

Written evidence submitted by the Medicines and Healthcare products Regulatory Agency (MI00)

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 2002¹) 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
 - c. Directive 98/79/EC on *in vitro* diagnostic medical devices (IVDD)².
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 Europe³. 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.

¹ <http://www.legislation.gov.uk/ksi/2002/618/contents/made>

² http://ec.europa.eu/health/medical-devices/documents/index_en.htm

³ <http://ec.europa.eu/enterprise/newapproach/nando/index.cfm?fuseaction=directive.main>

8. The overarching legislative framework for medical devices is part of the EU's 'New Legislative Framework'⁴ (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 country⁵.
10. These general principles are explored in further detail in relation to medical implants in the following section.

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. Annex 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

⁴ <http://ec.europa.eu/enterprise/policies/single-market-goods/regulatory-policies-common-rules-for-products/new-legislative-framework/>

⁵ <http://www.mhra.gov.uk/Howweregulate/Devices/index.htm>

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 pre-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 Body⁶.
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 AIMDD⁷. 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 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

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>

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 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. Annex B provides an example of how the MHRA has fulfilled this role in the past in relation to a medical implant, and Annex C sets out further information and statistics in relation to the MHRA's role in medical device vigilance⁸.

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 Prosthète (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 implants⁹;
 - c. the Health Select Committee report on PIP breast implants and regulation of cosmetic interventions, published on 28 March 2012¹⁰;
 - 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 implants¹¹; and
 - e. the forthcoming revision of the Medical Devices Directives¹².
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

⁸ See also <http://www.mhra.gov.uk/Howweregulate/Devices/Vigilance/index.htm>

⁹ For terms of reference for both reviews see <http://mediacentre.dh.gov.uk/2012/01/24/department-of-health-sets-out-scope-of-pip-implant-and-cosmetic-surgery-reviews/>

¹⁰ <http://www.parliament.uk/business/committees/committees-a-z/commons-select/health-committee/news/12-03-22-pipreport/>

¹¹ <http://europa.eu/rapid/pressReleasesAction.do?reference=IP/12/119&format=HTML&aged=0&language=EN&guiLanguage=en>

¹² http://ec.europa.eu/health/medical-devices/documents/revision/index_en.htm

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 EU¹³. 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

¹³ http://ec.europa.eu/enterprise/newsroom/cf/_getdocument.cfm?doc_id=4854

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 area¹⁴.
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

¹⁴ <http://www.nbog.eu/> has details on peer review and best practice guidance

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 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 year¹⁵. 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

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

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.

43. The MHRA has also been pressing for the concept of post-market clinical follow-up (PMCF) studies to feature in the revised Directives. PMCF studies complement clinical evaluation prior to being placed on the market by continuing the assessment of a device once it has been CE marked, allowing further clinical data to be gathered once a device is in more widespread use. PMCF is one aspect of post-market surveillance, but is particularly relevant for medical implants since a long-term assessment of the ongoing safety and performance of a device is critical.
44. **Traceability** – one key aspect of improving post-market surveillance of medical implants is in improving their traceability – accurately recording an exact code that identifies the implant a patient has within an existing dataset and then using this information to link with all relevant outcomes. The aim of this is to move post-market surveillance of medical implants from relying largely on adverse incident reporting to a more sophisticated proactive analysis of the ongoing performance of an implant over its lifetime.
45. The benefits of using outcomes to analyse the performance of devices have been demonstrated recently by the central role that the National Joint Registry of England and Wales (NJR) played in identifying problems with metal-on-metal hip replacements in 2010 – analysis of information from the NJR on the revision rates of the DePuy ASR system led to a worldwide voluntary recall of the device, and has subsequently brought about rapid changes in clinical practice in the UK¹⁶.
46. 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 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 globally¹⁸.

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http://www.njrcentre.org.uk/njrcentre/MetalonMetalHipImplants/tabcid/237/Default.aspx#DePuy_ASR_Device

¹⁷ <http://www.dh.gov.uk/health/2012/01/it-systems-coding/>

¹⁸ <http://www.imdrf.org/> and <http://www.ghtf.org/documents/ahwg/AHWG-UDI-N2R3.pdf>

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 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 removed²⁰.

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

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 to patients and the public²¹. 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 following²², 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.

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²¹ <http://www.eucomed.org/newsroom/8/19/EU-regulatory-system-brings-Europeans-fastest-access-to-medical-technology-without-compromising-safety/> and

<http://www.eucomed.org/newsroom/13/19/European-patients-have-access-to-new-medical-technology-sooner-than-American-patients/>

²² e.g. <http://in.reuters.com/article/2012/02/03/breast-implants-regulation-idINDEE81208U20120203>

Annex A – 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:

'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:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,*
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*
- investigation, replacement or modification of the anatomy or of a physiological process,*
- control of conception,*

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;

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

Any device which is intended:

- to be totally introduced into the human body or,*
- to replace an epithelial surface or the surface of the eye,*

by surgical intervention which is intended to remain in place after the procedure.

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:

'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;

'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.

Annex 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.

Annex 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:

| Year | Adverse Incident reports received |
|------|------------------------------------|
| 2007 | 8,634 |
| 2008 | 8,910 |
| 2009 | 9,096 |
| 2010 | 10,282 |
| 2011 | 10,967 (a 27% increase since 2007) |

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:

| Year | Medical Device Alerts issued |
|------|------------------------------|
| 2007 | 100 |
| 2008 | 88 |
| 2009 | 85 |
| 2010 | 98 |
| 2011 | 113 |

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 Jane Edwards (MI 01)

With reference to the Inquiry into the **Regulation of Medical Implants**, I wish to make the following points in answer to the questions to be raised.

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

Current legislation is not fit for purpose, hence the vast numbers of cases which require revision surgery and compensation claims should be urgently addressed.

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

Evidently not very effectively since it appears they gather the information but cannot act upon it.

3. How could the legislation and regulations be improved?

More comprehensive trials to force manufacturers to be more open and honest (stop hiding behind takeovers, stop rushing new items through before thorough testing or taking the cheapest component option) and ensuring patients are given all the necessary tests (i.e. blood and allergy tests) before the type of implant is considered.

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?

By using less biased assessment of engineering results (assessment by other than the manufacturer of the implants). Greater impartial (non-manufacturer) engineering involvement in final development stages.

I trust the Select Committee will ensure that the above points are taken into consideration.

April 2012

**Written evidence submitted by Dr. Stephen A. O'Connor, C. Eng., FIPEM, C. Phys., FInst P, Hon.
FRCP (MI02)**

Introduction

I have worked in the clinical and regulatory area of the medical device industry for many years. My current position is Director of Clinical and Regulatory Affairs for a United States company with a novel implantable cardioverter defibrillator, Cameron Health Inc. I am, however, not representing my employer with my comments, but the Institute of Physics and Engineering in Medicine, an institution within which I am an active Fellow. I am also a Fellow of the Institute of Physics and an Honorary Fellow of the Royal College of Physicians.

I am delighted to have the opportunity to provide information for your deliberations, conclusions and hopefully your impact on the new medical device regulations being prepared by the European Commission.

Current legislation

Unfortunately, current legislation is vague in relation to the term ‘medical device’ or ‘medical implant’. These terms include active devices, such as pacemakers and defibrillators, passive devices such as joint replacements, cosmetic systems such as breast implants, but not breast fillers such as Macrolane. Whilst the MHRA brief is to ensure that medical devices both ‘work and are acceptably safe’, it should be immediately evident, even with the limited examples above, that the methodology to do this differs between devices types.

I would recommend that there be absolute clarity in the definition and designation of “medical devices” in the new medical device regulations.

MHRA in the UK

The award of the CE Mark is delegated to the Notified Bodies by the Competent Authorities. The Notified Bodies are audited frequently by the Competent Authorities. Notified Bodies review documentation down to the finest detail of product dossiers including design dossiers, toxicology of implanted material and pre-clinical testing dossiers. Notified Bodies scrutinise, review and approve protocols for clinical trials designed to gain CE Mark. However, Competent Authorities must also review the clinical protocols. MHRA, the UK Competent Authority, also requests additional items including product and design dossiers etc. etc., which have been already submitted to and reviewed by the Notified Body. This is most certainly duplicitous and a cause of delay in processing what should be strictly a protocol review at MHRA. My experience of other Competent Authorities is that they have confidence that the Notified Body has done their review appropriately and therefore, perform only a clinical protocol review.

Competent Authorities have 60 days to review a clinical trial protocol and give their opinion to ‘object’ or ‘raise no objection’. MHRA, in my experience, has made decisions very close to the 60th day. This, I feel sure, is at least partly due to the additional data that MHRA requests and reviews, in contrast to other Competent Authorities. External reviewers employed by MHRA can fail to respond in an appropriate time frame, a consequence of which is that new questions can be raised with the study sponsors late in the

60 day cycle. The sponsor is then under extreme pressure to respond adequately within a very limited time. If the sponsor fails to do this, MHRA are obliged to ‘object’ so as not to be delinquent on giving their opinion within the 60 day period. MHRA then inform all other Competent Authorities of their decision without explanation. This, in turn, causes concern, and in some cases alarm, within other Competent Authorities and firefighting on the part of the sponsor to explain the specific UK situation.

I would recommend that the 60 day clock commences when a complete application is acknowledged by the Competent Authority. The clock should then stop when questions are raised by MHRA and restarted only when replies are received by MHRA. This, however, would require a major change in the workings of MHRA. Currently MHRA, send out lists of questions on an almost daily basis, after receipt of an application, from their in-house personnel, often with the same questions being repeated due to lack of consolidation internally. Inter-departmental communications on clinical protocols within the MHRA would therefore have to be greatly improved.

The public face of MHRA at medical congresses is that they are friendly, helpful, inclusive, communicative and only too pleased to work with companies wishing to perform clinical trial intended to gain CE marking. The reality could not be further from this media image when trying to communicate with MHRA about an upcoming application, during the 60 day review period, during the study itself and finally the reporting stage. In summary, they are difficult to contact, have different personnel dealing with the same issue in an uncoordinated manner, appear to have short working hours and a lack of awareness of the technology with which they are dealing. The latter leads to a defensive attitude and contributes to MHRA’s adversarial approach, championed by their senior management.

One suggestion that I was given for a new defibrillator study protocol was to implant the study defibrillator as well as a conventional transvenous defibrillator, thereby demonstrating a complete lack of understanding of the technology and, unfortunately, a total disregard for the study participant.

Competent Authorities are allowed to meet with sponsors of studies. However, my experience with MHRA has been that they try to avoid face to face contact. This may be a reflection of their insecurity and lack of coherent inquiry. Such meeting should be encouraged as they can save time and avoid misunderstanding.

MHRA appears more favourable in their dealings with the larger medical device companies compared with smaller or start-up companies. Company size and / or status must not affect their relationship with MHRA.

Improvement in legislation and regulation

Clarity of the legislation and regulation is essential. I sincerely hope that this will be achieved in the new draft later this year.

I have heard suggestions that medical device companies seek out the Notified Bodies who they believe ask the least demanding questions and approve ‘easily’, alleging that the Notified Bodies are more interested in repeat business rather than rigorous standards. I have even heard suggestions that medical device companies change their Notified Body in the hope of easing the passage for a specific product. Whilst considering this, it must be remembered that the Notified Bodies are commercial businesses. If there was substance in these allegations, it would indicate that the delegation of the award of the CE Mark

by Competent Authorities to Notified Bodies is not working uniformly as intended across Europe by the Medical Device Directive, despite frequent Competent Authority audits of the Notified Bodies. If this is proven, legislation must be introduced to stop what would be a shameful practice. However, I am personally unaware of this occurring.

Specific regulation should differentiate between medical device types and required testing, as mentioned earlier.

Prevent hindrance to the introduction of innovation in medical technology

I would recommend that one complete, concise, thorough review of a clinical protocol be performed. Notified Body or MHRA should examine the entire product dossier, not both.

The current UK situation entails the following groups all reviewing a clinical protocol with different application forms and different time scales:

Notified Body, MHRA, NHS R&D, Lead Ethics Committee, Individual local Ethics Committees, NHS New Medical Device / Interventions Committee.

This must be streamlined to make UK competitive for innovation and the ability to take part fully in clinical studies. Time and effort is spent to move through the review processes outlined above by hard pressed dedicated clinical practitioners and researchers. Unfortunately, and despite these efforts, multi-national studies are often completed, or almost completed, before the UK centres have negotiated their way through the minefield, resulting, at best, with minimal enrolment.

UK has wealth of world class scientists and medical practitioners, who are only too willing and able, not only take part, but also lead world class research in innovative medical devices. The UK regulatory climate precludes them in many cases. It must be realised that this also precludes UK patients becoming clinical trial participants on innovative products, which could potentially be to their benefit. This was highlighted by Sir Paul Nurse FRS in the Richard Dimbleby Lecture earlier this year, 2012.

MHRA should embrace the opportunity for face to face contact with study sponsors and ensure that their personnel are proficient in the areas of endeavour. This should assist in defusing the current adversarial and defensive approach towards sponsors.

MHRA should accept that there are other Competent Authorities in Europe with whom they can collaborate, share information in full and even learn.

April 2012

**Written evidence submitted by Sheila Sunley,
Member of the Altogetherhip Patient Support Group (MI03)**

I am a patient currently treated at York District Hospital. In the last 7 years I have undergone 3 hip replacement operations, two of which were Metal on Metal, and am being monitored for high chromium/cobalt levels. I would like to comment on the lack of legislation and regulation as follows:

1. Current legislation and regulations are not fit for purpose. 2 years of laboratory testing is not enough. Clinical trials are needed with volunteer patients to ascertain the effect of implants on the body, ie; on bone and soft tissue damage.

Metal on metal hips and the subsequent wear releasing metal ions into the bloodstream are an example.

2. The MHRA is a toothless organisation influenced by manufacturers not patient care.

My own experience is that the directive to withdraw Metal on Metal hip implants was issued a full year after I had had my implant removed. There should be a process where surgeons report back sooner and if implants are failing they should be removed from the market immediately. There was concern in other countries (Australia) about hip devices in 2007 and the MHRA were slow to react.

3. Improvements in legislation should include making it illegal to give incentives to surgeons for using a manufacturers product. If the implant is good enough it should not need to be 'sold' to the medical profession.
4. The introduction of implants to the market is expensive and I would suggest there being an independent body supported by the government, to thoroughly test products and report back to the MHRA who in turn have the power to withdraw an implant from use.

I would welcome the opportunity to be involved with the inquiry process and hope that my above comments will be taken into consideration.

April 2012

**Joint written evidence submitted by the Centre for Evidence-Based Medicine
and the British Medical Journal (MI04)**

This response reflects the research and investigation studies that the British Medical Journal and the Centre for Evidence-Based Medicine have undertaken in this area. These include analyses of UK and US regulators as well as studies on metal-on-metal hip implants and research into medical device recalls and the device regulation process in the UK. These studies are used in the construction of this response and referenced at the end; full copies are available upon request.

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

Lack of pre market clinical data

Concerns exist about the lack of premarket clinical data on the effectiveness and safety of medical devices. These concerns have previously been expressed by Susanne Ludgate of the MHRA, who stated in 2010 that she was “appalled at how many devices are brought to market with a lack of appropriate clinical data.”¹

Our research into European device directives that form the current legislation reveals the extent of the problem. First, it is left to the discretion of the Notified Bodies (as to the extent and nature of clinical data required for the approval of even the highest-risk devices).^{2 3} We have found that whatever clinical data are reviewed by Notified Bodies, on behalf of the manufacturer, none are available to independent scientific scrutiny. This means that the normal level of evidence required to demonstrate the effectiveness or safety of new pharmaceutical agents is simply not required for medical devices under the current legislation. Given the large number and potential risk of medical devices, this lack of clinical data at the outset seems unacceptable, particularly for implantable devices (such as cardiac pace makers, artificial joint implants, stents etc.) which are those that present the highest risk.

