics without providing modern equipment to save lives. There are weekly NHS scandals and considerable litigation costs due to current limitations. More complicated and protracted device regulation and licensing will not solve these problems.

13 June 2012

Written evidence submitted by Jacqueline Minor, European Commission

I would like to thank the Members of the House of Commons’ Science & Technology Committee for having given me the opportunity to provide the European Commission’s views with regard to medical device regulation in the EU.

As I mentioned at the session on 13 June 2012, enhancing transparency of the regulatory system is one key element of the revision of the existing medical devices directives. The European databank on medical devices (Eudamed) should be further developed and become the central piece of an EU portal storing information regarding medical on the EU market and giving access to such information.

In future, Eudamed should be composed of the following electronic systems:

— an electronic system on Unique Device Identification (to allow traceability of medical devices),
— an electronic system on registration of devices and economic,
— an electronic system on information on certificates issued by notified bodies,
— an electronic system on clinical investigations in relation to medical devices,
— an electronic system on medical device incidents (vigilance), and
— an electronic system for sharing information on market surveillance activities of the Member States.

In the impact assessment carried out to prepare the draft legislative proposals, we estimated the approximate costs for setting up the future Eudamed databank with its various integrated electronic systems at EUR 2mio/year for a period of four years, followed by annual maintenance and development costs of EUR 1.8mio/year (including software for statistical analysis of reported incidents for signal detection).

Unfortunately, I cannot share with the Committee the draft legislative proposals which the Commission plans to adopt by the end of September 2012.

But I have compiled some draft provisions which relate to the subject-matter of my oral witness statement and which aim at enhancing the transparency of the system, ensuring traceability of medical devices, achieving a high level of commonality in the designation of notified bodies and making the vigilance system more effective.

Those provisions are part of the draft proposals which are currently subject to the consultation of the various Commission departments and remain internal documents. I would therefore ask you to keep this enclosed document strictly confidential.25

As part of Commissioner John Dalli’s plan for immediate action to restore trust in the regulatory system after the PIP incident, the European Commission is currently working, in cooperation with the Member States, on measures to strengthen the implementation of the existing medical devices directives. One measure aims at bridging the gaps in the practices of the Member States in relation to the designation and monitoring of notified bodies. The other measure aims at setting uniform criteria to be followed by notified bodies during the audits they perform under the medical devices directives. I enclose the two measures in their draft versions which are currently subject to stakeholder consultation and are therefore not confidential.

25 Not printed
Written evidence submitted by BSI Healthcare

Introduction

On 26 March 2012, the House of Commons Select Committee on Science and Technology announced its plans to examine the regulation of medical implants and invited written submissions from interested parties. This document contains BSI Healthcare’s submission to the Select Committee.

In the UK BSI operates a full scope Notified Body (NB number 0086) that certifies products under the Medical Devices Directive, Active Implantable Medical Devices Directive and the In Vitro Diagnostic Devices Directive. It is designated to do so by the MHRA. The German competent authority designates BSI Germany’s Notified Body (NB number 00535) to certify medical devices and in vitro diagnostic devices. The notified bodies operate separately from BSI’s National Standards Body.

Between 8 May and 2 July 2008, the European Commission consulted stakeholders on the revision of the legal framework for medical devices. Many of the issues the Commission raised are pertinent to the Select Committee’s enquiry.

1. Are current legislation and regulations on safety and efficacy of medical implants fit for purpose?

Since 1993 (mandatory from 1998) the Medical Device Directive 93/42/EC has provided the framework for medical devices to achieve EU market access, during this period (as accepted by the recent EC report prior to revision 2007/47/EC) this framework has largely been recognized as appropriate for the regulation of medical devices within Europe.

The framework has demonstrated flexibility and adequacy in providing appropriate regulatory paths for 10,000’s of types of medical devices with only limited need for adjustment or reclassification to address specific concerns. The major stakeholders have in the main been satisfied with its functioning.

