



**Government Response to the House of Commons
Science & Technology Committee Report of Session 2012-13:
Regulation of medical implants in the EU and UK**

Presented to Parliament
by the Secretary of State for Health
by Command of Her Majesty

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Table of contents

Introduction	4
Pre-market approval.....	5
Transparency of evidence.....	9
Comparisons with the FDA	11
Notified bodies	11
Post-market surveillance.....	14
Responding to adverse incidents.....	18
Auditing manufacturers	20
Conclusions.....	21

Introduction

The Government welcomes the Committee's¹ report and its focus on the importance of increasing transparency and accountability in the regulation of medical implants.

The regulation of medical implants is currently being revised by three strands of work, all of which are reflected in the Government's response to the Committee's recommendations.

Firstly, the Government began negotiations with the other Member States of the European Union (EU) in October 2012 to agree a revised regulatory framework for medical devices, including implants. Secondly, Member States and the European Commission are currently agreeing implementing legislation which will amend the current legislation and improve aspects of the regulatory framework in advance of the wider revision. Thirdly, Member States are implementing a voluntary programme of action, coordinated by the Commission, in light of lessons learnt from the events involving fraudulent Poly Implant Prothèse (PIP) breast implants.

Thus the Committee's report is timely and its recommendations are being taken into consideration as this work progresses.

¹ Throughout this response, the term 'Committee' refers to the House of Commons Science and Technology Select Committee, except where the context requires otherwise.

Recommendations and responses

Pre-market approval

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 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.

1. The Government agrees with the Committee that the best way to improve the safety of medical implants for patients is to build on the current regulatory framework, rather than fundamentally change it. The existing system has created an innovation-friendly market that provides patients with rapid access to life-changing and life-saving medical technology.

The use and analysis of equivalence data

2. The Government agrees that there should be clearer rules on when it is appropriate for manufacturers to use clinical data which is sourced from studies on a similar device (termed 'equivalence'). The proposed regulation on medical devices² sets out the circumstances where equivalence may be used: the devices must have the same intended purpose and their technical and biological characteristics and the medical procedures must be so similar that there would

² http://ec.europa.eu/health/medical-devices/files/revision_docs/proposal_2012_542_en.pdf

not be a clinically significant difference between their safety and performance. In addition, the legislation carries forward the existing requirement for a manufacturer to give due justification if they do not intend to perform specific clinical investigations on a class III or implantable device.

3. More broadly, the Government considers that, regardless of whether equivalence is used, manufacturers must thoroughly evaluate the relevant clinical data in order to demonstrate the safety and performance of their device. We are pleased to see that the proposed regulation on medical devices improves this in two ways. Firstly, the regulation sets out that a manufacturer's clinical evaluation must include a critical evaluation of the relevant scientific literature, with a requirement to conduct a clinical investigation where existing clinical data is insufficient. Secondly, with oversight from Member States, the European Commission will adopt common technical specifications on specific devices or groups of devices, which can be used to clarify the requirements on manufacturers when they conduct a clinical evaluation for certain devices or types of device. Manufacturers will have to comply with these common technical specifications unless they can demonstrate how they have met the equivalent level of safety and performance by other means.
4. It is also important that manufacturers' clinical evaluations are properly assessed and the use of equivalence critically appraised by notified bodies. The proposed regulation on medical devices requires notified bodies to have personnel with clinical expertise, as well as access to external national expertise, in order to scientifically challenge the clinical data presented by a manufacturer and make an objective clinical judgement about the assessment of the manufacturer's clinical evaluation.
5. As the new European legislation will not come into effect until at least 2017, Member States are also taking additional voluntary action to check and improve the quality of notified bodies. The Medicines and Healthcare products Regulatory Agency (MHRA) has rigorously audited the six notified bodies which assess the highest risk devices, including implants, in the UK and taken action to support their assessment of clinical evidence.