The level of clinical data required for a new device can be minimal. For example, a directive would include as evidence for approval “a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device”. This is a very low level of evidence and could be obtained in a few days, contrasting markedly with the type and extent of clinical trial data required for new drugs.⁴

The specific council directives 93/42/EEC and 90/385/EEC allow studies of other similar devices to be sufficient in a literature review for regulatory approval

- *B COUNCIL DIRECTIVE 93/42/EEC and 90/385/EEC*
 - *(k) ‘clinical data’ means the safety and/or performance information that is generated from the use of a device.*

Clinical data are sourced from:

- *clinical investigation(s) of the device concerned, or*

¹ Carl Heneghan: *Lack of clinical data for medical devices is putting patients' lives at risk*. The Guardian, 16 May 2011 <http://www.guardian.co.uk/science/2011/may/16/medical-devices-lack-clinical-data>

² Carl Heneghan, David Langton, M Thompson. *Ongoing problems with metal-on-metal hip implants* BMJ 2012; 344 doi: 10.1136/bmj.e1349 (Published 28 February 2012) Cite this as: BMJ 2012;344:e1349 <http://www.bmjjournals.org/content/344/bmj.e1349>

³ Cohen D, Billingsley M. *Europeans are left to their own devices*. BMJ. 2011 May 13;342:d2748. doi: 10.1136/bmj.d2748. <http://www.bmjjournals.org/content/342/bmj.d2748>

⁴ Thompson M, Heneghan C, Billingsley M, Cohen D. *Medical device recalls and transparency in the UK*. BMJ. 2011 May 13;342:d2973. doi: 10.1136/bmj.d2973. <http://www.bmjjournals.org/content/342/bmj.d2973>

- *clinical investigation(s) or other studies reported in the scientific literature, of a similar device for which equivalence to the device in question can be demonstrated, or — published and/or unpublished reports on other clinical experience of either the device in question or a similar device for which equivalence to the device in question can be demonstrated.*

Use of "equivalence" in regulatory approval of devices

A major problem with the current system is the use of "equivalence" (as outlined above) for approval of devices. That is, if a device is similar to another manufacturer's device on the market, then there is no need for clinical trials and device manufacturers can seek regulatory approval based on a far lower level of data than devices not considered under this fast track pathway. Regulators find it incredibly difficult to judge if a device is "equivalent" to another on the market.⁵ As an example we have recently demonstrated for metal on metal large diameter hip replacement prostheses, that small changes to the design had sizable negative impact on the effectiveness and safety of the device. Rather than improving the device, the small change led to an unacceptably high failure rate with serious actual and potential impact on patients' health. However, in the US regulators suggested that: "*The design, while not identical to the predicates, does not raise any new issues of safety or effectiveness.*"

The current system of 'equivalence' and the acceptance of studies of other devices reported in the scientific literature are one of the main drivers of poor quality under-researched devices on the market today. Of more concern, the guidelines in the EU for manufacturer's state: "The depth and extent of clinical evaluations should be flexible and not unduly burdensome." The current CE regulatory framework allows clinical evaluations to be based on existing technologies rather than the actual performance of the new device.

Disparity in evidence requirements between US and EU

Similar concerns have recently been raised in the US, by the highly prestigious and independent Institute of Medicine about the FDA's fast track approval route known as 510k. Indeed legislation is currently before Congress to limit the use of this approval route by the FDA.⁶ Their report on the 'Public Health Effectiveness of the FDA 510(k) Clearance Process'⁷ recommends:

The Food and Drug Administration should obtain adequate information to inform the design of a new medical-device regulatory framework for Class II devices so that the current 510(k) process, in which the standard for clearance is substantial equivalence to previously cleared devices, can be replaced with an integrated premarket and postmarket regulatory framework that effectively provides a reasonable assurance of safety and effectiveness throughout the device life cycle.

There are profound differences in evidence requirements for regulatory approval between the US and EU, with far higher requirements in the US for approval of the same device. For example, evidence submitted for EU approval of a "GuardWire" developed by PercuSurge for use during angioplasty, required a 22 patient study with no control group. In the US, in contrast, for the same device FDA regulators required an 800 patient multicentre randomized controlled trial. Although it is inevitable perhaps that different countries will have different processes and evidence requirements for medical devices, the magnitude of the disparity suggests an unacceptable level of risk for patients in the EU compared to the US.⁸

⁵ Cohen D. *How safe are metal-on-metal hip implants?* BMJ. 2012 Feb 28;344:e1410. doi: 10.1136/bmj.e1410.

⁶ Carl Heneghan: *Hip replacement fiasco highlights regulatory failings in Europe.* The Guardian. <http://www.guardian.co.uk/science/blog/2012/feb/29/hip-implant-fiasco-regulatory-failings>

⁷ *Public Health Effectiveness of the FDA 510(k) Clearance Process*

<http://www.iom.edu/Activities/PublicHealth/510KProcess.aspx>

⁸ Ibid.

As a result a number of devices that were rejected by the FDA have been approved by the EU regulatory system.⁹ This list of EU approved devices that were rejected by the FDA includes the PIP breast implant which has so spectacularly failed patients in the UK and Europe at enormous additional cost, and the now recalled metal on metal hip resurfacing prosthesis, the ASR, which resulted in joint failure and further risky and expensive surgery for large numbers of patients.

Rejected Devices by FDA that were approved in the EU:

Covidien PleuraSeal lung sealant system

This device went on the EU market in November 2007 and is used during elective pulmonary resection as an adjunct to standard closure techniques for visceral pleural air leaks. However, the Investigational Device Exemption (IDE) study (a clinical study for FDA regulatory purposes) produced unexpected interim results. In October 2010 Covidien announced a worldwide recall of all PleuraSeal lung sealant systems

Medtronic Chronicle

The Chronicle is an implanted system designed to measure and record haemodynamic variables continuously. In March 2007, an FDA panel refused to approve the device, citing statistically insignificant results as “lack of clinical effectiveness.” It was nonetheless approved in Europe.

PIP breast implants

In 1991, breast implants manufactured by Poly Implant Prosthese (PIP) received a CE mark for its silicone breast implants. But in 2001 they changed the gel, so that it was different from the one described in the CE marking file. This modification led to rupture rates higher than silicone implants made by other manufacturers. On 30 March 2010, the French regulator—AFSSAPS—issued a recall of all pre-filled silicone breast implants manufactured by PIP, affecting an estimated 35 000-45 000 women worldwide.

Trilucent breast implants

First marketed in the UK in 1995 by LipMatrix, Trilucent implants were recalled and withdrawn from the market in 1999. The filler of the implants, which was derived from soybean oil, broke down in the body and leaked through the shell, causing ruptures. The breakdown of the filler was significantly different from that predicted during preclinical testing, and many patients had to have implants removed.

Conor CoStar drug eluting stent

CoStar is a cobalt, chromium, paclitaxel eluting coronary stent and received EU approval in 2006. In May 2007, Johnson and Johnson announced that a pivotal clinical study of the device had failed to find a significant difference on the primary end point, possibly because patients got a suboptimal therapeutic dose of paclitaxel. The trial did not identify safety issues. As a result of this trial, Conor terminated ongoing clinical trials and chose not to conclude the submission of its US premarketing approval. Conor discontinued the sale of the stent in Europe, Asia, and Latin America.

Changes to a device

In the US, even changes to the device which are regarded as minor - and which can be justified as not risking any material change to the risk-benefit equations for the patient - still need to be notified to the FDA 5 days beforehand. This is not the case in Europe. This is how the silicon in the PIP Breast implant could be changed without requiring notification, whereas in the US, any such change would require notification to the FDA approval.¹⁰

⁹ Cohen D, Billingsley M. *Europeans are left to their own devices*. BMJ. 2011 May 13;342:d2748. doi: 10.1136/bmj.d2748. <http://www.bmjjournals.org/content/342/bmj.d2748>

¹⁰ Heneghan C. BMJ. 2012 Jan 11;344:e306. doi: 10.1136/bmj.e306. *The saga of Poly Implant Prosthese breast implants*. <http://www.bmjjournals.org/content/344/bmj.e306>

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

MHRA lacks access to clinical data submitted for device approval

The absurdity of the current system is highlighted by the minutes of a meeting of the MHRA's safety of devices committee in 2009 which stated: 'It was also noted that MHRA does not see the clinical data that is generated from a clinical trial prior to it being submitted to a Notified Body as part of a conformity assessment process. The only way they see it is if there is an adverse event or concerns raised. It is not mandatory for manufacturers to present their final report to the Competent Authority.'¹¹

This leaves us in a situation where no one really knows, including the regulators, what data was submitted by whom, and on what date, for a device to be allowed access to the European market. Indeed, there is no complete list of medical implants that are on the market. It is difficult to understand how a regulator can function effectively without actually knowing what they have approved.

Unlike in Europe where both the public and, bizarrely, the regulator are kept in the dark, in the US, the FDA does itself see the data and provides public access to it on their website at the time of regulatory approval.

Slow responsiveness of MHRA

In addition to the lack of access to data prior to approval, we are also concerned about the slow response of the MHRA when safety or effectiveness concerns are raised on devices that are already approved or in use. For example, an unpublished trial of a metal-on-metal total hip replacement implant was stopped early due to problems with the device, but it took more than a year for the UK regulator to inform orthopaedic surgeons not to use the implant. Indeed, the MHRA confirmed that they did not know the trial was underway.¹²

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. Because of a lack of formalised post-marketing surveillance studies, the MHRA relies on either clinical registers to report failures (such as the national joint register) or issues being raised in the published literature. Both of these systems have their flaws—not least publication bias or under-reporting—and are not good for early warning systems or for spotting new conditions as they emerge. For example, joint registers only include patients who have had revision surgery, which may be many years after symptoms first occur.¹³

Lack of post market surveillance

We appreciate that a proportion of devices will fail owing to problems which were not noted prior to approval, in the same way that some medications need to be withdrawn from the market or their use restricted due to safety concerns. However, it is interesting that car manufacturers appear to be more successful at identifying and acting on possible faults in new cars than medical device manufacturers. This may be because there is currently no formal system for post market surveillance of medical devices in the UK and many vested interests that disincentivise manufacturers and clinicians from highlighting problems as they arise. Registries of devices are used in two main areas, orthopaedics and cardiovascular devices. However, these are ad-hoc and often not formalised. They may also not be totally independent of manufacturers and data can be difficult to access.

¹¹ Cohen D. *How safe are metal-on-metal hip implants?* BMJ. 2012 Feb 28;344:e1410. doi: 10.1136/bmj.e1410.

¹² Cohen D. *Study on metal-on-metal hip implants was halted a year before UK regulator banned their use.* BMJ. 2012 Apr 13;344:e2698. doi: 10.1136/bmj.e2698. <http://www.bmjjournals.org/content/344/bmj.e2698>

¹³ Cohen D. *US regulator seeks advice on health risks of metal on metal hip implants.* BMJ. 2012 Mar 30;344:e2460. doi: 10.1136/bmj.e2460. <http://www.bmjjournals.org/content/344/bmj.e2460>

Unfortunately registries are limited to devices within these categories. And even in these limited clinical specialties, there is no way of knowing which patients in the UK have a device (even an implanted device), since this information is not available on GP records, and is not routinely noted on hospital records (or discharge summaries). Therefore, if a device is found to be faulty there is no way of notifying GPs or their patients.

This seems unacceptable given that the devices were purchased using NHS funds, and when devices fail the NHS is responsible for any costs incurred—unless there is ensuing litigation. A further consequence of this is that without systems to identify which devices are used in which patients, it is not possible to perform the large scale research on safety and effectiveness on medical devices using the many excellent sources of national data available to researchers in the UK (such as Hospital Episode Statistics, General Practice Research Database etc.). This contrasts with the situation for medications, where prescribing data are routinely available and widely used for studies in the UK. The addition of correct coding of devices in patient records would involve minimal cost, but potentially large benefit.

Lack of post market monitoring of performance

It is currently the case that CE marked devices can enter widespread use without any organised monitoring of the outcomes of their use. The MHRA itself has reported that “*Long term outcomes of implanted devices are a particular concern.*”¹⁴

The MHRA also reported to the BMJ that it relies on a “statutory vigilance or voluntary adverse incident reporting system” to regulate—in other words, governmental regulation really starts when devices are already on the market.^{15 16}

Under-performance of post-marketing surveillance by manufacturers

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. Steve Owen, head of Devices Policy, European and Regulatory Affairs at the MHRA, has stated that he finds it “staggering” how many manufacturers fail to fully fulfil their legal responsibility to collect product data once their device is on the market.

And according to an MHRA report: “Post-market surveillance has not been addressed sufficiently in the past, as many manufacturers do not focus on this area, and it is not ‘policed’ vigorously enough by Notified Bodies.”

Manufacturers cannot be simply relied on to undertake post-marketing surveillance. Post-marketing studies, requested by the FDA for breast implants in 2006, have lost so many of the women they were supposed to follow up that they are unlikely to offer any insight into the long term safety of devices. After three years, a study by Mentor, the maker of Memory Gel implants, lost 79% of the patients enrolled, whereas Allergan, the maker of Natrelle implants, has lost nearly 40% of its participants after two years.¹⁷

¹⁴ *Long term outcomes of implanted devices are a particular concern.* MHRA

<http://www.mhra.gov.uk/home/groups/clin/documents/websiteresources/con082076.pdf>

¹⁵ Cohen D. *Revision rates for metal on metal hip joints are double that of other materials.* BMJ. 2011 Sep 20;343:d5977. doi: 10.1136/bmj.d5977. <http://www.bmjjournals.org/content/343/bmj.d5977>

¹⁶ Cohen D. *Out of joint: the story of the ASR.* BMJ. 2011 May 13;342:d2905. doi: 10.1136/bmj.d2905. <http://www.bmjjournals.org/content/342/bmj.d2905.full>

¹⁷ Carl Heneghan: *Hip replacement fiasco highlights regulatory failings in Europe.* The Guardian. <http://www.guardian.co.uk/science/blog/2012/feb/29/hip-implant-fiasco-regulatory-failings>

3. How could the legislation and regulations be improved?

Independent scrutiny of premarket approval data

There appears to be a concerning lack of transparency in the data available for independent scrutiny of medical devices. We recently quantified the number and types of medical device failures in the UK, the health consequences from these failures, and the data that had been supplied for premarket approval. These appeared to be straightforward questions—ones that someone else would have already asked—but unfortunately our research threw up numerous hurdles. Indeed, we were not able to gain access to any data submitted by device manufacturers for regulatory approval, and thus were not able to judge whether device failures could have been predicted by lack of clinical data prior to approval.

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. As noted above, this lack of independent assessment of data is not acceptable, and contrasts with the UK's highly regarded systems for evaluating clinical evidence via NICE etc.

Lack of clinical trial data and cost effectiveness

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. With drugs, the likes of NICE are able to use the data generated in regulatory approval to make decisions about the best use of NHS funds. We have been told by similar institutions across Europe about the impossible task in trying to prioritise healthcare spending for devices. 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.

We urge the Committee to push for increasing the access to pre-market approval clinical data used by Notified Bodies to submit for regulatory approval.

Failures to identify and recall devices when concerns are raised

A second problem highlighted by our research is that information about the number of recalled devices, the risk of harms to patients, and the premarket approval process was not available from the MHRA. These data are held by the manufacturer and the Notified Body. Since both the Notified Bodies and the manufacturers are exempt from freedom of information legislation, we decided to contact them directly by email. We started with the manufacturers of 192 devices recalled by the MHRA over a 5 year period, each of which lists a contact responsible for the recall. Unfortunately, despite our best efforts (based on high level clinical research expertise) only four (2%) companies provided any clinical data. We were informed by the Notified Bodies that information was confidential and not available for scrutiny.¹⁸

In addition, our attempts to obtain how many adverse events had occurred for specific devices were also unsuccessful. The Freedom of Information Act is over-ridden by medical device legislation in the EU. Article 20 of the EU medical devices directive states: “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.”

¹⁸ Carl Heneghan, David Langton, M Thompson. *Ongoing problems with metal-on-metal hip implants BMJ* 2012; 344 doi: 10.1136/bmj.e1349 (Published 28 February 2012) Cite this as: BMJ 2012;344:e1349 <http://www.bmjjournals.org/lookup/doi/10.1136/bmj.e1349>; Cohen D, Billingsley M. *Europeans are left to their own devices. BMJ.* 2011 May 13;342:d2748. doi: 10.1136/bmj.d2748. <http://www.bmjjournals.org/lookup/doi/10.1136/bmj.d2748>; and Thompson M, Heneghan C, Billingsley M, Cohen D. *Medical device recalls and transparency in the UK. BMJ.* 2011 May 13;342:d2973. doi: 10.1136/bmj.d2973. <http://www.bmjjournals.org/lookup/doi/10.1136/bmj.d2973>

Therefore we urge the Committee to strengthen the Notified Body assessment in terms of demonstration of competence, impartiality and transparency, providing for timely and uniform action in the areas of vigilance and reinforced market surveillance. In addition we add the need to allow independent third party scientific scrutiny of data supplied.

Post marketing surveillance

At a minimum there is a need to eliminate the use of multiple predicates (equivalence) in 510(k) and CE approval and put in place robust post marketing studies to detect devices that are failing.