Over time opportunities for improvement have been identified and the latest review 2007/47/EC, along with the new regular meetings of NBOG and the Borderline and Classification Work Group, has addressed outstanding issues as they have been identified. In fact the preamble to 2007/47/EC indicates there is a lot of support from all stakeholders for the existing framework. The EU Medical Devices Directive based on the New Approach has achieved significant consensus and consistency in understanding and implementation. The current status of agreement and common understanding is the outcome of significant stakeholder investment and many man years of effort and work, the value and cost of this understanding and consensus should be weighed carefully when considering the benefits of any substantial change to the current framework.

The current framework provides key benefits that include:

(a) A comparable record of device safety with other mature regulation frameworks (eg, US FDA), which is demonstrated by the relatively low occurrence of recalls and clinical issues.

(b) Timely product evaluations compared to other approval based regulatory schemes, such as drugs and plant protection products, and to devices under other regulatory frameworks outside the EU.

(c) Available regulatory review resources and competences that have already been established and demonstrated to support safe, timely product evaluations.

(d) A system that is adaptable and does not stifle innovation.

Timely efficient review of medical devices is important to Europe from several perspectives:

(i) Patients benefit from access to the most advanced, safe and effective “state of the art” technology;

(ii) Healthcare systems and payers benefit from a competitive supply environment that drives device manufacturers to continuously improve devices and that ensures an available selection of competitive devices to drive competitive pricing; and

26 Not printed
27 BSI submission to the European Commission’s Consultation into the revision of the Directives http://ec.europa.eu/enterprise/newsroom/cf/_getdocument.cfm?doc_id=4901, and is attached to this submission for convenience.
(iii) A strong, vibrant, innovative medical device sector is beneficial for European economic stability and development.

In general BSI considers the current regulatory framework for medical devices in the EU as satisfactory but has concerns over the consistent implementation and that addressing these aspects would deliver further improvement in the quality, integrity and consistency of evaluations.

2. How effectively does the MHRA implement the Directive in the UK?

The MHRA is one of the leading and most respected Competent Authorities in Europe. It is responsible for the designation of Notified Bodies under the Medical Directives and has designated BSI under the MDD, AIMD and the IVDD. The MHRA regularly audits BSI in respect of its procedures and processes in implementing conformity assessments under this designation. BSI considers the audits to be thorough which are conducted by technical and clinical experts.

3. How could the legislation and regulations be improved?

As mentioned before, BSI believes the basic regulatory framework is robust and protects patients appropriately; it is likely the forthcoming EU Commission revision will propose improvements that will help with consistency and implementation of the rules, in a number of areas which BSI would welcome.

Notified Bodies

Notified Bodies like BSI are independent third party organizations designated by Member State authorities, such as the MHRA. Their control and oversight is by National Authorities who often have different approaches to the role, and there are inconsistencies between National Authorities in terms of the rigour with which Notified Bodies have been designated and controlled. Any new regulation should focus on consistent, mandatory EU level rules and standards, and the development of better control mechanisms. Policy makers should focus on oversight of Notified Bodies’ performance, rather than introduce further steps in the regulatory process.

Vigilance and post market surveillance

Member states need a robust and transparent system of sharing data efficiently between national Competent Authorities. BSI feels that the system can be improved, starting with improved reporting of incidents within the healthcare authorities. BSI provided the following statement in 2008 at the time of the European Commission’s Consultation into the revision of the Medical Directives:

One or more proposals to improve the vigilance system could be foreseen to be appropriate. In each case can you give an estimate of the socio-economic impact of the particular proposal?

Proposal 1: Establish an obligation for the medical institutions and healthcare professionals to report incidents and to invite patients to do the same, to introduce timelines for reporting and corrective actions, to give certain publicity to the corrective actions of the manufacturer:

An obligation on users of devices to report incidents seems to have merit, such a systems must ensure that all reports are made available to the appropriate medical device manufacturers so that manufacturers can fulfill their vigilance reporting and incident investigation obligations.