The environment for clinical investigations

6. The Government agrees with the Committee on the importance of improving the environment for clinical trials in the UK. The Government is making it faster and easier to undertake high quality health research in England through a range of initiatives, together with the work that the Health Research Authority (HRA) is taking forward to simplify the approval processes for ethical research. In addition, we are currently working to expand the remit of the HRA to Northern Ireland.
7. Established in 2006, the National Institute for Health Research (NIHR) Clinical Research Network helps life science companies, including medical device manufacturers, deliver leading edge research within the NHS in England. It has developed specific tools and processes for medical technology company sponsored studies in order to speed up the contracting process and support value for money.
8. In December 2011, changes were introduced to the NIHR's contracts with providers of NHS services, which aim to make performance in starting and delivering research more transparent and to make the NHS accountable for its performance:

- the NIHR's contracts with providers of NHS services introduced incentives for the initiation and delivery of research, including a 70 day benchmark to recruit the first patient to a trial;
 - reporting on recruitment of patients to time and target is required for commercial trials; and
 - from 2013, the performance against these requirements will affect payment to trusts.
9. With the support of the NIHR, the NHS Confederation and the Academy of Medical Sciences, the Department of Health has held a number of events in England over summer and autumn 2012 to enable NHS trusts to share early learning from those already subject to the new contract requirements. These events brought together teams from trusts to encourage partnership working and make research in the NHS faster and easier.
 10. In May 2011, the Government launched, through the NIHR, a framework of good practice and standard procedures to facilitate consistent local research management, which helps NHS trusts in England to speed up their performance. This framework is complemented by the Co-ordinated System for gaining NHS Permission for Research on the NIHR Clinical Research Network portfolio. This system allows a central review of all issues that only need to be considered once, so that individual trusts can focus on site-specific issues.
 11. In addition, a model clinical investigation agreement for medical technology industry sponsored research in NHS hospitals has been agreed by the UK health departments and the Association of British Healthcare Industries. It was developed to speed up the contracting process for medical technology industry sponsored clinical research, carried out in NHS hospitals, whether conducted pre- or post-CE marking.
 12. In Scotland, NHS Research Scotland has made progress to remove much of the bureaucracy and delay associated with beginning clinical trials. The introduction of a single costing and contracting process across Scotland has significantly streamlined the process of obtaining R&D permission, which is frequently cited as a major barrier to research.
 13. In Northern Ireland, the small scale and relatively non-complex health and social care structures have streamlined processes, which facilitate faster and easier start-up of clinical trials and other studies.
 14. At European level, the rules on clinical investigations are updated in the proposed regulation on medical devices. The Government is also currently negotiating the proposed regulation on clinical trials for medicinal products³, which aims to address the decline in clinical trial activity in the EU due to unnecessary administrative and regulatory burdens. Whilst there is typically not the same level of burden on clinical investigations for medical devices, we will ensure that any experience gained on how to better regulate clinical trials will be picked up in the rules on clinical investigations for devices in the draft regulation on medical devices.

³ http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf

Scientific advice

15. It is worth noting that not all of the European Commission's plans to make scientific advice available to manufacturers and notified bodies, which were presented to the Committee during the call for evidence, were included in the final legislative proposal. Notably, the Commission has not proposed to establish a Scientific Advisory Board.
16. However, the European Commission has proposed to establish EU reference laboratories for medical devices, which will:
- provide scientific and technical assistance and advice to notified bodies, Member States and the Commission;
 - respond to notified bodies' requests for scientific opinions;
 - contribute to developing testing and analysis methods which notified bodies should use when assessing the conformity of a device with the regulatory requirements;
 - collaborate with notified bodies on best practices when assessing the conformity of a device with the regulatory requirements;
 - contribute towards international standard setting;
 - verify the compliance of the highest risk *in vitro* diagnostic devices (IVDs) with the applicable common technical specifications or equivalent; and
 - test samples or batches of the highest risk IVDs as part of the conformity assessment procedure.
17. In principle, EU reference laboratories could be an effective way to raise standards across the EU and increase access to scientific expertise. However, the Government is currently considering whether they will deliver tangible benefits which outweigh the cost which notified bodies will have to pay to receive their scientific advice. This is particularly important given that the additional cost for notified bodies will then be passed onto manufacturers.