Funding medical device safety with an insurance based system

No initial regulatory evidence can safely assume that there will not be harms in the long term, so devices could come with an insurance based funding system to allow for this—companies go bankrupt and harms take a long time to manifest. In effect the greater evidence of safety would lead to reduce premiums at the time of implantation.¹⁹

Transparent approach to conflicts of interest

It is important regulators remain impartial and take a view point that is important, not only for industry, but also for patient safety. The use of impartial advice is paramount in regulatory decision making processes where substantial sums of money are at stake. To achieve this, the regulator and the regulations need to have a consistent and transparent approach to dealing with conflicts of interests.

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?

Failures of medical devices cause harm and cost money. More stringent requirements to provide evidence from clinical trials for the efficacy and safety medical devices before they are approved should therefore be welcomed by patients, clinicians and the medical device industry. Devices which are safe and effective provide a win-win situation where both the company gains market shares, and NHS patients benefit from improved clinical outcomes. Innovation is only of real value to health if it does genuinely improve outcomes—unfettered innovation may have the opposite effect.

Different levels of evidence

The European Commission should consider different levels of evidence depending on what is currently available. Where multiple devices for the same condition currently exist (e.g., hip replacements, pacemakers), then the bar for seeking market entry should be higher. Where in contrast little or no devices are currently available and patient care is clearly suboptimal, then consideration can be given for earlier or faster approval of innovative devices which are clearly filling clinical gaps. This parallels the lessons from the pharmaceutical industry, where for example HIV drugs underwent fast track approval in their early years due to overwhelming patient need, but now with many combinations of HIV drugs now available a higher level of scrutiny is now needed.

We believe that there is a need for a clearer understanding of evidence requirements for new devices.

Better methods for surgical innovation: the IDEAL framework

The IDEAL (Idea-Development-Exploration-Assessment-Long term study) framework and proposals are being developed by an international group of methodologists and clinicians.^{20,21}

¹⁹ Heneghan C. BMJ. 2012 Jan 11;344:e306. doi: 10.1136/bmj.e306. *The saga of Poly Implant Prostheses breast implants.* <http://www.bmjjournals.org/content/344/bmj.e306>

²⁰ Barkun J, Aronson J, Feldman L, Maddern G, and Strasberg S (2009). *Surgical Innovation and Evaluation 1: Evaluation and stages of surgical innovations.* The Lancet, 374:1089-96; Ergina P, Cook J, Blazeby J, Boutron I, Clavien P, Reeves B, and Seiler C (2009). *Surgical Innovation and Evaluation 2: Challenges in evaluating surgical innovation.* The Lancet, 374:1097-104; and McCulloch P, Altman D, Campbell B, Flum D, Glasziou P,

IDEAL promotes: the development of innovative study designs for early phase innovation in interventional therapy in surgery, including the development of implantable devices, and a comprehensive international agreement on best practice in conducting and reporting clinical case series in surgery. The IDEAL group also recommends that regulators of medical devices provide rapid, flexible, and expert ethical oversight for early-stage innovation, link provisional approval to evaluation or registration of all cases and raise the burden of proof for full licensing of new devices to demonstration of efficacy level.

Much has been made of the difference between medicines and implantable devices.²² However, it is worth noting that if an implantable device is faulty or fails, the reversal procedure carries risks in itself. There are the risks of having to undergo an anaesthetic plus there may be other risks from the procedure itself, for example haemorrhage, infection and venous thromboembolism. The current system should strive to incentivise innovations that improve patient care and reduce the harms to patients.

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and Marshall J (2009). *Surgical Innovation and Evaluation 3: No surgical innovation without evaluation: the IDEAL recommendations*. The Lancet, 374:1105-12.

²¹ <http://www.nds.ox.ac.uk/conferences/ideal>

²² Godlee F. *The trouble with medical devices*. BMJ 2011; 342 doi: 10.1136/bmj.d3123 : BMJ 2011;342:d3123 <http://www.bmjjournals.org/content/342/bmj.d3123.full>

Written evidence submitted by Carol Holland, Altogether Hip Support Group (MI05)

I would like to make the following comments to the Select Committee looking into the totally inadequate regulation on medical implants:

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

Obviously not or else why am I currently no better off than before I had my hip operation in March 2007. I had less than 18 months of renewed life before I had to have my hip revised in June 2010 because the joint used was a DePuy ASR XL. I am now only just 60 but the damage done to my muscles by the toxic fluid formed by the defective joint has left me with the mobility of an 80 year old and I consider myself one of the fortunate ones! There are others in our Support Group who have been left in a far more serious condition with one poor chap having no hip joint left at all.

- 2) *How effectively does the MHRA implement the Directive in the UK?*

The MHRA seems to be a totally ineffective body working on behalf of the corporations rather than patients. If the ASR was withdrawn in Australia in 2009, why was it still being fitted in this country at the end of 2010. It was never even authorised in the US, so why should we, in this country, be guinea pigs? They appear to have listened to nobody's concerns at all and shown absolutely no interest in patient welfare – after all what do patients matter?

- 3) *How could the legislation and regulations be improved?*

The legislation needs to be simplified and a much more thorough system of testing introduced. It is just not good enough to say this joint is similar to those already out there. If it is, why do we need it anyway? Are surgeons offered inducements by the likes of DePuy? Surgeons should, by law, have to disclose their interests so patients can have some chance of discovering why a particular joint is chosen. Patients should be told what is on the market, the advantages and disadvantages of them all and what tests they have undergone. All companies involved in the manufacture of implants should be legally required to show exactly what tests have been carried out.

The MHRA should be a totally independent body with enough experts on board to evaluate the information and test results properly before any licence is issued. Mistakes happen and if another bad joint slips through the system, action should be taken immediately not wait years and allow thousands of patients to be crippled.

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, even though, as in this case it is generally not their fault. If all surgeons were forbidden to take inducements, and were forced to report problems, then they would all be on a level playing field. Far from them looking incompetent if they could prove that they had acted promptly in notifying problems, patients would start to believe that someone actually cared about them as people and were not just treating them as pound signs.

- 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?*

If a product really is innovative, even the more reason to have it tested more thoroughly. Could the MHRA set up their own testing centre so that smaller companies could rent time rather than have to

buy their own expensive equipment. After all, if the innovation works after tests, the company involved is eventually going to make loads of money.

Could a licence be issued and renewed on an annual basis with the annual cost helping to contribute to the running of the MHRA test centre. Before renewal the Joint Registry would check to see if any problems had been reported.

The MHRA needs to be a financially independent body working for the good of the patient.

I could not believe the arrogance and attitude of Sir Kent Woods of the MHRA when he talked to Jeremy Paxman on Newsnight. Of course things can and should be tested - he obviously hasn't been unfortunate enough to need a new hip.

April 2012

Written evidence submitted by Professor Alan Murray (MI06)

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

There are two main issues confronting regulation of medical devices. They are sometimes taken as a single issue in the recent, often confusing, debates in the press. The first is over CE marking, and the second is over the follow up of devices that have been implanted. These have already been identified by the Committee as “provisions relating to market surveillance, vigilance [for follow up] and the functioning of notified bodies [for CE marking]”.

Many patients and clinical staff have called for medical implants to face the same style of clinical trial as for drugs. This 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 remove. Nevertheless, manufacturers must provide sufficient data to show that their device is both safe and effective. The current regulations require manufacturers to provide these data in the Technical Files that they make available to Notified Bodies. It is essential that all Notified Bodies review these data in a consistent way. There is a great danger that the process could become more bureaucratic with little effect on the outcome. The regulations could provide more information on what data has to be provided and how it is to be examined. Some limited information on this assessment could be made available openly in the public domain. This could include whether the data were published and give the source, and also the numbers of patients studied. There also needs to be a way of monitoring how Notified Bodies in different countries are performing, by publishing information that could be compared between bodies.

I believe that market surveillance and vigilance are much more important. If we accept that clinical trials for medical implants are much harder to conduct than for drug trials, we need a mechanism to detect when things go wrong, and to be able to do this quickly. Follow up of all implants would provide much stronger clinical and scientific data than any formal clinical trial. It would be much larger, and would not be constrained by the use of selected patient groups. The data collection and analysis would be difficult, but should be confronted. All implants should be registered to each patient. There is no current requirement for this, and some professional bodies have developed their own databases and voluntary recording systems. This includes pacemakers and hip joints. If records are to be held showing which patient has which implant, how this is to be done should be thought through carefully before it is implemented to ensure that it is practical and can be analysed quickly and anonymously. It will not be easy.

Recommendations:

- Ensure that Notified Bodies assess safety information in a consistent way, and that there is a European wide system of monitoring Notified Bodies.
- Make some limited data available in the public domain of this assessment.
- Ensure that all medical implants are registered to individual patients, and that anonymous data can be analysed quickly.

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

The MHRA as the UK's Competent Authority deals with vigilance according to current regulations. They publish data annually on incidents reported to them, mainly through manufacturers' reporting via the vigilance system and from NHS hospitals that are required to report incidents. There are about 10,000 medical device incidents reported to them annually. MHRA staff investigate serious incidents and publish Device Alerts and Hazard Notices for action by manufacturers and medical establishments.

My assessment is that they follow the Directive in a legal way. They do exactly what is required and take great care not to break manufacturer's confidentiality. There is no harm in that, but they lack the

ability or drive to make improvements beyond the current legislation. I am sure that this is in part related to their current finances and expertise. The older versions of the devices arm of the MHRA had more technical expertise than is currently available to them. Also, the legal framework in which they operate tends to delay any necessary action in case the advice is wrong and there are subsequent legal cases.

The MHRA works with nominated hospital contacts (Liaison Officers), but from my experience these contacts tend to do what is required and no more. I believe there is still confusion over what should be reported. If a patient experiences some pain with a hip joint or a pacemaker fails after say four years, is that an incident? Probably not, in the view of most clinicians, but could be very relevant in assessing implants. Relevant data should be collected, provided it is done for all devices in consistent ways. If the press says there is a potential problem with a specific device, side effects will be reported for that device and probably not for other different devices, and this unhelpfully skews the data making it difficult to evaluate any potential problem.

Currently the MHRA has not been involved in committees dealing with device standards, when in the past they often took a leading role, and this helped promote international safety. I suspect they are no longer in a position to do this.

Recommendation:

- MHRA do what is required of them by the Medical Devices Directives, and probably do this work better than most (or all) other European Competent Authorities, and should be thanked for that, rather than being at the end of much press criticism. However, they need to go beyond the legal framework and help develop a better more future looking vigilance system.

3. How could the legislation and regulations be improved?

I have nothing to add to the above.

Recommendations:

- Improve vigilance, in particular by developing methods to follow up all patients with implants. Ensure that all notified bodies are monitored, and that they examine and assess the safety data in manufacturers' Technical Files in a uniform way.
- Require implantable devices to be registered to specific patients and the data analysed quickly and anonymously.

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?

We need to avoid attempts to introduce medical device clinical trials in the same way as for drugs. Manufacturers need to know exactly what is required of them when submitting clinical data in their Technical Files so that different Notified Bodies do not interpret these requirements differently. The Directives also need to state explicitly that we expect devices to be improved and new devices to be introduced. Manufacturers are mostly providing a great service that allows us all to live longer, and there needs to be general approval that this is good.

Also I would recommend that the regulations are simplified. To take one example, I have heard much more discussion about which Class a device might fall into and which Annex of the Directive a company should follow (all pretty complex stuff) rather than on how to achieve better safety.

Recommendations:

- Implantable medical devices should be allowed to follow different approaches to clinical trials than for drugs.
- Promote development of improved and new devices.

- Simplify existing regulations.

Background: Alan has been employed in the NHS and University departments all his working life. He has been the director of a large medical physics and bioengineering service. He has worked informally with the devices arm of the MHRA and its predecessors since the 1970s. In his clinical roles he has promoted clinical safety. The book he co-authored on “Medical Devices: Use and Safety” was published in 2011 in India for the Asian market where there is a growing realisation that medical safety is a problem that can and must be improved. He is a member of international standards committees, chairs the British Standards Institute’s Sphygmomanometer Committee, is a Registered Clinical Scientist and Chartered Engineer, and is a Fellow of both the Institute of Physics and Engineering in Medicine and the Institute of Engineering and Technology.

April 2012

Written evidence submitted by Action on Hearing Loss (MI07)

About us

Action on Hearing Loss is the new name for RNID. We are the UK's largest membership charity supporting people who are deaf or hard of hearing. We're experts in providing support for people with hearing loss and tinnitus and provide day-to-day care for people who are deaf and have additional needs. We supply communication services and training whilst offering practical advice to help people protect their hearing. We campaign to change public policy around hearing loss issues and support research into an eventual cure for hearing loss and tinnitus.

Introduction

1. Hearing loss is a major public health issue affecting over 10 million people in the UK – one in six of the population. 800,000 people in the UK are severely or profoundly deaf¹.
2. 10,000 people in the UK use a Cochlear Implant.² These implants can improve people's ability to hear and understand speech if they can't benefit from hearing aids, devices which amplify sounds to a level that the individual can hear – but only if someone has residual hearing.
3. When someone is profoundly deaf, it is usually because most of the hair cells in the cochlea have stopped working. A Cochlear Implant bypasses lost or damaged sensory cells in the cochlea and consists of an internal part (a receiver which is surgically implanted in the mastoid bone behind the ear, with electrodes inserted into the cochlea, part of the inner ear) and an external part (a microphone and speech processor which convert sound into an electrical signal that is sent to the electrodes in the inner ear). The implant works by stimulating the hearing nerves in the inner ear directly, sending a sensation of sound to the brain.
4. Cochlear implants enable children who are deaf to learn language, speak intelligibly and perform better at school. Adults are able to communicate more confidently, regain their independence, and stand a better chance of getting a worthwhile job.
5. We expect to see further advances made in the coming years to greatly improve the function of cochlear implants, so we need a regulatory environment for medical implants that not only ensures patient safety but also one that does not hinder the introduction of innovative new technology.

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

6. Yes, the current system has largely proven effective but there are some difficulties when working across different countries. These include;
 - a. Poor coordination of post-marketing surveillance between Member States.
 - b. Differences between Member States in how they transpose the European Directive on Medical Devices into national law and the criteria used to approve clinical trials.
 - c. Notified Bodies being inconsistent.

How could legislation and regulations be improved?

¹ Action on Hearing Loss (2011) Hearing Matters.

² <http://www.actiononhearingloss.org.uk/your-hearing/about-deafness-and-hearing-loss/cochlear-implants.aspx>

7. Improvement could be achieved through the criteria used to approve clinical trials being clearly specified in the Directive. Increased transparency is needed in order to bring improvements. For example, publicly available databases of approved products, clinical trials, adverse events and recalls.

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?

8. The flexibility of the current ‘new approach’ system has worked well and should be maintained. A change to an approach similar to that taken by the United States Food and Drug Administration (FDA) would increase the time taken to gain approval for a new product, thereby increasing levels of bureaucracy and delaying patient access to new implants that could significantly improve their quality of life.

9. The European Commission should ensure that each Member State implements the Directive consistently to support studies across different countries. Achieving this consistency between Member States would be aided by the removal of areas of uncertainty through the production of clear regulations for the industry instead of directives.

10. In the future there is likely to be an increased convergence between medical implants and pharmaceuticals in the future. For example, cochlear implants could deliver drugs to reduce inflammation or to improve the health of the auditory nerve. Authorities need to develop an integrated approval route for this type of mixed product. Traditional drug approval requires thousands of subjects, but medical devices may gain approval after being tested in only 50 patients. To support innovation work needs to be done to bring these two areas together.

April 2012

Written evidence submitted by the Association of British Healthcare Industries (MI08)

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.

1. Introduction and Overview

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 £37.2million (Bevan *et al*, 2011).

2. The term 'implant' covers products ranging from active (i.e. 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)
 - c) Directive 98/79/EC on *in vitro* diagnostic medical devices (IVDD).
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.

4. How the current legislation delivers innovation to patients

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.

12. The role of the MHRA

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.

13. How can the legislation and regulations be improved?

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
- effectively foster and support innovation

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

15. Notified Bodies

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.

17. Vigilance and post market surveillance

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.

19. Clinical Evaluation

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.

21. Mechanisms for consistent implementation

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.

23. Confidentiality

The confidentiality requirements under the current Medical Devices Directives are seen by some stakeholders as being too restrictive (e.g. 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.

25. Unique Device Identification

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.

26. Coordination and Management

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.
28. *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?*

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.

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April 2012

Written evidence submitted by the Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians of the United Kingdom (MI09)

A medical device, is any device that is used for diagnosis, prevention, monitoring, treatment and alleviation of diseases. In the EU, the government of each member state is required to appoint a competent authority responsible for medical devices. In the UK, it is the Medicines and Healthcare products Regulatory Agency (MHRA) which acts as the competent authority. The competent authority in one member state does not have jurisdiction in any other member state but they do exchange information and try to reach common positions.