Proposal 2: Create an obligation for the Notified Body to periodically review the manufacturer’s vigilance system:

This is already required by the Directive and should be applied by the Notified Bodies. Today the vigilance system should be a routine part of each Notified Body audit of medical device manufacturers. If this is not the case enforcement is the responsibility of the DA.

4. How could the European Commission ensure that potential changes to the Medical Devices Directive do not hinder the introduction of innovations in medical implants to the market?

Overall, BSI considers that the EU medical device regulatory system as it stands provides an adequate framework to deliver safe devices to the market that are fit for purpose but it is recognized that all stakeholders need to make full use of the powers available to them under the Directives and for the designation and monitoring of the implementation of those measure to be consistently applied across the EU.

After 20 years, however, notwithstanding the various updates to the regulations there is always scope to improve some aspects. The improvements in medical implants in that time have improved the quality of life of millions of patients and this has been possible because the sector’s regulatory system has enabled the speedy introduction of safe innovative product. There have been criticisms that the system is not stringent enough and suggestions that devices need a regulatory regime like that applied to pharmaceuticals, with pre market approval by a centralized authority and randomized controlled trials.

However, medical devices are different to pharmaceuticals. The extremely diverse range of technologies is subject to more frequent design changes and a rapidly evolving state of the art. Unlike pharmaceutical products,
implantable medical devices have significant reliance upon surgeon skill and accessory products to achieve successful outcomes. This makes the pharmaceutical approach to regulation unsuitable for medical devices.

The Medical Devices Directives and many of the associated European regulatory guidance documents have been updated in the last few years; we are not yet seeing the full benefits of these changes. European policy makers should implement changes that reinforce standards and consistency within the current framework to continue to support a thriving industry that develops and introduces innovative medical devices that improve millions of people’s lives.

April 2012

Supplementary written evidence submitted by BSI Healthcare

During the Select Committee Session on 13 June 2012 and during the questioning regarding the potential for manufacturers to “shop around” and find a Notified Body (NB) which would accept lesser standards, I was asked to provide further information following the meeting. These aspects were covered within Q55 and Q56 of the meeting transcript.

BSI issues more than 300 new certificates to medical device manufacturers under the Medical Devices Directive each year. Those certificates are comprised firstly of Conformity Assessment certificates covering the Quality System and additionally, in the case of the higher risk devices a product related Design or Type Examination certificate.

In respect of the QMS certificates, BSI does not consider there to be a great deal of “forum shopping” although there is an amount of turnover where manufacturers, for one reason or another, would choose to switch Notified Bodies. BSI does not view this to be a widespread or high risk practice, although in a number of cases, there may be some correlation between those manufacturers moving to another Notified Body and the number of issues identified over previous audits. Due to the many factors involved it is difficult to evaluate the exact reason for manufacturer deciding to change to a different NB. When this does occur there is an expectation, although not currently mandated, that the “new” NB would communicate with the original NB to determine whether any specific problems existed. This process of exchange of information and communication is generally adopted by most of the recognised NBs but it is in no way universally implemented.

The main concern that BSI sees with “forum shopping” is in respect of the higher risk devices for which a product related Design or Type Examination certificate is required from a Notified Body prior to the manufacturer being able to declare compliance with the directive and place product on the market. In these situations there is the potential for a manufacturer, faced with demands from the Notified Body to submit more comprehensive information, particularly clinical data to support device safety, to withdraw an application and seek another NB. BSI has been aware of situations where a manufacturer has withdrawn an application and has been successful just a few months later, clearly without any further clinical data, to gain certification through another NB.

A review of our records has shown that BSI is aware of seven clear cases over the last five years where a manufacturer has successfully had a device certified through another NB following an application whereby it had been deemed by BSI that the available clinical data was not adequate in meeting the requirements of Annex X of the MDD.