The Health Research Authority

18. The Government welcomes the Committee's comments on the HRA, which was set up in 2011 to protect and promote the interests of patients and the public in health research in England. The HRA has the National Research Ethics Service at its core and is working with the MHRA and the NIHR to create a unified approval process for health research and to promote consistent and proportionate standards for compliance and inspection. Its functions in connection with facilitating and promoting health research include research that involves medical devices. Earlier in 2012, the HRA published plans to deliver its objectives, which includes a feasibility study into how HRA assessment could facilitate approval to undertake research in the NHS.
19. The *Health Research Authority Directions 2011* require the HRA to produce an annual report; the first was published in July 2012⁴. The Government's autumn statement gave an update on the progress that has been made on the 2011 *Plan for Growth*⁵, which announced that the Government would establish the HRA. In addition, the Government recently published the *Strategy for UK Life Sciences: One Year On*⁶ which provides an update on the work and future plans of the HRA. Therefore, the Government does not consider that a further report on the HRA is required.

⁴ <http://www.official-documents.gov.uk/document/hc1213/hc03/0312/0312.pdf>

⁵ http://www.hm-treasury.gov.uk/d/growth_implementation_update_dec2012.pdf

⁶ <http://www.bis.gov.uk/assets/biscore/innovation/docs/s/12-1346-strategy-for-uk-life-sciences-one-year-on.pdf>

Transparency of evidence

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 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.

Transparency of clinical data

20. The Government wholeheartedly agrees with the Committee on the importance of transparency. Transparency can significantly improve the safety of implants by empowering patients and healthcare professionals, increasing scrutiny on industry and public authorities, and ensuring that market surveillance information is better shared between Member States and more quickly acted upon. The proposed regulation on medical devices goes some way towards improving transparency by removing the presumption of confidentiality that exists in the current legislation. However, the Government is committed to analysing where the proposed regulation can go further on transparency and negotiating for this with other Member States and the European Parliament. The Government started

a ten-week public consultation on 12 November 2012⁷, which seeks stakeholders' views on various aspects of the Government's proposed negotiating position, including how transparency can be further improved.

21. The Government considers that more information on the quality and safety of medical devices, including implants, needs to be made available. We are pleased that the European Commission has proposed to require manufacturers of implants to produce and publish a summary of safety and performance information, which will be publicly available on the new central European database ('Eudamed'). However, we think it may be valuable to provide more detail in the proposed regulation on medical devices on what level of information these summaries should include to ensure that they are a valuable resource for clinicians and patients. In light of the Committee's report, we are carefully considering whether this requirement could be expanded to include data from clinical investigations or an indication that the manufacturer has relied on equivalence data.
22. Eudamed will also store other publicly accessible information. Registration information on devices and economic operators, the electronic traceability system for devices and information on certificates will be publicly accessible. The proposed regulation on medical devices delegates power to the European Commission to define the public accessibility of information on clinical investigations and vigilance. We are currently examining to what extent this delegation of power is appropriate and whether more detail should be put on the face of the legislation.
23. Furthermore, the outcome of peer reviews between different national authorities responsible for notified bodies, reports from each Member State on how they have monitored their notified bodies and statements from notified bodies on their independence and impartiality will be made public.

The publication of clinical data

24. The Government notes the Committee's recommendation to make all clinical data about a device publicly available. This is currently under discussion at European level for medicinal products during the negotiations of the proposed regulation on clinical trials. Currently, manufacturers must notify the national regulator of a summary of the results from a clinical trial. The Government supports greater transparency and we would look to reflect any improvements in this area onto the new rules on clinical investigations for medical devices in the proposed regulation.

Committee on the Safety of Devices

25. The Government disagrees with the Committee's criticisms on the transparency of the Committee on the Safety of Devices (CSD). Since the CSD's inception in 2001, the meeting minutes have been published and are available on the MHRA website⁸. Whilst papers and presentations to the CSD are not proactively published, they are available on request and have been routinely supplied.
26. Members of the CSD act as external assessors for clinical investigation applications made to the MHRA and they also support the MHRA by carrying out an independent annual audit of the clinical investigation system and the adverse event system. The MHRA makes information available to the public wherever

⁷ <http://www.mhra.gov.uk/Publications/Consultations/Deviceconsultations/CON205361>

⁸ <http://www.mhra.gov.uk/Committees/Devices/CommitteeontheSafetyofDevices/index.htm>

possible but aspects of this work are subject to the confidentiality provisions in the current legislation, where the Government does not have discretion over publication. By negotiating to remove the presumption of confidentiality and increase transparency, the Government expects that the MHRA will be able to publish more information about the wider work of the CSD under the new legislation.