Medical devices are classified into Class I, IIa, IIb and Class III. The classification of medical devices is risk-based, dependent on the device's duration of body contact, its invasive character, its use of energy source, its effect on the central nervous system and the central circulation, its diagnostic impact, or its incorporation of a medicinal product. To simplify the discussion, the focus of this feedback is mainly on Class IIb and Class III, which are the implantable medical devices. Below is the summary of the feedback from the members of the Medical Devices Special Interest Network of the Faculty of Pharmaceutical Medicine to the four questions of the House of Commons Science and Technology Inquiry on medical devices.

1) Are current legislation and regulations on the safety and effectiveness of medical implants fit for purpose?

Safety and Effectiveness

In order to assess whether the current EU legislation/regulation of medical implants is fit for purpose, we need to assess other regulatory regimes and whether they are better or worse than the current state of affairs in the EU.

The US Food and Drug Administration (FDA) makes much greater demands for non-clinical and clinical testing of medical implants than do notified bodies in the EU. These demands usually manifest as insistence on controlled data and on long-term follow up data. This begs the question of whether this increased stringency by the FDA prevents unsafe or ineffective devices reaching the US market. Or put another way; do the lesser demands for non-clinical and clinical data made by notified bodies result in unsafe or less effective devices being placed on the market in the EU?

Advamed (the US medical device trade association and lobbying group) released a report in November 2010, which summarized a survey of over 200 medical device firms. The report claims that on average, the FDA process delays approval of medical implants (or at least of medical devices needing a premarket approval (PMA) in the US) 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. We believe that these latter data were based on comparing medical device withdrawals from the market in the US and EU.

Examples of medical devices that have been approved in the EU on little or no clinical data but which are being or were subjected to extensive clinical trialling in the US include:

- Dural sealant: approved with no clinical trial data in the EU; controlled trial versus current standard of care with 12 month follow up in the US.
- Intra-abdominal pump: approved with uncontrolled clinical study data in 30 subjects followed for six months in the EU; controlled trial with larger numbers of patients and follow up for 12 months in the US.

- Intra-articular injection: approved in the EU with marginally positive clinical trial data; large, controlled trial ongoing in the US with six months' follow up and stringent statistical demands on the analysis.

None of these three products has so far resulted in any safety concerns or field safety corrective actions in the EU. All three devices are apparently effective in that market uptake has approximated what was predicted by the manufacturer.

Recent examples of major safety issues on marketed products in the EU include hip implants (metal on metal and leachable substances from plastics in the devices), breast implants, and drug-eluting cardiac stents. These long-term safety problems with devices were apparently not found sooner by the more rigorous FDA process.

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. For instance, the recent recall of metal-on-metal hip prostheses demonstrated a mismatch between the competent authorities' assessment of post-market vigilance reports and the notified bodies' assessment of risk at the product approval stage. It would seem that the vigilance expertise within competent authorities is not directly brought to bear on the product approval process, which may expose patients implanted with medical devices to additional risk.

The current Medical Device Directive (MDD) is clear about how to reach a decision about whether a specific clinical trial is needed for a particular medical device. A clinical evaluation report is written, which assesses all known published and unpublished safety and effectiveness data for the device in question and devices similar enough for meaningful extrapolations to be made. The conclusions of the clinical evaluation report include an assessment of whether all the essential requirements appropriate for the class and type of device can be met using current information, or whether additional clinical testing is needed. From members' experience, it is clear that some notified bodies are not expert enough in the assessment of clinical data, of likely safety risks in clinical use, and of issues such as "dose" ranging, to make an effective critical assessment of whether a de-novo clinical trial is needed and whether long-term safety data should be gathered in a formal way.

The current MDD relies on the ability for manufacturers to claim similarity to other devices on the market in order to demonstrate safety and effectiveness/performance. In other words, Device Y is going to be used for the same indication, is made of the same materials, is the same shape, and has the same action as Device X: since Device X is on the market with no published safety issues, Device Y should be approved for use in the same indication. The flaw in this logic is that:

- there may be unpublished safety issues with Device X;
- there may be subtle differences in the use of Devices X and Y which result in safety and effectiveness differences that are not explored clinically prior to marketing the device;
- no two devices are exactly the same and so extrapolating data from one device to another may be flawed (for example, subtle changes in the shape of a hip prosthesis may result in dramatically different wear patterns, with subsequent safety issues for patients implanted with those devices);

- 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 and currently there does not seem to be a good assessment of the clinical implications of such iterative changes in device design.

When there are product recalls, the responsibilities of the manufacturer, the competent authority, the health care professional using the device, and the notified body need to be very clearly defined to ensure that patients who have been implanted with concerning devices have recourse to continuing care.

The Faculty believes that formal periodic safety reporting should be a requirement for higher risk medical devices. Currently we believe that periodic assessment is undertaken by notified bodies during their ongoing audit programmes, but that periodic safety reporting and assessment does not have to be submitted to the competent authorities, which receive the expedited safety reports for marketed products.

Members also felt that whichever body was approving higher risk medical devices for marketing should have the power to demand post-market surveillance programmes and be able to undertake minimum notice audits of manufacturers to ensure their compliance. An increased use of registries to gather long-term safety data on implanted devices was considered to be a useful addition to safety monitoring.

Inconsistency and Unfairness

A likely issue with the current EU system for medical implant approval is inconsistency. There are many notified bodies and it is possible that different NBs could make different demands on companies for clinical trial data for similar devices. This would certainly be unfair as companies try to get their devices approved in the EU.

In theory, any inconsistency could have an impact on the assessment of safety and effectiveness of medical implants.

The Future

As medical devices become more sophisticated, it is unknown whether the assessors within the notified bodies are going to be able to assess safety and effectiveness effectively. The devices themselves are more complex from an engineering and programming stance; they are often combined with medicinal products and biologics, whose contribution to safety and effectiveness may be difficult to assess; devices are being used now to treat more and more chronic conditions, for which gathering meaningful clinical data is increasingly challenging.

We conclude that there is some evidence that the current system allows unsafe or ineffective devices onto the EU market, and there is little confidence that notified bodies have the internal expertise and ability to assess complex devices for chronic conditions, often with medicinal products as part of the mix, in the future.

2) How effectively does the MHRA implement the Medical Device Directive?

This is an odd question in the context of approval of medical devices in the EU: the competent authorities are removed from the assessment and approval of individual devices and have input only to clinical trials (via clinical trial approvals) and post-market safety (via vigilance reports for marketed devices).

In terms of clinical trial approvals, the MHRA implements the Medical Device Directive appropriately. However, their input to clinical trial design and execution is limited, since the MHRA is not the audience for the final clinical data during the product approval process.

Competent authorities do control, audit and license the notified bodies in their country, so the MHRA may be very active at making sure the UK-based notified bodies are up to scratch. However the MHRA is powerless to take direct action against a notified body from another country if it approves devices that should not be approved, and the local competent authority takes no action.

The MHRA was noted to have been very active in closely monitoring various sources of safety signals in the case of metal on metal hip prostheses, including various national joint registries. The MHRA implemented medical device safety alerts as a result of this.

3) How could the legislation and regulations be improved?

The scope of this inquiry should have been Class III devices, not just medical implants.

Any issues with inconsistency and the inability (perceived or real) of notified bodies to adequately assess complex medical devices, devices used to treat chronic conditions, or combination products (not already regulated as drugs), would be addressed by having Class III devices assessed by a central agency, staffed with experts in medical device regulation including those with expertise in assessing clinical data. This central agency could also be responsible for licensing notified bodies throughout the EU, which would ensure consistency of standards across borders.

It may not be necessary to change the conformity assessment pathway for Class III devices; it would just be that one organisation instead of potentially a hundred organisations would be responsible for the assessment.

The current system does not really allow a transparent translation of medical policy from public opinion to legal implementation. In other words, notified bodies are a large step away from government control as they are private commercial companies that undergo periodic licensing by the competent authorities. In the recent public furore about hip prostheses, the notified body that actually approved the device for marketing was not mentioned in all the media coverage. Too much public pressure may be a bad thing, but no public accountability is equally dangerous.

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.

A central body, perhaps part of the European Medicines Agency (EMA), overseeing higher risk device approvals would facilitate designation of combination products. These products are well-defined and their regulatory path clearly laid out by the FDA, but in Europe there is much confusion as to how to define a combination product and which regulatory path (device or drug or both) is appropriate. As medical devices become more complex and incorporate biological, pharmaceutical, and cellular products, a central body that could be consulted to determine the appropriate regulatory and developmental pathway will be helpful in commercialising innovation at the same time as protecting patients.

4) How could the European Commission ensure that potential changes to the MDD do not hinder the introduction of innovations in medical implants to the market?

If a product is truly innovative, and has incremental benefit to patients, it is unlikely that increased regulation will hinder its introduction to the EU market.

The primary driver for regulatory oversight must be patient safety. There is evidence that the current system sometimes fails patients in this regard. Therefore a clearly defined and robust regulatory framework with a focus on short and long term patient safety, should serve patients and industry well.

However increasing the bureaucracy surrounding product development is seen as a negative influence on introducing innovative products to the EU market. Often increasing layers of bureaucracy slow research and increase costs, without adding any appreciable benefit in terms of increased patient safety. So great care must be taken to increase the quality of regulatory oversight, without increasing bureaucratic hurdles to the point of blocking ground-breaking research from proceeding at a reasonable pace.

The main issue with devices that are subjected to large clinical trials is that they are rather similar to their competition or controls, and therefore not that innovative!

April 2102

Joint written evidence submitted by Dr Thomas Joyce and Dr Pauline McCormack (MI10)

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] “were 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”.*¹

“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)

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.

¹ Professor Sir Kent Woods, Chief Executive, MHRA <http://www.bbc.co.uk/news/health-17200330>

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.²

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)

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.

² <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm>

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)

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Written evidence submitted by Medtronic (MI11)

About Medtronic

Medtronic is the global leader in medical technology, alleviating pain, restoring health and extending life for millions of people around the world. With deep roots in the treatment of heart disease, Medtronic now provides a wide range of products and therapies - every four seconds, somewhere in the world, another life is improved by a Medtronic product or therapy.

The company was founded in 1949 in Minneapolis, Minnesota, USA, by Earl E. Bakken and Palmer J. Hermundslie. In the UK, Medtronic has been based in Watford for over 35 years. Further, Medtronic has long-established research and development, manufacturing, logistics, and sales and clinical support facilities throughout Europe.

Notes on this Submission

This document focuses on the four questions asked by the Select Committee.

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

1. Medical implants are regulated in the European Union (EU) through the Medical Devices Directives. This set of legislation is designed to provide a high degree of protection of public health by ensuring that only acceptably safe devices are placed on the market as well as enabling the free movement of goods.
2. Medical technology benefits patients through improving the longevity and the quality of life. The industry also contributes significantly to the UK's economy generating employment and exports. In 2011 there were over 3,000 medical technology companies in the UK with a combined annual turnover of £15bn. These companies employ 64,000 people in the UK.¹
3. The success of the medical technology industry in meeting clinical needs is dependent on the ability to innovate and this in turn relies on the existence of an appropriate regulatory framework. This must ensure that patients have access only to safe and high quality products but also allowing for the timely introduction of innovation.
4. European Union Council Conclusions in June 2011 reaffirmed European Member States commitment to the current legal framework of the Medical Devices Directives citing not radical changes but rather focused attention to essential amendments to the current system that guarantee future innovation and safety in medical devices.²
5. Medtronic also believes the current legal framework has served the European Union well. However, we recognise that the legislation needs to be regularly reviewed and updated on the basis of experience and advances in the technical, regulatory, and clinical states of art. The Medical Devices Directive will be revised later this year with draft proposals expected to be published by July 2012. We support the review undertaken by the European Commission and member states. Medtronic through the UK medical technology trade association – the Association of British Healthcare Industries (ABHI) – and the European medical technology trade association – Eucomed – have contributed to consultations issued by the European Commission. We look forward to commenting on the draft proposals when they are published.

¹ <http://www.abhi.org.uk/key-issues/uk-market/valueofmedtech.aspx?searchText=economy>

² Council conclusions on innovation in the medical device sector - 3095th EMPLOYMENT, SOCIAL POLICY, HEALTH and CONSUMER AFFAIRS - Council meeting, health issues, Luxembourg, 6 June 2011

Question 2 - How effectively does the MHRA implement the Directive in the UK?

6. As 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.
7. The MHRA has long played a recognised leadership role at European level in the development, implementation, and application of the medical device directives, e.g., in the Medical Devices Expert Group and the Notified Bodies Operations Group.
8. MHRA is also recognised by national regulatory authorities in third-countries as an example of a medical device regulator with sound practices and well-established expertise.

Question 3 - How could the legislation and regulations be improved?

9. It is crucial that regulation governing the use of medical technology is transparent and consistent across the European Union. Although the European Commission issues guidelines designed to ensure the consistent implementation of the Medical Devices Directive across EU member states, it is very clear that there remains wide disparities in implementation. 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.
10. The revision of the Directive must also deliver greater overall transparency and access to information for patients, consumers, healthcare professionals and industry. Information on the functioning and decision making processes of ‘notified bodies’ and ‘competent authorities’ such as the (MHRA) is too often withheld on confidentiality grounds. This jeopardises the level of public confidence that should exist in the system.
11. The operation and coordination of the individual Member State notified bodies should also be addressed through the revision of the Directive. The oversight of these notified bodies by Member States differs enormously again causing consistency problems for industry. Mandatory EU wide levels of oversight would help with issues of transparency, trust and legal certainty.
12. Efforts to improve post market surveillance should always be a key driver when reviewing legislation and regulations. The sharing of data and information between ‘competent authorities’ is crucial, as is consistency when they react to doubt about product performance. We believe a better defined legal framework on vigilance and greater harmonisation of Member States’ market surveillance activities would deliver significant benefits for overall patient safety allowing centralised reporting and surveillance.
13. As harmonised European norms are one of the elements of the EU medical device regulatory scheme, the UK should renew its involvement in European standardisation work.

Question 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?

14. Present EU medical device regulation has generally allowed for the timely and appropriate introduction of innovative technology and implants to the market – improving the lives of millions of patients in the UK and Europe. Revisions to the Medical Devices Directive should continue to support the development of new products through innovation and patient access.

15. The fundamental differences between the pharmaceutical industry and the medical technology industry should be clearly understood when revising the regulation. Medical technology is generally based on engineering rather than chemistry and a regulatory system suitable to the pharmaceutical industry – involving randomised controlled trials – would not be appropriate for all kinds of medical technology. It could have a detrimental impact on the development of innovation. The regulatory system should also recognise, and encourage, the rapid iterative innovation process of most medical technologies.

April 2012

Written evidence submitted by Nuffield Health (MI12)

Executive summary

Context and background

Nuffield Health has run independent ‘not-for-profit’ hospitals for over 50 years, and has the UK’s third largest portfolio of independent hospitals providing services including elective surgery, rehabilitation and diagnostic tests.

Nuffield Health is an interested party in the House of Commons Science and Technology Committee’s inquiry into the regulation of medical devices as a high quality provider of acute independent healthcare. Nuffield Health is unique in being the only independent provider to be accredited at Level 3 for compliance with NHS Litigation Authority (NHSLA) risk management standards and having been assessed corporately as fully compliant by the Care Quality Commission (CQC) for the management of medical device, quality and patient concern outcomes.

In the interim report of the expert group convened under the chairmanship of Professor Sir Bruce Keogh (NHS Medical Director) to review policy in relation to breast implants from the French company Poly Implant Prostheses (PIP), it was acknowledged that Nuffield Health was the first provider to announce that it would review and treat patients in their clinical interest at no cost. This was done immediately to reassure patients and on a no fault basis, not precluding any future legal action we may intend to take. We consider that the improvements for the management of patients, products, professionals and providers set out in the Nuffield Health 12 point plan (Annex 1) are relevant to this inquiry.

Nuffield Health submission in response to questions:

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

Nuffield Health considers that the fitness for purpose of the current legislation and regulations on the safety and efficacy of medical implants has been called into question in light of the apparent failures of implementation and process control. Given that the European Commission has already stated that it will use the opportunity of the review on medical devices Directive to strengthen existing legislation, particularly provisions relating to market surveillance, vigilance and the functioning of notified bodies, then the existing processes must be considered to be less effective than they could be.