Of the seven cases identified, there were four US manufacturers, one Canadian, one European and one from Japan. The devices concerned have included orthopaedic joints, spinal implants, bone graft substitutes, coronary implants, vascular stents and an intra-ocular lens.

It should be emphasised that the instances of this nature are relatively rare but the consequences of each individual case could be very significant in respect of patient safety.

June 2012

Supplementary written evidence submitted by the Association of British Healthcare Industries

I am writing to you following the oral evidence session on 13 June 2012. First of all I would like to thank the Committee for giving ABHI the opportunity to discuss the important issue of medical implant regulation with the Committee.

I will address the points raised during the session. On the issue of Notified Bodies (NB), I would like to express industry’s support for the principles of the current system. Unfortunately, there are areas where the NB system has shown signs of weakness. Industry believes the following measures will help improve the system:

— Precise and mandatory requirements for the designation of Notified Bodies;
— EU-wide mandatory accreditation standards for Notified Bodies, which include standards for competence, training, staffing, transparency and expertise of Notified Bodies;
— Precise, binding, transparent measures for Competent Authorities to control and monitor the activities and performance of Notified Bodies;
— Audits of Notified Bodies by joint teams composed of different national Competent Authorities and the European Commission;
— EU-level oversight of the way Member States designate and monitor their Notified Bodies.

In regards to manufacturers “shopping round” for less rigorous NBs, ABHI does not believe this to be common practice. Medical device manufacturers work closely with their NB throughout the process of developing a compliance dossier for a medical device. It is not the case that they simply choose a NB at the end of the process and submit their evidence. Moreover, the process of changing from one NB to another is expensive and time consuming. It involves the need to carry out new conformity assessments, other checks on manufacturing facilities and costly re-labelling programmes.

Also discussed during the session was the issue of evidence sharing and transparency of information. At present, the current arrangements for the control of data are seen by many as too restrictive. Industry believes that information regarding devices on the market, vigilance, market surveillance, clinical investigation and CE certificates should be widely available to patients, consumers, healthcare professionals and manufacturers, NBs, national Competent Authorities and the European Commission. Obviously the level of information available could vary according to the intended recipient as was suggested in the evidence submitted by Mrs. Minor from the EU Commission.

At present the oversight of medical devices is highly decentralised and largely controlled by Member States. This approach makes it possible to manage the 400,000 products on the market and the thousands of new products introduced each year. The current system does, however suffer from disparate national approaches. There is therefore a need for some added coordination at EU level to iron out some of the discrepancies between EU Member States. This could be facilitated by a central body would have a key role in overseeing the auditing of NBs and coordination of vigilance reporting systems.

However industry does not believe that establishing a single organisation that carries out CE marking centrally is a workable system for medical devices. The establishment of such a body would be very expensive and fraught with difficulties. We do not believe that a more centralised system would make a real difference to patient safety. In our opinion it would be an expensive way to slow down patient access to innovative treatment and would indeed be a heavy burden on the public purse.

A final area of improvement is around the coordinated and rapid sharing of information in relation to products on the market. Industry supports a better defined legal framework on vigilance and greater harmonisation of Member States’ market surveillance activities are needed to ensure rapid and consistent EU-wide risk identification and response. This would require a centralised reporting system based on an EU portal for reporting of key data and situation assessment by Member States and the European Commission.

I hope you found our evidence useful. Patient safety is of paramount importance to our industry. We work alongside the NHS in a relationship of mutual dependency. If this relationship is to continue to be a success and deliver innovative new treatments to patients, then we will need a regulatory regime that industry, clinicians and patients have faith in. Like any system dealing with innovative technologies, the regulatory regime for medical devices will have to constantly evolve and keep pace with the technologies it regulates. The medical device industry believes the ideas listed above, and those from our original submission will help deliver a regulatory system that gets innovation to patients whilst maintaining the highest standards of patient safety.

June 2012