Comparisons with the FDA

Recommendation 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.

27. Europe can learn from some aspects of the regulatory system in the United States, for example their strong emphasis on transparency. However, the Government considers that the principles of the European system are sound and agrees with the Committee that adopting a more centralised regulatory framework, as exists for medical devices in the United States, would not be desirable.
28. Instead it is important to address the weaknesses in the European system, highlighted in the Committee's report and the Government's evidence to the Committee, by building on the current regulatory framework. This way we can deliver a system that ensures a high-level of patient safety from pre-market assessment of devices by notified bodies to common European standards to rigorous post-market surveillance by manufacturers and competent authorities.

Notified bodies

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 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.

29. The inconsistent quality of notified bodies across the EU is an acknowledged weakness of the regulatory system on medical devices and must be significantly improved.

The risk of forum shopping and improvements to the quality of notified bodies

30. The risk of forum shopping must be reduced by ensuring that notified bodies are aware when this may be taking place and the practice must be disincentivised by raising the quality of notified bodies across the EU. In the proposed regulation on medical devices, the Government is pleased to see that the European Commission has proposed that manufacturers will be unable to apply to more than one notified body at the same time for a conformity assessment. In addition, notified bodies will be required to inform other notified bodies when a manufacturer withdraws its application.

31. The Government is currently considering how information can be declared more transparently to make the system even more robust. As the Committee recommends, one option would be to require notified bodies to publish records of all approaches by manufacturers. Another option would be to require manufacturers to declare in their application for conformity assessment whether they have already approached another notified body to assess the same device previously.

32. More broadly, the European Commission has proposed to consistently improve the standard of notified bodies across Europe in four ways in the proposed regulation on medical devices:

- i. Competent authorities will be obliged to peer review, and be peer reviewed, in alternate years to assess their competence to monitor notified bodies. The exchange of experience between competent authorities will also be better organised.
- ii. A Member State may have its concerns about a notified body considered by the Commission and action taken where the Member State responsible for that notified body does not take action itself to address the identified weaknesses.
- iii. Every year competent authorities will visit each notified body in their Member State and assess whether it still meets the regulatory requirements. This includes an audit of the clinical data used to support CE marking. Every three years, a team of experts from different Member States will also participate in the review. The Government agrees with the Committee that this will strengthen national assessments of notified bodies' competence and ensure a more consistent application of the rules. To make progress more quickly, the Government is pushing for an accelerated introduction of this joint audit programme on a voluntary basis, which is due to commence in 2013.

- iv. Stricter criteria on notified bodies are set out, which stretch from their independence and impartiality to their quality management system to the requirements on their resources and processes.
33. In parallel to negotiating the new legislation, Member States are voluntarily auditing the quality of the notified bodies of high risk devices, including implants. Following an audit of the six relevant notified bodies in the UK, the MHRA has not reduced the scope of any of the notified bodies because there were no gaps in the expertise of technical reviewers. As outlined previously, the MHRA has taken action to support notified bodies in how they assess clinical evidence.
34. The Government is also working with other Member States and the European Commission on implementing legislation to ensure that competent authorities consistently apply the same criteria when deciding whether an organisation is qualified to be designated as a notified body. The Commission will also adopt a non-binding check list of items to be verified by notified bodies during an audit of a manufacturer and a minimum number of unannounced audits that notified bodies should perform, which we expect to be published in early 2013.
35. The Government welcomes the Committee's comment that the European Commission's proposal to add an additional layer of bureaucratic oversight of high risk devices and implants during the pre-market phase will not add value in patient safety but will simply delay patients' access to innovative technology. We are committed to negotiating to seek to remove or improve this provision and ensure that tighter requirements are placed on notified bodies so that they are assessing the conformity of devices with the regulatory requirements in a consistently rigorous way for all manufacturers across Europe.
36. Moreover, a move to a centralised system like that in the United States would likely result in substantially increased and potentially prohibitive costs for small and medium sized enterprises. The Government therefore supports building on the current system whilst balancing the dual aims of the legislation: protecting patient safety and supporting innovation through the single market.