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

Nuffield Health is concerned that the MHRA, as the UK Regulator of medical devices, has permitted the Regulations to be supported by ‘principles’ which are inconsistently applied and thereby impact on the assurance framework for providers, who are in turn required to protect and promote patient safety. Furthermore, the concerns raised by a representative of the National Patient Safety Agency (NPSA), regarding the CE marking process, have not been followed up by clear actions by the Committee on the Safety of Devices (CSD).

3. How could the legislation and regulations be improved?

Nuffield Health considers that the legislation and regulations could be improved by requiring manufacturers to take account of biological issues and lessons learnt from recent issues ensuring the requirements on post-marketing surveillance are improved and made more consistent. Nuffield Health considers that the clinical trial methodology must be able to allow end user professionals to interrogate

that data to ensure that the claims being made about the device are valid. Furthermore, for implantable medical devices there is an opportunity to align more with the regulation and surveillance processes used for medicines, including using a similar process to update healthcare professionals as MHRA ‘Drug Safety Update’.

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?

Nuffield Health agrees with the position stated in a recent article³ for The American Society for Clinical Pharmacology and Therapeutics: “*Although future policies must minimize disincentives to innovation they also need to recognize the societal harms associated with costly therapies for which supporting evidence of comparative effectiveness is lacking.*” In addition, Nuffield Health agrees with the recent editorial in the British Medical Journal⁴ that “*Large well conducted clinical trials performed before mass marketing of new implants combined with postmarket surveillance are imperative to promote innovation in the best interests of patients, surgeons, and implant manufacturers.*”

Nuffield Health is concerned that the fundamental lessons learnt from medicine regulation following Thalidomide in the 1960’s have not been transferred to implantable medical device regulation in the UK. Medicines are granted a Marketing Authorisation (MA) by MHRA, however they are only placed on the market subject to a period of intensive post-marketing surveillance. This Black Triangle status is clearly communicated to all professionals and requires an intense level of reporting using the Yellow Card System of all side-effects, however minor. Nuffield Health also considers that the key is that patients are informed of the risks by ensuring that Patient Information is provided in a consistent manner including the numerical likelihood and severity of the risk.

Context - Nuffield Health as an interested party:

Nuffield Health is an interested party in the Commons Science and Technology Committee’s inquiry into the regulation of medical devices as a high quality provider of acute independent healthcare.

Nuffield Health hospital activities are registered with the relevant healthcare regulator including in England, the Care Quality Commission (CQC). The CQC essential standards have been written to protect services users across all the regulated activities, including acute services providing surgical operations. The CQC essential standards are written in terms of patient focused outcomes including; outcome 11 on medical device management, outcome 16 for monitoring the quality of service provision and outcome 17 for ensuring patient concerns and complaints are managed effectively.

In March 2012 (in response to Professor Sir Bruce Keogh’s request for a review of the cosmetic providers) Nuffield Health was subject to a review and assessment of the systems in place at a corporate level to monitor and manage the use of equipment including medical devices, the systems for monitoring and assessing the quality of care and how complaints are managed. CQC found Nuffield Health to be fully compliant in respect to Outcomes 11, 16 and 17.

Quality standards and procedures are very important to Nuffield Health. Integrated Governance is the mechanism used to challenge and measure quality – responding quickly to safety concerns, measuring customer feedback and understanding and evaluating where things have gone wrong and embedding lessons learnt. Nuffield Health was awarded NHS Litigation Authority Level 3 in 2011, including full compliance in medical device management and training. Nuffield Health is the only independent sector provider with this level of accreditation from the NHS for our governance policies, practice and monitoring, and indeed only a small number (approximately 20) of NHS Trusts are accredited at NHSLA Level 3.

In the interim report of the expert group convened under the chairmanship of Professor Sir Bruce Keogh to review policy in relation to breast implants from the French company Poly Implant Prostheses (PIP), it was acknowledged that Nuffield Health was the first provider to announce that it would review and treat patients in their clinical interest at no cost. This was done immediately to reassure patients and on a no fault basis, not precluding any future legal action we may intend to take.

Nuffield Health considers that much of the 12 point safety plan (Annex 1) that we put forward for cosmetics could also be adopted for a range of treatments, including all implantable medical devices across healthcare to provide patients with the assurances they seek regarding their safety and continuing care. In simple terms the priority can be summarised into effective monitoring of the four P's:

- Patient: Improve the monitoring of patients (points 1-4/6 on NH plan) including the introduction and maintenance of registers for implantable medical devices.
- Product: Improve the monitoring of the product (points 7-8 on NH plan) including controls for putting CE marked products onto the market and medical device surveillance.

- Professional: Ensure services are led by registered professionals, who are monitored (point 9 & 11 on NH plan) including the relevant speciality register of the General Medical Council.

- Provider: Ensure all providers are regulated, insured and effectively monitored (points 5, 10, 12 on NH plan) by the Care Quality Commission (CQC) (or similar for home countries).

Context - Nuffield Health background:

Nuffield Health has run independent ‘not-for-profit’ hospitals for over 50 years, and has the UK’s third largest portfolio of independent hospitals providing services including elective surgery, rehabilitation and diagnostic tests. Two thirds of the British population are within an hour’s drive of a Nuffield Health Hospital.

Nuffield Health:

- Operates 31 Hospitals (with 1,345 beds, 111 theatres and 1,500 procedure types)
- Operates 65 Fitness & Wellbeing Centres
- Have 41 Medical Centres
- Have over 200 on-site workplace fitness and wellbeing contracts
- Are the UK’s leading employee wellbeing provider
- Have the largest network of physiotherapists outside of the NHS
- Operates the UK’s largest health assessment programme
- Are the UK’s leading report imaging provider
- Sterilise over 12 million instruments a year
- Have over 20 million member visits a year to our Fitness & Wellbeing Centres.

New services continue to be developed in conjunction with consultant partners to meet patient demand. For example, weight management services including Bariatric Surgery have been introduced in ten Nuffield Health hospitals.

Our not-for-profit status has enabled high levels of continual investment in equipment and infrastructure, from the building of advanced hospitals in Leeds, Oxford and York to new theatres in Chichester and major refurbishments in Guildford, Leicester, Tunbridge Wells and Brighton. This investment will continue to ensure that Nuffield Hospitals remain first choice for patients and consultants.

Context – changing healthcare market

It is important to note that elective surgery is at the forefront of the changing healthcare market and regulations and standard setting must be flexible enough to reflect wider healthcare trends such as:

- Personalisation – the service is more commoditised with patients researching the range of products and services available to them. Any changes in regulation of the industry need to focus on the patient to ensure adaptability with the pace of change.
- Model of health system delivery – the patient may have the choice to move from NHS to the independent sector and within the independent sector. Standards that are predicated on a long term relationship with a single provider or professional are likely to result in patients being lost to the system.
- Globalisation – products are moved around the world and purchases increasingly involve internet purchasing. In addition, the concept of travelling to purchase products and services has become common place. The issues of counterfeit healthcare products are increasing and regulations, standards and the relevant agencies from individual countries must be able to work more closely together and share intelligence to protect patients and the public.

Nuffield Health submission in response to questions:

Firstly, and before responding to the specific questions below, Nuffield Health would like to draw attention to the recurring issue of poor engagement with providers of healthcare. As an example the MHRA Medical Device Technology Forum (MDTF)¹ held on 4/11/11 aimed to explore the difficulties in promoting innovation in the orthopaedic field whilst maintaining patient safety.

Participation in the workshop is recorded including regulatory bodies (MHRA, FDA), British Orthopaedic Association, British Hip Society, National Joint Registry, Orthopaedic Patient Data Evaluation Panel, Industry and Notified Bodies. The MDTF stated this was “*to ensure a comprehensive overview of the system with the aim of producing guidance to help all parties in bringing a new hip implant safely to market*”.

- Nuffield Health is disappointed to note that providers of healthcare, and moreover the Regulators of healthcare such as the Care Quality Commission, are not seen as relevant stakeholders in producing guidance to help all parties bring new hip implant safely to market. When there are safety concerns, it is the healthcare providers (not Consultants or their associations) that are required to manage the alerts, recalls of products, recalls of patients, and are responsible for ensuring a safe system of work for patient safety.

There needs to be recognition by MHRA, and others, that part of the system is how (and where) the patient is treated within the regulated healthcare provision. Hospitals are regulated under the Health and Social Care Act 2008 (Regulated Activities) 2010 (in England) which includes compliance with specific regulation (Regulation 16) regarding the safe management of medical devices and equipment.

- Nuffield Health considers that there should be a ‘whole system’ view as healthcare provision is an integral part of the quality and safety system for patients and not an ‘end process’ that may be taken for granted. Furthermore, the increasing costs of managing the consequences from safety concerns adversely impact the providers of healthcare at a time when new resources are limited.

Nuffield Health considers that the outputs from the MHRA MDTF meeting to be a useful element on which to record our feedback to the inquiry. The conclusions and recommendations of that meeting, and other meetings, are discussed and referenced below.

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

The Medicines and Healthcare products Regulatory Agency (MHRA) is the Government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe. The MHRA is an executive agency of the Department of Health.

Following the Dispatches programme on 16/05/11, Nuffield Health wrote to MHRA for assurances on CE accreditation and received an email stating: “*The MHRA is satisfied that the Medical Devices Regulations are fit for purpose. However as with any regulatory system there is room for improvement. The MHRA and other Member States are working with the European Commission on the current revision of the medical devices Directives to improve the system even further. What is acknowledged though is that the current system works well in terms of protecting patients and there is no evidence to support the view that it requires a radical overhaul.*”

¹ MHRA Medical Device Technology Forum, Conclusions and Recommendations of the orthopaedic workshop: joint replacement implants: Are we ensuring patient protection whilst facilitating the introduction of potentially beneficial technologies? “Beyond Compliance”. London: MHRA 4 November 2011

- Nuffield Health does not concur with the above statement. We understand that the broad definition of medical devices means that application of a single process for medical device regulation is inappropriate. However, the current differential controls that are in place e.g. for Class III medical devices such as implants, must require a greater level of accountability throughout the supply chain from manufacture to use. This must include improvement in the accountability for the management of post-marketing surveillance and any associated requirements for Field Safety Notices.

By November 2011 the conclusions and recommendations of the MHRA MDTF meeting acknowledged that “*The confidence of the public and professionals in how novel medical devices are brought to market, has been compromised*” and went on to state “*Nowhere is this more apparent than with orthopaedic implants*”.

- Nuffield Health agrees with these statements and would add that the providers of healthcare services have also lost confidence in the processes for how medical devices are brought to market. Nuffield Health considers that the fitness for purpose of the current legislation and regulations on the safety and efficacy of medical implants has been called into question in light of the apparent failures of implementation and process control. Given that the European Commission has already stated that it will use the opportunity of the review on medical devices Directive to strengthen existing legislation, particularly provisions relating to market surveillance, vigilance and the functioning of notified bodies, then the existing process must be considered to be less effective than they could be.

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

It is noted that the European Directive on medical devices will be revised later this year with draft proposals expected to be published by July 2012.

- Nuffield Health only operates hospitals in the UK and therefore has no experience of direct working with other competent authorities under the European Directive.

There is confirmation by the MHRA MDTF that there is an issue of consistency of implementation with the required safety principles, as the report states “*Although the Regulations set out overarching principles for clinician investigations, post-market clinical follow-up studies and post-market surveillance including vigilance, these principles are not always universally implemented*”.

- Nuffield Health is concerned that the MHRA, as the UK Regulator of medical devices, has permitted the Regulations to be supported by ‘principles’ which are inconsistently applied and thereby impact on the assurance framework for providers, who are in turn required to protect and promote patient safety.

The conclusions of the MHRA MDTF state that that the safety of certain devices that the Regulator has allowed onto the market is unclear: “*Many of these devices have been CE marked on grounds of equivalence with similar devices due to the iterative nature of designs in this range of device. This has meant that clinical investigations have often not been performed on new (joint replacement) implants or on significant modifications and hence the safety and risks of the device may be unclear at the time of the device coming to market.*”

- Nuffield Health has significant concerns that the MHRA is permitting medical devices to be put onto the market without a clear understanding of the safety and risks of the device.

It was noted by the House of Commons Health Committee into PIP Breast implants² from March 2012 that Professor Sir Kent Woods (Chief Executive, MHRA) expressions of ‘sincere hope’ was not an adequate basis for regulation. The committee stated (paragraph 22) that “*there needs to be a more reliable method of communicating Medical Device Alerts to the private sector, that requires a positive response that the communication has been received and acted upon in the same way as in the NHS*”.

- Nuffield Health has supported this approach for many years and has managed, through its own efforts, to ensure one way communication from the Central Alerting System (CAS). All Medical Device Alerts (MDA - and other alerts) and received into Nuffield Health from CAS for central review and organisational-wide dissemination via our Datix risk management system. However, to date, Nuffield Health has been unable to achieve access to provide a return through CAS on compliance to alert implementation as this is deemed as ‘NHS only process.’ This results in MHRA/National Patient Safety Agency (NPSA) ‘blind-spot’ in relation to management of alerts (and adverse event reporting to NPSA).

The minutes of the Committee on the Safety of Devices (CSD) meeting of 07/07/11, show that Professor Brian Toft (Professor of Patient Safety/NPSA Reference Group Chair) had contacted the MHRA expressing concern about the CE marking process. The minutes note that Professor Toft referred studies stating that “*...in this instance the CE mark as applied to this category of instrument has not guaranteed the safety of the expected performance requirements of the instruments in question*”. A further quote from 2004 “*...these facts suggest that the present mechanism, a CE marking for control and quality of suitability of this particular product in the UK may not be sufficiently robust...*” A further study in 2005 “*...it is apparent from this study that at present there is no guarantee that a single use instrument will be of an acceptable standard when used even if they carry a CE mark*”.

- Nuffield Health is concerned that the CE marking process was being vigorously defended by MHRA on the one hand (in response to Nuffield Health in May 2011) whilst it is evident from the minutes of the CSD meeting (secretariat support by MHRA) that questions had been raised over a number of years regarding the robustness of the CE mark.

The minutes of Committee on the Safety of Devices (CSD) meeting of 03/11/11 state that, in response to the concerns raised by Professor Toft the “*CSD had canvassed Competent Authorities, and of the 27 countries which were approached 12 responses were received there were no major concerns raised by these countries regarding the quality of new instruments.*” The minutes then Medical Implants – go onto to state that “*The Chair indicated that it was up to the purchasing system within Trusts to use manufacturers who provide quality products, and the user has to be alert to when something goes wrong*” and further that “*The Chair added that the problem with the surgical instrument manufacturers or the distributors is, if you find a problem with an instrument they are delighted to change it and give you a new one, and ultimately in the hospital you will then acquire a set of 100% perfect instruments, but unfortunately the quality control step is the hospital.*”

- Nuffield Health is not assured by the comments made by the CSD with reference to the robustness of the CE marking process for medical devices, particularly in respect to the activities in the 15 countries that did not respond (we note this is in respect to instruments rather than implants). It is unclear from the minutes if Professor Toft has been assured by the response given

² HC 1816 The House of Commons Health Committee, PIP Breast implants and regulation of cosmetic interventions. London: The Stationery Office Limited, 28 March 2012

by CSD. Furthermore the statements relating to the fact that the ‘quality control’ process was to be undertaken by the purchaser (Trust/other Provider) could be likened to a ‘buyer beware’ position, which is inconsistent with a process which is deemed to be highly controlled by regulation. Indeed the MHRA state that on their website that: “*The Regulations implement the EC Medical Devices Directives into UK law. They place obligations on manufacturers to ensure that their devices are safe and fit for their intended purpose before they are CE marked and placed on the market in any EC member state.*”

3. How could the legislation and regulations be improved?

The MHRA MDTF conclusions and recommendations state that during the pre-marketing stage manufacturers “*..should include methods that take into account biomechanical functions and ideally biological issues relating to the materials used..*” and “*..have in place a system of post-market surveillance which should feed into the ongoing risk assessment; and a system for collecting data on adverse events, assessing these and reporting such serious events to the relevant Competent Authority*”.

- Nuffield Health considers that the legislation and regulations could be improved by requiring manufacturers to take account of biological issues and from lessons learnt from recent issues ensuring the requirements on post-marketing surveillance are improved and made more consistent. Furthermore Nuffield Health considers that the clinical trial methodology must be able to allow end user professionals to interrogate that data to ensure that the claims being made about the device are valid.