Limits to the burden on industry

37. The Government recognises that increasing the scrutiny of notified bodies will raise their costs, which will be passed onto manufacturers. In line with the Government's commitment to better regulation, our priority is to ensure that these costs do not fall disproportionately on small, medium and micro manufacturers. We are seeking views in our public consultation on how this burden can be kept to a minimum while still ensuring that notified bodies are rigorously scrutinised and public confidence in the safety of medical devices and implants is improved.
38. It is worth noting that the UK medical technology industry welcomes the European Commission's proposal to introduce stricter controls and monitoring of notified bodies⁹. More broadly, the Commission's impact assessment foresees net benefits for manufacturers because of elements of the proposed regulation on medical devices which streamline their reporting requirements. For example, the cost savings to manufacturers from introducing the central registration of

9

<http://www.abhi.org.uk/multimedia/docs/press/New%20Folder/ABHI%20Response%20to%20MDD%20Proposal.pdf>

economic operators and devices at European level is estimated to bring savings between €81 to €157 million¹⁰.

Post-market surveillance

Recommendation 13: Manufacturers should publish the results of post-market surveillance studies.

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 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.

Recommendation 19: We recommend that the inclusion of data from explanted medical implants should be a requirement of the Eudamed registry.

¹⁰ http://ec.europa.eu/health/medical-devices/files/revision_docs/revision_ia_part1_en.pdf

Transparency of post-market surveillance

39. The Government agrees with the Committee on the importance of using post-market surveillance to continue to monitor the safety and performance of devices on the market and welcomes aspects of the proposed regulation on medical devices that address this. Most notably, manufacturers will be required to put together a plan for post-market clinical follow-up (PMCF). Where notified bodies assess the conformity of a device with the regulatory requirements, this will include an examination of the PMCF plan. The clinical evaluation of a device will also need to be updated based on experience from post-market surveillance.
40. There are not, however, any requirements for this post-market surveillance information to be published. This is of concern and the Government considers that there should be a requirement in the proposed regulation on medical devices for manufacturers to keep the publicly available summaries of safety and performance information updated in the light of post-market surveillance. In this way the most relevant information will be available to clinicians and the public. Equally, it will become apparent which manufacturers are not undertaking adequate post-market surveillance because they will not provide updated, relevant information in these summaries.
41. The Government is also taking on board learning from the implementation of new European rules on pharmacovigilance, which includes introducing risk management plans into post-market surveillance plans.
42. The Committee will be interested to learn that the Government is currently piloting a scheme that is supporting the introduction of new hip and knee implants to the market in the UK. This voluntary scheme, termed 'Beyond Compliance', will provide manufacturers with advice to support the phased introduction of new implants into clinical use in the UK. In this way, its aim is to significantly enhance manufacturers' ability to undertake high quality post-market surveillance and the ongoing generation of clinical data.

Black Triangle Scheme

43. The Government welcomes the Committee's recommendations on the introduction of a Black Triangle Scheme for medical implants on the basis of equivalence data and will give this proposal careful consideration. For context, the Black Triangle Scheme currently in place for medicines in the UK is a voluntary scheme¹¹ which will be replaced by a mandatory European scheme in the new legislation on pharmacovigilance¹². Under the UK scheme, a Black Triangle is assigned to a medicinal product if the drug contains an active substance that meets certain conditions, including if it has been newly licensed for use in the UK or if it contains a new combination of active substances. This signals to healthcare professionals and patients that the MHRA strongly encourages reports of suspected adverse reactions associated with Black Triangle products. The MHRA also intensively monitors all Black Triangle products.
44. The Government has reservations about whether a mandatory scheme for medical devices could be introduced solely in the UK because this would likely be seen as a barrier to the internal market under European rules. This may,

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<http://www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/Reportingsuspectedadversedrugreactions/Healthcareprofessionalreporting/BlackTriangleScheme/index.htm>

¹² <http://www.mhra.gov.uk/Howweregulate/Medicines/Pharmacovigilancelegislation/index.htm>

therefore, be an objective that the Government could pursue in the negotiations on the proposed regulation on medical devices.