The function of Notified Bodies is pivotal to safe devices coming to market and remaining on the market. The Commons Health Committee² (paragraph 56) heard that the “*concerns about the performance of PIP implants began to emerge in 2006. Following an increase in reports of ruptures, the MHRA raised concerns with PIP and the notified body, and was told that the trend was due to an increase in sales of the implants and improvements in PIP’s reporting criteria. The MHRA raised further concerns in 2009.*” The Commons Health Committee went on to state that “*Procedures for the follow-up of the CE mark certification have been shown to be inadequate by what has happened in this case. Sir Bruce’s review should examine how to strengthen the CE mark system — for example by ensuring that certified devices are subject to routine review. There must be a procedure whereby the concerns of national regulators regarding implants manufactured in another European country can be acted upon and investigated.*”

- Nuffield Health considers the role of the Notified Bodies needs to be reviewed to ensure there are measures to ensure consistency of approach and that unscrupulous manufacturers are not able to exploit the limitations of the current processes. There needs to be a process whereby the output metrics of various Notified Bodies can be compared and contrasted by Competent Authorities to ensure there is confidence that clinical trial data, equivalence data, modification requests and post-marketing surveillance is robust.

As with other areas, the MHRA process for communicating adverse events or emerging issues for medicines and medical devices is divergent and there is an opportunity to improve the position. The MHRA website provides information on safety alerts and recalls for medicines which is up-to-date and intuitive to navigate. However the MHRA information under medical device alerts has several sections of old information on Advice Notices (AN - 1999 and before), Device Alerts (DA – 2002 and before), Hazard Notices (HN – 2002 and before), Safety Notices (SN – 2002 and before) and up-to-date information is less easy to navigate and often requires multiple clicks to other sites, for example the statement on biological effect of wear debris generated from metal on metal bearing surfaces. Having no

process for regular, simple updates has resulted in the MHRA becoming increasingly reactive to published papers and media interest for example PIP and Polyurethane-coated breast implants.

- Nuffield Health consider that there should be more consistent and accessible communication of changing risk profiles of medical devices for example as similar to MHRA ‘Drug Safety Update’. This is accessible and can be easily cascaded from email alerts. This provides new information and updates on previous issues (for example withdrawal of Co-proxamol) as well as information on learning about reducing medicines risks and quick links to reporting safety problems. The MHRA state that “*Drug Safety Update is essential reading for all healthcare professionals, bringing you the very latest information and advice to support the safer use of medicines.*” However there is no similar communication mechanism for medical devices and in particular those that are implanted. Nuffield Health considers that the trivialisation of safety concerns with medical devices (mainly equipment) in the MHRA ‘One- Liners’ series should also be reviewed.
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?*

The MHRA MDTF reports states “*if regulators were to insist on prolonged clinical trials prior to the free market of these devices, innovation would be stifled and the public denied access to improved developing technologies*”.

- Nuffield Health hospitals have been at the forefront of supporting innovation in orthopaedic implant surgery. However, Nuffield Health not only agrees with MDTF that “*a balance needs to be struck, allowing new devices to be produced, whilst reducing the risk to the patient population*”, we consider that the key is that patients are informed of the risks by ensuring that Patient Information is provided in a consistent manner including the numerical likelihood and severity of the risk.

The main aim of the Devices sector of the MHRA is to protect public health and safeguard the interest of patients and users by ensuring that medical devices and equipment meet appropriate standards of safety, quality and performance and that they comply with relevant Directives of the European Union.

- Nuffield Health considers that the roles and responsibilities of the groups that support the MHRA in ensuring that medical devices and equipment meet appropriate standards require clarification. The MHRA website states that the Committee on the Safety of Devices (CSD) can make recommendations however, since the committee does not make decisions, it is not subject to independent review or audit. Nuffield Health considers that the title of the CSD should reflect the advisory capacity of the committee. Furthermore, given the CSD is not responsible, Nuffield Health considers that its position in establishing Expert Advisory Group (AEG) is reviewed. The roles and responsibilities of the EAG on the ‘Biological effects of metal wear debris generated from hip implants: genotoxicity’ should be reviewed and the transparency of the programme of meetings and reports improved (meetings in 2006/7 then one in 2010 and none recently despite increased issues identified in this area). In addition, the responsibility of the individual members of the EAG requires definition, for example the role of the manufacturer Smith and Nephew within this forum. The responsibilities between the various bodies in the area of patient safety in respect to medical device implants is less than transparent e.g. MHRA, CQC, NPSA, NICE, CSD, EAG (and the relationship to the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment). The responsibilities must be clarified to avoid duplication or gaps in management of a safe system of work.

The requirements of the European Directive are limited and non-specific with regards to post marketing phase.

- Nuffield Health is concerned that the fundamental lessons learnt from medicine regulation following Thalidomide in the 1960's have not been transferred to implantable medical device regulation in the UK. Medicines are granted a Marketing Authorisation (MA) by MHRA, however, they are only placed on the market subject to a period of intensive post-marketing surveillance. This Black Triangle status is clearly communicated to all professionals and requires an intense level of reporting using the Yellow Card System of all side-effects, however minor. The Black Triangle intensive surveillance process has identified a number of products that have been withdrawn from the market or the indications/dose/side-effect profile changed for example Cisapride, Cox-2 inhibitors and thiazolidinediones. Nuffield Health do not consider that the Black Triangle process confers on the medicine a 'conditional' MA (as has been suggested by members of MHRA), rather it provides a process for increasing the data collection process for a wider patient group than can be achieved in any clinical trial phase. Nuffield Health considers a similar scheme should be implemented for implantable medical devices along with the compulsory requirement to submit data to implant registers to support the improvement in adverse event reporting, monitoring outcomes and thereby allowing rapid response to concerns.

The requirements for 'prescribing' implantable medical devices should be more aligned with the process for prescribing medicines including the evidence base for the 'off-label' use of medical devices. The July 2011 meeting of the CSD reported that the 'mixing and matching' of hip replacement components, including metal on metal, was common place however it was against the manufacturers advice. The CSD deferred a decision to issue a Medical Device Alert regarding this practice. The November 2011 CSD meeting concluded that the best thing was for them to write to the British Orthopaedic Association (BOA) and await a response. At the time of writing it is not clear if the BOA have responded

- Nuffield Health is concerned about the patient safety implications of this closed debate regarding the use of implantable medical devices, and particularly with reference to off-label use. Nuffield Health considers that the changes to the Medical Devices Directive should not hinder the introductions of innovations in the healthcare market, however, we consider that the changes need to reflect the operational reality of how devices are used. Nuffield Health agrees with the position stated in a recent article³ for The American Society for Clinical Pharmacology and Therapeutics: "*Although future policies must minimize disincentives to innovation they also need to recognize the societal harms associated with costly therapies for which supporting evidence of comparative effectiveness is lacking.*" In addition, Nuffield Health agrees with the recent editorial in the British Medical Journal⁴ that "*Large well conducted clinical trials performed before mass marketing of new implants combined with postmarket surveillance are imperative to promote innovation in the best interests of patients, surgeons, and implant manufacturers.*"

April 2012

³ RS Stafford, American Society for Clinical Pharmacology and Therapeutics, Volume 9, Number 5, Off-label use of Drugs and Medical Devices: A Review of Policy Implications. Nature Publishing Group, May 2012

⁴ Leela C Biant, British Medical Journal, Hip resurfacing or stemmed arthroplasty for young active patients? Both can deliver good function in the short term but longer term outcome data are needed. BMJ 2012;344e2663 19 April 2012

Annex 1

Nuffield Health 12 Point Cosmetic Safety Plan:

1. The guidance for all medical devices to be re-examined to ensure patients can be tracked quickly and effectively if concerns are raised around any implants they received.
2. Standardised data collection methods to be used to improve outcome data.
3. The Government to reintroduce a National Implant Registry for all breast and other cosmetic implant medical devices (as with the hip, knee and ankle registries).
4. A review to take place of all other voluntary registries (such as the bariatric surgery registry) and consider extending to other implants (such as pacemakers and cataract lenses).
5. The introduction of standards for patient information and informed consent with ‘cooling off’ period for all cosmetic surgery.
6. International collaboration to allow monitoring of the issues and complications which can arise from breast implant surgery.
7. A review of the actions and guidance provided by the MHRA on PIP implants and of the CE marking scheme for medical devices.
8. The MHRA to make it clearer to doctors on how to report issues with medical devices.
9. The implementation of wider safeguards for patients of all cosmetic treatments, injectables, fillers and medical lasers. Fillers to be reclassified as prescription-only medicines. Deregulation of lasers to be reversed.
10. A ban on direct consumer cosmetic advertising (as exists for medicines).
11. For all cosmetic practitioners to be appropriately registered on the GMC Specialty Register for plastic and reconstructive surgery.
12. The consideration of an industry “bond” scheme (along the terms of ABTA / ATOL in the travel industry) where all cosmetic providers are required to provide a guarantee scheme to protect patients. This must include the provision of hospital facilities and follow-up to manage complications, longer-term follow-up and specialist care when required by patients.

Written evidence submitted by the Royal College of Surgeons (MI13)

The Royal College welcomes the opportunity to submit evidence to this important and timely inquiry by the Science and Technology Committee. The College is a professional body with a remit covering England, Wales and Northern Ireland. The College has a particular interest in medical implant regulation as surgeons are core users of such devices in the delivery of treatment, and therefore must have confidence in their safety and efficacy for the patient.

Medical implants and devices more widely have brought significant benefits to patients, and therefore continual innovation in this field must be encouraged and facilitated. This should not however happen at the expense of patient safety. In this submission, we set out how we believe this balance can be achieved through improved European regulation and its implementation in the UK.

Key points

- Transparency: The College firmly believes that transparency and access to information need to be addressed in the revision of medical device regulation. Improvement in this area will likely have multiple benefits including greater efficiency in regulation, better monitoring, and increased public confidence in the system.
- Role of the surgeon/clinicians: The expertise of clinicians can be better harnessed for implant regulation than it currently is (particularly post-market surveillance) by mandating auditing and reporting responsibilities in this area and making it as easy as possible for these responsibilities to be fulfilled.
- Maintaining consistently high regulatory standards across Europe: Implants and devices once approved can be used throughout the EU, regardless of which Member State has conferred this approval. Therefore it is in the best interests of UK patients to ensure parity of regulatory standards in each EU country through increased cooperation and coordination.

Transparency

The College firmly believes that transparency and access to information are central themes to be addressed in the revision of medical device regulation. A recent College seminar¹ on this subject, *New Techniques and Technologies: Ethics and Patient Safety*, indicated that this is a view shared by many stakeholders including the medical device industry, the regulator and patient groups.

Improvement in this area is likely to have multiple benefits including greater efficiency in regulation, better monitoring, and increased public confidence in the system.

In order to address the issue of transparency, we recommend the establishment of a central information service which can provide details of the notified bodies in each EU Member State. We also believe that there should be a centrally available database of approved implants and devices with key information on their manufacturer, approving notified body, evidence base, post-market surveillance and safety corrective actions where applicable.

Whilst we acknowledge that the recommendations suggested are a significant undertaking, requiring substantial initial investment, we believe that it will in the longer term prove cost effective as a tool that can benefit every area of regulation from speeding up approval decisions, to earlier indication of implant safety issues, and driving up regulation standards through increased potential for public scrutiny.

¹ 1 RCS New Techniques and Technologies: Ethics and Patient Safety Seminar, October 2011 – Seminar videos and written summary available here: [http://www.rcseng.ac.uk/policy/policy-seminars/new-techniques-and-technologies-ethics-and-patient-safety-seminar](http://www.rcseng.ac.uk/policy/policy-seminars/new-techniques-and-technologies-ethics-and-patient-safety-seminar/new-techniques-and-technologies-ethics-and-patient-safety-seminar)

Role of the surgeon/clinicians

Ensuring the safety and performance of medical implants must involve a joint approach by regulators, industry, clinicians, patients and other stakeholders. There is a need to clarify the roles and responsibilities of each stakeholder, to ensure that the system is effective.

The clinician's role is vital and should be acknowledged as such – particularly in the monitoring of implant performance once on the market. It is important to define and mandate at European level how surgeons and other health professionals must report performance and safety concerns regarding an implant.

In the UK it is important that changes are made to ensure reporting is made as easy as possible by considering the wider safety reporting responsibilities of clinicians (e.g. incident reporting to the NRLS, and Yellow Card reports to the MHRA regarding adverse drug reactions etc) and streamlining these wherever possible to minimise complexity and administrative burden.

Additionally, there is great potential for surgeons to fulfil a mandatory implant monitoring duty through audit and procedure registries. 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. For example; see the National Joint Registry² and the Society for Cardiothoracic Surgery³ annual reports.

Consistent regulatory standards across Europe

The College is concerned about the current potential for variability in the standards and expertise of national Competent Authorities and the Notified Bodies to which they delegate responsibility for approving medical devices. 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 College believes that only the Notified Bodies who have the highest expertise and use the highest standards should be able to approve devices. We call for greater Member State collaboration and coordination in order to develop more stringent harmonised standards and criteria for notified bodies – in consultation with all Member States and stakeholders within them. This would enable national competent authorities to consistently assess performance of their notified bodies and hold them to account in a more transparent manner. This would also increase accountability of the competent authorities themselves if a notified body is consistently underperforming. We also think there is greater scope for notified bodies and competent authorities in different member states to work together in order to achieve high standards where an improvement need has been identified.

The College would also support the principle of decreasing the number of notified bodies undertaking regulatory duties in the EU – particularly for medical implants which are in the class three (highest risk) device category. Fewer notified bodies would decrease the likelihood of variation and make pan-EU quality assurance and accountability more feasible.

Regarding regulation in the UK, we query the capacity of the MHRA to effectively monitor the performance of a notified body assessing implants when they do not have that explicit functional expertise in-house. Addressing this issue, we believe that public confidence in the system would be

² 2 National Joint Registry 2011 annual report.

<http://www.njrcentre.org.uk/NjrCentre/Portals/0/Documents/NJR%208th%20Annual%20Report%202011.pdf>

³ 3 Society for Cardiothoracic Surgery (SCTS) 2011 annual report: Maintaining patients' trust: modern medical professionalism. <http://www.scts.org/modules/resources/info.aspx?id=32>

improved if the MHRA as the national competent authority were to take on the direct regulation and assurance of the highest risk devices (including implants).

April 2012

**Written evidence submitted by Independent Healthcare Advisory Services (IHAS)
(MI14)**

1. Introduction

1.2 IHAS provides advisory and support services in the areas of regulatory compliance and policy setting across the independent healthcare sector in the UK.

1.3 IHAS core objectives are to:

- facilitate effective communication between subscribers, the government and external organisations
- strive to develop and drive policy advancement through shared subscriber input and consultation
- deliver focused, practical information and guidance in all areas of regulation and policy, sharing and distributing knowledge

1.4 IHAS's primary focus is in the area of operational policy and the regulation of the sector. As such it seeks to:

- Facilitate the development of operational policy, through consultation with its member organisations
- Provide its members with accurate and timely information regarding regulatory and policy matters
- Administer an independent complaints and adjudication process and promote best practice
- Develop a range of quality initiatives to raise awareness of good practice within independent providers
- Represent independent health care providers to government, external organisations, and the public, providing a channel for effective communication and dialogue.

1.5 IHAS wishes to strengthen the assessment, registration and manufacturing quality of medical devices ultimately leading to better patient safety and outcomes. IHAS believes there is significant scope to strengthen the existing medical device directives and guidelines which will ultimately lead to better quality medical devices being made available. IHAS understands that, within the pending update of the Medical Devices Directive (MDD), the MDD will clearly define that all implants or injections, including those products for 'cosmetic intent', will come under its auspices and control. IHAS will be pleased to give evidence in person to this inquiry.

2. Treatments You Can Trust and medical Implants

2.1 Treatments You Can Trust (TYCT) is a government and industry backed independent self regulatory scheme for the cosmetic treatments industry. TYCT gives authoritative advice about registered providers of injectable (botulinum toxin and dermal fillers) treatments. For the public it is a guide to treatment providers who have been checked and registered by TYCT. Registered Providers are fully qualified, trained and insured and they will deliver treatments which comply with the TYCT standards delivered in facilities which are clean, hygienic and comfortable.

2.2 It is important to differentiate a pharmaceutical product from a medical device as there are different EU Directives governing these two classes of product. Pharmaceutical or medicinal products achieve their principal action by pharmacological, metabolic or immunological changes within or on the body. Medical devices are defined by the fact that they do not achieve their principal intended action in or on the human body by pharmacological, immunological or metabolic means. It is also important to note that the MDD goes on to state that devices may be assisted in their function by these means. As regards this definition, fillers are classified as medical devices by most Regulatory Agencies (including the Food and Drug Administration in the US (FDA)) as their primary intended action is mechanical (“filling effect”). In 2005, dermal fillers were re-classified as class III (the highest class) in the EU Medical Device Directive (MDD). In 2010, the MDD 93/42/CE was reinforced with additional requirements, especially around the need to demonstrate clinical effectiveness.