45. The Government is, however, unsure about the merits of imposing such a scheme only on implants brought onto the market with equivalence data. As the Government stated in its evidence, there is a limited amount of clinical evidence that can be gathered before a device is placed on the market. We consider it to be critical that all manufacturers continue to monitor the safety and performance of their devices once they have been placed on the market, irrespective of whether a clinical evaluation has included a bespoke clinical investigation for that device. Such a scheme might therefore be more appropriately applied more generally to novel and innovative high risk devices.

Reporting of serious adverse incidents by healthcare professionals

46. The Government agrees that reporting by healthcare professionals is an extremely valuable source of information about the ongoing safety of devices. We therefore recognise the rationale for the Committee's recommendation to make reporting of serious adverse incidents mandatory for healthcare professionals; indeed, this is something that the Government has given consideration to previously. The importance of improving reporting by healthcare professionals was highlighted as a key recommendation in the report on the review of the actions of the MHRA and Department of Health that was undertaken by Earl Howe, Parliamentary Under Secretary of State for Quality¹³ following on from concerns about fraudulent PIP breast implants.
47. As a result, the MHRA has begun a programme of work designed to improve the culture of reporting among healthcare professionals. This includes work with Royal Colleges and the relevant professional bodies to connect with the relevant safety committees and improve links to the MHRA's reporting web pages. It also involves designing enhanced systems to join up the facilities for reporting by introducing interactive on-line reporting facilities and improving links with the National Reporting and Learning System. The Government is committed to fully considering all of the options to improve reporting by healthcare professionals and will take the Committee's recommendation into account as we take forward this work.
48. In addition, the MHRA is further developing its systems to trend and recognise post-market safety issues with medical devices through further improvements to the trending systems it first introduced in April 2011 and the acquisition of new signal detection software.

Publishing raw data from the National Joint Registry for England and Wales

49. The Government will give further consideration to the Committee's recommendation for the National Joint Registry for England and Wales (NJR) to publish raw data. It is not, however, usual practice for registries to publish data before validation and a first level of analysis has been undertaken owing to the risk of misinterpretation which may have an impact on post-market surveillance and patient confidence.

13

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_134044

50. Following an initial consultation with the NJR in light of the Committee's inquiry, the NJR stressed that the publication of raw data carries significant potential risks:
- clinicians may reduce their participation in a registry if they are concerned about how the data will be used;
 - third parties may misinterpret or misunderstand the complex raw data which requires analysis to take into account the varying factors which may impact on the performance of a joint;
 - patients may receive confusing and damaging mixed messages as a result of unregulated and unscientific analysis of the raw data; and
 - the NJR's role to facilitate post-market surveillance may be jeopardised by inappropriate interpretation of the raw data.
51. The NJR explained that they have a responsibility to ensure that proper data governance arrangements are applied to sharing data with third parties, which enables it to effectively monitor and manage data access and use and avoid these potential risks.
52. With these systems in place, the NJR actively encourages the analysis of its data by the wider research community and industry and there has been an unprecedented increase in the use of NJR data for research purposes. The NJR publishes data for surgeons, manufacturers and hospitals on secure electronic feedback systems, which allows these stakeholders to access the relevant raw data and enables the surveillance and performance monitoring of both the surgeons' and implants' performance.
53. More broadly, the Government is committed to make more data open and accessible, to support greater accountability, improve services and support growth. In line with this agenda, we are actively looking at how best to make more detailed data available from audits and registries such as the NJR. Work undertaken through the Department of Health's Health and Social Care Transparency Panel recognises the huge potential value of such audit data but also the need to consider the issues identified above regarding the potential risks of publishing raw data. It has recommended that while the data that underpins published annual reports should be made freely available for use, the release of more detailed data to third party organisations should currently continue to be under a data sharing agreement. The process for applying for data to be released under such agreements should be transparent, proportionate, simple and quick.

Analysis of explanted joints

54. The Government does not consider that it would be feasible to undertake the routine analysis of explanted joints. Thousands of implants a year are explanted, analysis is a costly exercise that requires significant expertise and there are only a small number of centres that can undertake such work. We recognise that explanted joints can provide valuable evidence but we consider that this is more appropriately undertaken on a targeted basis.
55. Following an initial consultation, the NJR for England and Wales agreed that the analysis of explanted joints can provide useful information but warned that the costs and logistics involved in this task would be very high. For example, this would require the collection of essential data for examination, such as x-rays and blood test results, which the NJR does not currently collect and would need to be gathered from participating trusts. The NJR highlighted that a number of joint

replacement retrieval centres carry out analysis on explanted joints and they could advise on which targeted explant studies would provide most added value.

The NJR and Eudamed

56. The Government welcomes the Committee's support for the NJR and agrees that it should be the 'gold standard' for implant registries. To clarify, however, the NJR and the proposed new Eudamed database are two quite different systems. The NJR collects information on the performance and effectiveness of hip, knee and ankle joint replacements. The aim is to provide on-going clinical data to support the safety and performance analysis of a new device, significantly enhancing a manufacturer's ability to undertake high quality post-market surveillance. Registration data on Eudamed will be more basic information to identify a device, its manufacturer, authorised representative and importer, such as the contact details of the economic operator and the risk class of the device.
57. Eudamed will house six different databases with information on registration, an electronic traceability system ('Unique Device Identification'), certificates issued by notified bodies approving medical devices, as well as information on vigilance, market surveillance and clinical investigations. We can reassure the Committee that Eudamed will not replace the NJR given that they have quite separate roles. As such it would not be appropriate for Eudamed to collect data from explanted medical implants.

Responding to adverse incidents

Recommendation 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.

Responding to evidence about metal-on-metal hip implants

58. The Government is extremely concerned by the implication that the MHRA took several years to respond to evidence about problems with metal-on-metal hip implants before acting. The Government reiterates that analysis of data from the NJR was the trigger for the worldwide action to recall the DePuy ASR metal-on-metal hip system in August 2010.
59. The MHRA has played a leading role in ensuring that information on the safety of metal-on-metal hip replacements and that advice on the monitoring and clinical management of patients implanted with these devices is made available to healthcare professionals. In April 2010 the MHRA was the first regulatory authority to issue advice on monitoring and patient management and the Agency has continued to refine and update its advice as further information about the safety and performance of these devices emerges. The Agency has ensured that other regulators are made aware of these developments in a timely manner, by

issuing and circulating National Competent Authority Reports using established international systems for the exchange of regulatory information.

60. To clarify the order of events, in late April 2010, the NJR informed the MHRA that some types of DePuy ASR metal-on-metal hip replacements had been identified from registry data as having higher than anticipated rates of revision. The MHRA subsequently issued a Medical Device Alert, advising orthopaedic surgeons to follow-up all patients implanted with ASR hips and to ensure that the devices were implanted in accordance with the manufacturer's updated instructions for use. In late August 2010 DePuy informed the MHRA that they were carrying out a worldwide recall of ASR hips in the light of new data from the NJR about the performance of the implant. The MHRA issued a further Medical Device Alert in early September 2010 informing the UK health services of this recall. In both cases, the MHRA informed other regulators – both in Europe and internationally – of these actions.
61. Regarding data from the Australian joint registry, the Government has established that the Australian regulator, the Therapeutic Goods Administration (TGA), was in dialogue with DePuy in late 2009 based on data provided to TGA by the Australian joint registry. The TGA did not communicate this to the MHRA or other international regulators at that time. In March 2010, the MHRA was informed by DePuy that the ASR XL head System and the ASR Hip Resurfacing Platform were commercially discontinued in Australia in December 2009 due to the decline in their use.
62. The Government recognises that it would be desirable for the MHRA to be able to monitor information coming from all international device registries. It is the case, however, that the MHRA has finite resources and so has to rely on other regulators to interpret and share information coming from their own registries.
63. To facilitate the sharing of information, the MHRA holds regular teleconferences with its counterparts in the US and Canada, amongst others. The MHRA is currently exploring the opportunity to set up such an initiative with the TGA as well. The MHRA is also involved in producing guidance on requirements for worldwide auditing organisations involved in the inspections of medical device manufacturers. This is being produced under the auspices of the International Medical Devices Regulators Forum in an attempt to globally harmonise the requirements for such auditing organisations.