3. How effective and safe is the current regulatory framework for medical implants

3.1 Competent Authority

Under the current system, Notified Bodies are responsible for reviewing CE Marking applications, and grant approval for products to be placed on the market in Europe. Competent Authorities are not involved in product approvals. Under European law, the free market enables any CE marked device to be sold in any European country.

However, some EU countries require the manufacturer to notify the Competent Authority that they intend to place a device on the market in their country.

In the vast majority of countries where this requirement exists, the notification process is very limited, and requires only copies of labelling and approval certificates (CE and Declaration of Conformity) to be submitted. This simple notification process with no actual data being submitted is not adequate.

3.4 Clear guidelines for reporting changes

Under the current MDD, the legal manufacturer only needs to get approval from the Notified Body for changes which impact the compliance with the Essential Requirements specified in the Directive. This covers changes to risks, applicability of clinical data, product design and all other data created to get the original approval. While the MDD requires the manufacturer to have a process in place to assess whether a change is significant or not, it is up to the legal manufacturer to make this determination and decide whether the change does impact the elements of the Essential requirements.

3.5 Policies to define distribution

Unlike Pharmaceutical products, there are no policies or directives controlling distribution for medical devices. Device manufacturers are able to determine independently to whom they sell their devices.

3.6 ‘Legal manufacturer’ and the actual manufacturer

There is considerable confusion in medical device labeling regarding which company actually makes the devices and in which country. The term ‘legal manufacturer’, which is listed on all device packaging, refers to the CE Mark holder (the company with the responsibility for placing the product on a market). Contrary to what the name implies, the ‘legal manufacturer’ does not necessarily make the product. It is possible to have a ‘legal manufacturer’ based in the UK, while the product is actually made in China.

3.7 Inspections by Competent Authorities and Notified Bodies

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.

4. *The MHRA and how it implements the UK Directive*

4.1 There is a lack of transparency in the UK and European medical device agencies when compared with the FDA process in the US. There is no equivalent transparency of information on the MHRA website and in general the medical device information is limited when compared to medicines.

4.2 For a medicine in the UK access to the Summary of Product Characteristics (SPC) and a Patient Information Leaflet (PIL) is relatively straightforward via the electronic

Medicines Compendium (eMC). There is no equivalent for medical devices in the UK and this includes those products that are injected such as dermal fillers, which the public might assume are controlled in a similar way to medicines.

4.3 The transparency of the FDA information in relation to ‘Wrinkle Fillers’, provides unambiguous information on approved products and approved uses. There are 14 products listed, and although there is no easy method for ascertaining the number used in the UK, it is estimated at ten times that number. Botulinum Toxin is a medicine, the practice of remote prescribing that allows this to be administered by individuals without any clinical qualifications, is also an unacceptable risk to patients.

4.4 The broad definition of medical devices means that application of a single process for medical device regulation is inappropriate. However the current differential controls that are in place e.g. for Class III medical devices such as implants, must require a greater level of accountability throughout the supply chain from manufacture to use. This must include improvement in the accountability for the management of post-marketing surveillance and any associated requirements for Field Safety Notices from the MHRA.

4.5 The current definitions for medicinal product and a medical device are creating an issue with the logical and consistent approach to how certain products are handled. This is demonstrated in this example:

The legal classification for Water for Injection is a Prescription Only Medicine (POM) and this confers restrictions in obtaining, supply, prescribing and use.

It is currently inconsistent that this level of regulatory control is required for an injection of water whereas injectable fillers, that have been associated with patient harm in some cases, are classified as medical devices and can be obtained and used without the controls of a POM.

4.6 In addition to the inconsistencies in classification the differentiation of medical device and medicine result in inconsistencies in reporting and monitoring of adverse events. There is no MHRA ‘Black Triangle’ status and transparency of reporting for new medical devices onto the market as there is with medicines.¹

There is a difference in the relationship the MHRA afford the NHS compared to that of independent sector.

¹

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

5. Improving the regulatory framework and recommendations

Compulsory notification to the Competent Authority (CA)

Oversight by the Competent Authorities in all countries in Europe will clearly bring more governance to the medical device industry while allowing the CA to carry out its functions of assessment and inspection more effectively. This needs to ensure the notification process from manufacturers is far less limited than the current situation and any notification of a product includes adequate data submission.

Reporting changes

Clear guidelines defining what is meant by significant and non-significant changes would be a sensible step to strengthening governance of medical device manufacture instead of leaving it up to the manufacturers to set the parameters of a significant change.

Distribution

IHAS recommends the practice of the following manufacturers: Allergan; Merz Aesthetics; Galderma Q-Med and Lifestyle Aesthetics as best practice examples in their distribution of dermal fillers because they choose to limit distribution in the UK to registered doctors, dentists or nurses and select pharmacies. However, other medical device companies may choose alternative sales strategies.

Defining how medical devices are distributed and limiting who the products can be sold to would have a significant impact on controlling distribution of dermal fillers to the appropriate personnel, such as ensuring Beauty Therapists are not added in any circumstance to the supply chain.

Increase transparency regarding the ‘legal manufacturer’ and the actual manufacturer

IHAS believes that placing both the producer’s name/location alongside the license holder’s details within the *Directions For Use* will increase transparency about the origin of medical devices. This will help avoid the confusion about the legal manufacturer and misleading information.

Increase frequency and detail for inspections and audits carried out by the CA and the NB

For companies with the highest commitment to quality, raising the bar in terms of audits and inspections would not be onerous and should make improvements in standards.

Consider how the regulator of medicines and medical devices in the UK (MHRA) operates when compared with the FDA in the US. In particular access to information for professionals and patients that provides clarity of indication for use and thereby supports informed consent where the proportional link between vigilance and safety is clear.

CE marking is a key governance safeguard across all medical devices and the European Union CE marking scheme for medical devices. The robustness of this accreditation should be reviewed to ensure it is fit for purpose.

Mandatory reporting for medical devices should be escalated in visibility and ease of access for reporting clinicians. IHAS suggests the review of post market surveillance by the MHRA in terms of both outcomes monitoring and failure analysis. The analogy to the Black Triangle process for medicines should be adopted.

The MHRA document on the vigilance system for breast implants refers to the European Commission's Guidelines on a Medical Devices Vigilance System. Annex 3 of the European Commission document is a Report Form for Manufacturer's to the National Competent Authority. Section 9 of this form requires completion of the healthcare facility information. IHAS recommends that information on the vigilance should be shared with the healthcare facility in order to improve patient safety.

A National Implant Registry for cosmetic implant medical devices (as with the hip, knee and ankle registries) should be introduced. The issue of mandatory compliance for all registries should be explored with the appropriate clinical governance and information security safeguards. This should include standardised data submission.

6. Sustaining an environment of innovation in the medical implant market

Cosmetic surgery is at the forefront of the changing healthcare market and regulations and standard setting must be flexible enough to reflect wider healthcare trends such as:

- Personalisation – the service is more commoditised with patients researching the range of products and services available to them. Any changes in regulation of the industry need to focus on the patient to ensure adaptability with the pace of change.

- Model of health system delivery – the patient may have the choice to move from NHS to the independent sector and within the independent sector. Standards that are predicated on a long term relationship with a single provider or professional are likely to result in patients being lost to the system.
- Globalisation – products are moved around the world and purchases increasingly involve internet purchasing. In addition, the concept of travelling to purchase products and services has become common place. The issues of counterfeit healthcare products are increasing and regulations, standards and the relevant agencies from individual countries must be able to work more closely together and share intelligence to protect patients and the public.²

7. Conclusion

The CE mark is a European certification that is required before medical devices are placed on the market in all EU countries. However, as outlined above, local regulation in some countries requires notification of the certificate to the relevant national Competent Authority. This ensures that the Competent Authority has better control of the medical devices for sale in that country. It must be noted that medical device manufacturers selling products in the UK are currently not required to notify the MHRA unless the legal manufacturer happens to be based in the UK. Ensuring oversight by the Competent Authorities in all countries in Europe will clearly bring more governance to the medical device industry while allowing the Competent Authorities to carry out their functions more effectively.

April 2012

²

<http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/Counterfeitmedicinesanddevices/index.htm>

Appendix I

DRAFT PROPOSAL FOR THE ESTABLISHMENT OF A NATIONAL BREAST IMPLANT REGISTRY

Introduction

The National Joint Registry (NJR) of England and Wales was established in 2002. Its purpose is to define, improve and maintain the quality of care of individuals receiving hip, knee and ankle joint replacement surgery across the NHS and the independent healthcare sector.

BAAPS in conjunction with IHAS believes that a similar need exists to establish a Breast Implant Registry.

BAAPS and IHAS is proposing the establishment of a National Breast Implant Registry (NBIR) to be operated by QUIP with an identical purpose for individuals receiving Breast Implants across the NHS and independent sector.

IHAS believes that the lessons learnt during the establishment of the NJR and the principles behind the NJR Memorandum of Understanding can be applied in the development of a National Breast Implant Registry.

Principles of a proposed NBIR Levy

1. The National Breast Implant Registry would be self-funding through a levy placed on the sale of breast implants. As such, the cost of the scheme is ultimately passed on to the patient. These arrangements would apply to both NHS Trusts and independent healthcare hospitals in England and Wales. DN – if possible, Scotland and Northern Ireland
2. The NBIR Levy would be set by the NBIR Steering Committee (formed of INSERT) for the first year of NBIR operation at approximately ??£25 per implant and would be reviewed annually by the NBIR Steering Committee.
3. It is proposed that, as with the NJR, the NBIR Levy would include an administration fee (NBIR Administration Fee) to cover the costs of the suppliers collecting and processing the NBIR Levy. The NBIR Administration Fee would be included in the calculation of the NBIR Levy.

Principles of proposed Collection of Levy

1. The principle of funding proposed is that the supplier of a breast implant would collect a levy payment (the NBIR Levy) from the purchasing NHS Trust or independent healthcare provider for each applicable implant sold.
2. The NBIR Levy would be a separate line item on each invoice prepared by the supplier and will be payable directly to the supplier.

The NBIR Levy (including the NBIR Administration Fee) would attract Value Added Tax (VAT).

3. Within 10 working days of the end of each calendar month the suppliers would inform the NBIR Co-ordinating Centre of the number of implants sold during that month. The NBIR Co-ordinating Centre would use this information to provide a Statement of Account to the Department of Health.

Principles for the Establishment of the National Breast Implant Registry

Similar to the process to set up the NJR, the following structures would need to be established:

- A Steering Committee, with an independent chair, would need to be established to oversee the NBIR's activities. To ensure that all stakeholders are represented, its members should include patient groups, the surgical professions (25% of places), theatre nurses, implant suppliers, NHS Trust management and independent healthcare providers, the NHS Purchasing & Supply Agency, the MHRA, DH and Welsh Assembly Government. DN – if possible, Scotland and Northern Ireland.
- A NBIR Centre to manage the development and implementation phases of the database, as well as to manage dissemination of information.
- Establishing a network of Regional Clinical Co-ordinators (RCCs) to help promote the Registry throughout England and Wales. RCCs are practising plastic surgeons who act at a strategic level to facilitate feedback to surgeons and their teams, so enabling them to submit NBIR data and optimise their clinical practice.
- Developing a data entry tool that would work in the majority of hospitals with their existing IT systems; which was confirmed by carrying out an IT hardware 'health check' survey (in the case of the NJR).
- Implant suppliers, supported by the Association of British Health-Care Industries (DN Mr Fatah to confirm industries that are supportive)
- (ABHI), and the NBIR Centre working together to develop and populate the NBIR database with the relevant implant components. This incorporated coding components into product families to help make analysis simpler and faster, whilst also facilitating the analysis of new technologies as they become available.
- The NBIR Centre running a series of training roadshows in central locations across England and Wales in the weeks leading up to the launch. Involvement of RCCs in events with the launch of the NJR helped to attract attendance from well over 1,000 participants. The feedback from attendees helped to fine-tune both the system and reference manual ahead of the launch.

December 2011

Written evidence submitted by BSI Healthcare (MI15)

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 ²

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 (e.g. 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; and
- d) A system that is adaptable and does not stifle innovation.

¹ 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.

² Other stakeholders' responses to the Commission http://ec.europa.eu/health/medicaldevices/documents/revision/index_en.htm.

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
- 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 system 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 twenty 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

Written evidence submitted by The Harley Medical Group (MI 16)

The PIP crisis has affected our company significantly in the past two years: we are probably the largest single user of PIP implants in the UK, having used them in nearly 14,000 operations.

We feel that PIP patients have been totally let down by the European regulatory system, of which the various local health agencies are part, such as the MHRA, the Irish Medicines Board and the French AFSSAPS, just to name a few. We also feel that all the users of PIP implants, whether they be individual surgeons, national health services or private providers such as our group have been equally let down. I have laid out below what we feel are the main issues with the situation, and by implication, what we would recommend going forward. Please note that our recommendations are based on our experience with breast prostheses. We do not use other types of medical devices.

1. Testing before commercialisation starts

Before the PIP crisis broke out, we took the CE mark as a guarantee of safety. We knew that the CE mark was not an indication of efficacy, contrary to the FDA approval, but we assumed that CE-marked implants had been tested thoroughly and found to be safe. Of course when the crisis broke out we researched these matters to find, to our surprise, that the CE marking was an “after the event” mechanism, with testing and auditing by European agencies taking place after the product had been commercialised. We feel that the testing process by the regulator should take place before commercialisation, in the same way as happens with the FDA process.

2. Testing after commercialisation starts

The testing that currently takes place after commercialisation is not adequate and we recommend as follows:

- The visits to the manufacturer must be unannounced and must take place several times a year;
- There must also be visits to the distributors of the devices in each country. For instance, we feel that the MHRA should have inspected PIP’s UK distributors (Cloverleaf) annually on an unannounced basis, with sampling and testing of the stock and publication of the results (in the same manner as the Care Quality Commission inspects healthcare establishments and publishes the results of the inspections, for the public to see).

3. Gathering of adverse incident information

The PIP crisis has brought to light the inadequacy of the information gathering system for adverse incidents in the UK. Clearly this has been made worse by the disbanding of the Breast Implants Register in 2006. We recommend the following going forward:

- A compulsory breast implant register managed by the MHRA. Whenever implants are inserted, implanting centres would send data to the register, enabling the identification of the implanting centre, the implants and the patient.
- A compulsory reporting mechanism to the MHRA whenever there is a post-operative complication with a patient fitted with the implants. Again the implanting centres would generate this data, which would enable the identification of the implanting centre where the revision surgery takes place, the patient and the implant.

4. Accountability of regulatory authorities

We feel that there is a lack of accountability of the MHRA or the European regulatory authorities.

The PIP crisis is clearly the result of the failure of regulations of medical devices in Europe. As an organisation our first reaction when the PIP crisis broke out was to turn to these organisations for redress and help, on the basis that they are responsible for the safety of medical devices in Europe through the CE-marking. Much to our surprise and disappointment, they did not admit any responsibility or liability in relation to the situation. Worse, they put the onus on organisations such as ours and on individual surgeons to provide remedial surgery to PIP patients at no cost.

As things stand, many PIP patients who want their implants removed and / or replaced have to fund the revision surgery themselves, as providers such as THMG or individual surgeons cannot afford to offer free revision surgery to tens of thousands of patients. Their only route is litigation and there are currently many cases building up. This is not desirable for all parties involved, but for patients in the first place.

We feel that regulatory authorities should be made properly accountable for their failures (see insurance system below).

5. Insurance system

A similar crisis took place in the late 1990's with Trilucent breast implants. The manufacturers were suitably insured and organised, through BUPA and the UK private healthcare sector, for all Trilucent patients to be treated. All removals took place over a two year period in a managed and orderly manner and as a result litigation was minimal.

In the current situation, the manufacturers have disappeared and their insurance policy cannot be relied upon as fraud was committed. Going forward, we recommend that regulatory authorities should take insurance to be able to step in financially in such circumstances and fund the resolution and the management of such crises. The cost of that insurance should be passed on to the manufacturers. Overall this would increase the cost of medical devices but it would also ensure that the authorities can step in fast to address the anxieties of patients and providers and minimise litigation.

6. Transparency of regulatory authorities in their communications

We feel that the communications of regulatory authorities are, in some cases, a misrepresentation of the truth. For instance, the MHRA's website currently contains the following statements:

- “The MHRA’s mission is to enhance and safeguard the health of the public by ensuring that medicines and medical devices work, and are acceptably safe.”
- “The MHRA is fully accountable to both the government and the public”.