European cooperation on vigilance

64. More broadly, the Government is committed to improving how Member States in the EU share and act upon adverse incident reporting. The MHRA has led a task force to implement monthly operational EU vigilance teleconferences to improve cooperation and ensuring a coordinated response to common areas of concern. A number of European working groups on specific device safety issues have been initiated via these teleconferences in order to develop detailed co-ordinated actions, involving the relevant manufacturers.
65. The Government supports the early implementation of a common EU electronic vigilance reporting portal which would significantly improve the detection of safety signals and offer the first real possibility of fully co-ordinated analysis of adverse incidents across the EU. The MHRA is leading a task force of Member States to consider how such a system could be developed rapidly as a pilot before the regulation on medical devices comes into force. This would provide valuable

learning for the implementation of the Eudamed vigilance reporting portal which is included in the proposed regulation.

Auditing manufacturers

Recommendation 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.

Recommendation 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.

Audits of manufacturers by notified bodies

66. The Government welcomes the Committee's support for competent authorities enforcing unannounced audits of manufacturers by notified bodies, which has been proposed by the European Commission in the draft regulation on medical devices. We agree that introducing this change is an important lesson learnt from the events involving fraudulent PIP breast implants. The proposed regulation on medical devices delegates power to the Commission, with oversight from Member States, to decide the minimum frequency of unannounced audits. In addition, the draft legislation specifies that announced audits must take place at least once every 12 months.
67. As outlined previously, the European Commission will also adopt a non-binding check list in early 2013 of items to be verified by notified bodies during an audit of a manufacturer and a minimum number of unannounced audits that notified bodies should perform.

Potential conflicts of interest among notified bodies

68. As regards conflict of interest, as has been set out previously, the proposed regulation on medical devices and implementing legislation supplementing the current legislation tighten up the requirements on notified bodies, for example, by placing obligations on notified bodies to rotate personnel.
69. When notified bodies are properly monitored by competent authorities, the Government considers that the benefits of having for-profit notified bodies outweigh the risks of malpractice. As private sector organisations, notified bodies are able to specialise, react to market demand and add expertise and capacity in a flexible way that reflects the size and breadth of the market for devices.
70. The Government recognises the rationale behind the Committee's recommendation that notified bodies should audit manufacturers whose devices they have not approved. This is not something that would be possible under the existing legal framework and so would need to be pursued in negotiations on the proposed regulation on medical devices. However, we have concerns that this would be difficult to implement and may be disproportionately costly for manufacturers. For example, it is unclear how such an approach would work

contractually and commercially and it would be likely to result in a conflict of interest for the notified bodies involved. In addition, audits by notified bodies that have approved the device would need to continue, meaning manufacturers would have to pay for multiple audits.

71. The Government considers that competent authorities' market surveillance work is an important way to ensure that objective and neutral audits of manufacturers take place and that this is more appropriate than multiple audits by different notified bodies. Competent authorities are required to check the characteristics and performance of devices by reviewing documentation, undertaking sample checks or entering manufacturers' premises. To ensure that competent authorities are working to a consistently high level across Europe, the Government is pleased to see that the proposed regulation on medical devices will require Member States to make a summary of their market surveillance activity public.

Conclusions

Recommendation 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.

Recommendation 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.

Recommendation 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.

72. The Government welcomes the Committee's focus on improving the transparency and accountability of the current regulatory system, which we agree is a powerful lever to improve patient safety and public confidence.
73. Furthermore, the Government supports the Committee's conclusion that many of the changes proposed in the draft legislation on medical devices will strengthen the current regulatory framework. We agree that efforts to improve coordination and communication between Member States are also crucial. The Government is committed to negotiating strongly against any changes which are not backed by sound evidence and would introduce excessive centralisation at European level.
74. The Government agrees that it is imperative that patient safety is at the heart of the regulation of medical devices. The proposed regulation on medical devices makes this explicit in legal terms for the first time, following the changes brought about by the Treaty of Lisbon. The Treaty base of the proposed regulation on

medical devices comprises both Article 114 of the Treaty on the Functioning of the European Union (TFEU) on the internal market and Article 168(4)(c) on ensuring high standards of the quality and safety of devices for medical use. Recital two of the regulation sets out that 'both objectives are being pursued simultaneously are inseparably linked whilst one not being secondary to the other.'



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