Sadly, we have experienced at first hand the inaccuracy of both statements and we feel that until a proper testing and auditing system (see 1, 2 and 3 above) and an insurance mechanism (5. above) are in place, health authorities should tone down their claims and be absolutely transparent to the public about the shortcomings of the current regulatory system and the limitations of the recourses available to patients and providers in situations of crises such as the current one.

We hope that this crisis will give rise to an honest and thorough overhaul of the regulatory system in the UK. Please note that similar recommendations were already made in 2001 in the wake of the Trilucent crisis (see submission to the House of Commons Select Committee on Health by Paul Balen of Freethcartwright Solicitors, March 2001). Unfortunately, they were not followed. Let us not make the same mistake this time.

April 2012

**Written evidence submitted by the National Institute for Health and Clinical Excellence (NICE)
(MI17)**

Overview

1. NICE welcomes the opportunity to submit evidence to the Committee's inquiry. In our submission we outline the main areas of our work pertaining to medical technologies, namely the NICE Interventional Procedures guidance programme and the NICE Medical Technologies Evaluation Programme.
2. We work closely with the Medicines and Healthcare products Regulatory Agency (MHRA) but perform a distinct role: only once the MHRA has licensed a product for use in the UK does NICE produce guidance for the NHS.
3. There is often a lack of data to carry out thorough evaluation of medical devices, and we believe that the proposed revision of the European Directive on medical devices offers an opportunity to resolve this issue, and to develop more robust systems for data collection and analysis. This would lead to better outcomes for patients, and the quicker adoption of innovative technologies in the NHS.

Introduction

4. The National Institute for Health and Clinical Excellence (NICE) is the independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health.
5. NICE guidance supports healthcare professionals and others to make sure that the care they provide is of the highest attainable quality and offers the best value for money.
6. NICE runs a Medical Technologies Evaluation Programme (MTEP), which selects and evaluates new medical technologies, implants, devices and procedures (or new versions of existing ones) with the aim of ensuring that they are used more rapidly and more consistently in the NHS. The types of products that are evaluated include medical devices that deliver treatment such as those implanted during surgical procedures; technologies that give greater independence to patients; and diagnostic devices or tests used to detect or monitor medical conditions.
7. The programme evaluates technologies based on their potential to drive significant improvements in outcomes, patient experience (of treatment and recovery), ease of operator use, and/or the efficient use of resources.
8. The programme also plays a key role in identifying products that require further research prior to consideration for use in normal NHS practice, and makes recommendations on the nature of the research and how it should be undertaken.
9. NICE does not provide regulatory approval for drugs or other medical technologies to be marketed and used in the UK. For technologies to be evaluated by NICE, regulatory approval in the form of a CE mark and Medicines and Healthcare products Regulatory Agency (MHRA) approval must already be in place.
10. Medical technologies submitted to NICE for evaluation may follow one of the following pathways, each producing different types of guidance for the NHS:

Interventional procedures guidance focuses on the safety and efficacy of interventional procedures¹. Many of the procedures are new, but established procedures are also considered if there is uncertainty about their safety or how well they work. Unlike other types of NICE guidance, interventional procedures guidance does not provide advice on whether procedures are cost effective. Instead it provides advice on whether such procedures are safe and efficacious enough to be used in clinical practice, the circumstances in which procedures should be used, and whether special arrangements are needed for patient consent before the procedures are carried out.

A clinician intending to undertake a new interventional procedure in the NHS for the first time is required to check the NICE website and to notify the procedure to NICE if it has not already been notified. In addition, anyone may notify a procedure for consideration, and both device manufacturers and hospitals regularly do so. Interventional procedures guidance frequently refers to the need for additional evidence from data collection or other further research.

Medical technologies guidance identifies devices that offer advantages to patients and to the NHS, and promotes their adoption. Technologies are notified by manufacturers, who need to provide evidence about the advantage and cost savings of their product compared with current NHS practice. If the evidence supports the case for adoption, then NICE publishes guidance specifying what those advantages are, and using cost-modelling, describes the likely cost benefits to the NHS.

There may be evidence to suggest that a device is effective but there is uncertainty about whether it would produce the claimed benefits in normal NHS practice. Under those circumstances NICE can recommend and facilitate research to answer the relevant questions and to provide information to subsequently update its guidance to the NHS.

Medical Technologies guidance only recommends adoption of technologies that are cost neutral or reduce costs for the NHS, so that they offer better value than current practice. If the evidence fails to support clinical or cost advantages then guidance is published to that effect, stating that the case for adoption is not supported.

Technology appraisal guidance is probably the most well-known of NICE's guidance outputs. In technology appraisal guidance, whether on drugs or medical technologies, the focus is on clinical **and** cost effectiveness – essentially whether the increased patient benefits provided over and above existing NHS practice are worth the additional costs the NHS must pay for the drug or technology. If a technology is recommended by NICE for use in certain patients then there is a mandate on the NHS to provide those patients with access to its use. Technologies are selected for the technology appraisal process following detailed consideration and are referred to NICE by the Department of Health: this type of guidance tends to be restricted to technologies that are likely to have a major financial impact on the NHS.

¹ NICE defines an 'interventional procedure' as a procedure used for diagnosis or for treatment that involves making a cut or a hole to gain access to the inside of a patient's body (eg a cannula), gaining access to a body cavity without cutting into the body (eg endoscopy), or using electromagnetic radiation such as x-rays.

Clinical guidelines are recommendations by NICE on the appropriate treatment and care of people with specific diseases and conditions within the NHS. They usually include recommendations about the use of particular medical technologies.

11. NICE guidance is developed by independent advisory committees made up of clinicians and other healthcare professionals, health economists, patients, carers and industry experts. In developing guidance, the committees consider clinical studies, evidence from clinical and other experts and from patients and carers as well as cost analyses and social value judgements where relevant. All draft guidance goes through a period of public consultation, after which all comments received are considered by the committee or guideline development group. The guidance is then amended as appropriate. It is then scrutinised by NICE's officials (the Guidance Executive), on behalf of the Board, prior to publication. There is an opportunity for challenge by any party who believes that there has been a factual error or breach of process in the production of the guidance.
12. The MHRA, as the regulator for medical technologies, is represented by the MHRA Medical Director for devices on both the Interventional Procedures and Medical Technologies Advisory Committees. This enables good liaison between the MHRA and NICE in evaluating procedures and devices.

The Medical Devices Directive and the importance of data

13. Our experience of evaluating new devices and diagnostics shows that they often offer important benefits to patients and the NHS. But our experience also shows that there is often a lack of data making it difficult to judge the benefits a new technology brings, and therefore difficult to encourage and influence their uptake by clinicians and commissioners.
14. In order to carry out its evaluations, NICE needs data on both safety and efficacy. Clinical studies on medical technologies are often limited in quantity and quality, and they are typically poorer than equivalent evaluations for pharmaceuticals. One reason for this is that the regulation of medical devices in the EU does not require as much research data as does the regulation of drugs. Revision of the Medical Devices Directive offers an opportunity to change this situation, in a way that does not place an overwhelming burden on device manufacturers, many of whom are small companies that have little experience in research.
15. We suggest that during the revision of the licensing system, provision is made for devices that clearly show considerable potential but with limited data on their safety and efficacy – so that they could be used only in the context of a research study or well-designed and thorough data collection. The aim of this would be to gather information on safety and efficacy in clinical use.
16. Alongside this, NICE would like to see an improvement in the systems for collection of long term data for selected devices such as new types of implant. This would give proper support for hospitals and clinicians to allow them to follow patients up in the long term and also provide additional data for further evaluation.
17. In addition to clinical studies it would be beneficial to have information about the extent of the use of procedures (and associated devices) in the NHS and about their outcomes in everyday practice. Better information would lead to better outcomes for patients. Currently, the generation of this kind of information is inadequate because:

There is often no specific classification code for a new procedure. It is generally not possible to find out how many procedures, using a new device, have been carried out because the coding system used in the NHS does not allow them to be specified individually through routine NHS data collection. NICE has liaised with NHS Connecting for Health over several years and some progress has been made but this remains a real problem.

It is difficult to set up new registers. There are a number of national registers - databases of clinical outcome data and national audits used to measure the performance of procedures and devices, with the aim of improving the outcomes of care. Some new procedures can be incorporated into existing registers, such as those run by the National Institute of Cardiovascular Outcomes Research or the National Joint Registry, but they often require costly adaptation to receive data on particular new procedures. NICE would like to see the establishment of a system of data collection for any procedure about which the evidence is insufficient for 'normal' use. We have had some success in the setting up of registers, in collaboration with clinicians, but this has only been possible for a very small number of procedures.

April 2012

Written evidence submitted by Dr Gerry Armitage (MI18)

1. Contributor background

I am a health services researcher largely conducting work in patient safety, and holding the following posts: Senior Lecturer at the School of Health, University of Bradford; and Senior Fellow at the Bradford Institute for Health Research, Bradford Teaching Hospitals NHS Foundation Trust. I am co-investigator on a National Institute for Health Research funded programme grant (2009-2014) investigating patient involvement in patient safety, where my specific role is to lead a work stream which is developing and evaluating a patient designed, patient-led reporting scheme for safety incidents in acute hospital care. I am also lead investigator for an additional National Institute for Health Research funded study (2012-2015) which is developing a web based reporting scheme for quality and safety concerns within renal (kidney) services.

2. Scope of this contribution

I have been specifically asked to comment on that aspect of medical implant regulation termed '*post-market surveillance*'. I have been informed this could involve collating and learning from information taken from patients and the public who have concerns about their medical implants. I will provide evidence-based comment drawn from a recently published systematic review on patient reporting, and from the associated empirical research mentioned above. As most of my work is based in hospital care, I will simply put forward an overview of my work so the Committee might consider, if it is proposed to develop a reporting scheme for patients with medical implants, the current knowledge base around patient reporting and how such a scheme might be designed.

3. Policy context and published work

Recent health policy, as exemplified in the Government White paper *Liberating the NHS*, prioritises patient involvement and strongly emphasises the paramount importance of patient safety. It is also clear from numerous studies that while some learning is possible from staff-led patient safety incident reporting schemes, staff engagement with such reporting schemes is disappointing and the quality of reporting is poor.¹ My colleague Dr Jane Ward and I have recently published a systematic review titled: Can patients report patient safety incidents in a hospital setting: a systematic review.² This systematic review, based on thirteen papers, demonstrates that hospital patients *can* report safety and quality concerns, but the evidence base is rather ambiguous (Ward & Armitage, 2012).

4. Design of patient-led, patient safety (or quality) reporting schemes

¹See Armitage et al 2010, J. Evaluation Clinical Practice 16 1189-97

² See BMJ Quality and Safety <http://qualitysafety.bmjjournals.com/cgi/content/full/bmjqs-2011-000213>.

In light of the findings from our systematic review and aforementioned studies, we would argue, with some confidence, that any patient reporting scheme, where the prime purpose is to develop intelligent surveillance of patient concerns, should be co-designed and co-developed *with* patients. Previous studies of hospitalised patient reporting, (as detailed in our review), have attempted to measure the capacity of patients to report when actively solicited by researchers. In these studies, the researchers often framed their questions to patients using pre-defined categories, but did not consider the capacity of patients to report spontaneously (i.e. the patient can report what concerns them and when it concerns them, which we describe as 'hot reporting'). Further drawing on the findings of the review and our own research, we also argue that the design of a scheme should carefully consider structure and process, taking into account:

- a language that is understandable to patients yet also meaningful to clinicians (who may have to take action based upon the data)
- the optimum recall period for capturing accurate data;
- the means by which data is collected to gain relevant data as expediently and sensitively as possible.

Having collected reports from a wide range of patients about their concerns, we are aware that some patient reporters will be unwell and require considerable support, and others may feel threatened by the consequences of reporting something to an institution that, in their view, could be directly linked to the institution caring for them. We consequently recommend utilising *human factors* as a framework for design and implementation. A human factors perspective takes a multi-factorial, multi-level view of incident causation, with a much greater emphasis on systems than individuals, and attributes a high learning value to the reporting of near misses³. Additionally, we have found that hospitalised patients are more likely to engage with a reporting process if they know that the prime purpose is learning rather than the attribution of individual blame.

5. Preferred mode of patient reporting

Nine of the thirteen studies included in our systematic review used interviews based on a structured survey to collect patient reports. Based on more substantive data from our programme grant work, we have demonstrated that hospitalised patients can 'hot report' but have clear preferences as to the means of reporting, opting to share their concerns, face to face with another person, rather than in a written report or via a phone line. This has clear resource implications in choosing a person who is suitable to collect such reports - ideally not a member of the team directly caring for the patient, but someone who is independent of that team. This is likely to incur some cost in a health service continually facing cost improvement programmes. Although carefully trained volunteers might be

³ A near miss is where there has been an untoward incident or error but there is no patient harm

considered, this may be especially difficult to implement in a community setting. My more recent work on developing a web-based reporting scheme is at a very early stage, but of course we do know that the express advantage of this mode of reporting is the reach across both hospital and community settings. It is becoming clear, however, that patients have specific concerns about web based reporting: 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).

6. Nature of patient reports

When patients can report spontaneously, they will report concerns that are proximal to their care such as the nature of conversations between themselves and their nurse ('*I don't feel the nurse is taking my reports of pain very seriously*'). I have discussed this with other researchers doing tangential work such as Professor Rick Iedema at the University of Technology in Sydney and we recognise that this type of information may appear to be of little value and even idiosyncratic but it can be the precursor for a future medical error; where a perhaps subtle but significant change in a patient's condition is not recorded. We have found that patients can specifically comment upon basic care, medication safety, communication processes, service management and their physical surroundings. Such a wide range of topics suggests that patients can play a ubiquitous role in gathering intelligence about care, which is often delivered by numerous professionals, who themselves may not have a strong awareness of each other's performance.

7. Concordance with other established staff-led methods of collecting data on safety or quality incidents

Based on our systematic review, (where just five studies considered concordance) and our empirical evidence to date, the concordance between concerns reported by patients and those patient-centred incidents reported by staff is *not* consistently high. Whether patient reports have a higher false positive rate than staff reports is as yet unclear, although we do know that the existing range of established staff-led incident detection methods do not have a high degree of overlap.

8. Challenges in patient reporting

Engaging patients in reporting is not without challenges. Firstly, as mentioned above, some patients might be unwilling to report, believing the act of reporting suggests they are directly challenging those staff upon whom they may be reliant for essential care (this is, of course, a problem that would be unlikely to occur if the reporting patient is not directly receiving care). Secondly, by dint of asking patients to report, some patients may perceive that *they* are sharing the responsibility for

surveillance. Thirdly, and linked to a number of points raised above, staff should also be involved in any design of patient reporting schemes, which would not only add a sense of shared ownership but also make sure that the final product could fit into a clinical governance process.

9. Conclusion

The knowledge base for patient reporting is emergent, and as previously stated, our own work is largely focussed on hospital care. While some of our findings are relevant to hospitalised patients with medical implants, patients discharged into the community who need to report a problem may require a different approach and this might be web based. The comments on design are, nevertheless, broadly applicable to both settings. As a researcher in this field, I would advocate that any development of a patient reporting scheme for medical implants is evaluated stage by stage, using a range of methods.

May 2012

Written evidence submitted by Dr Peter Wilmshurst (PM19)

I am a consultant cardiologist and my work has required me to implant medical device, including coronary artery stents, permanent pacemakers and implants to correct structural cardiac defects, such as atrial septal defects and patent foramen ovale (commonly known as “holes in the heart”). Once implanted, if one of those cardiac implants fails to function properly or if it causes complications, it is usually very difficult to remove the implant from a patient unless major and high-risk cardiac surgery is performed. Since 2004 I have been a Specialist Advisor to the Interventional Procedures Advisory Committee of the National Institute for Clinical Excellence (NICE) and a Clinical External Assessor for the Medicines and Healthcare products Regulatory Authority (MHRA). Both roles have involved me providing advice about appropriate use of medical implants.

I understand that a balance must be struck between making available for patients effective implants as soon as efficacy is proven and doing sufficient checks to ensure that unsafe implants are not marketed. I am concerned that the correct balance has not been struck. I am also concerned that there is inadequate post-marketing vigilance to ensure that late complications are detected.

I find it difficult to understand why the evidence used to support licensing a drug in Europe or the USA is made public when the evidence for licensing a medical implant is kept secret from doctors and patients in Europe, but is published in the USA. When deciding on which implant to use in a particular clinical setting for an individual patient, doctors should be guided by knowledge of the full information about the available implants. This information should be available from the licensing body and from objective scientific reports published in medical journals and presented at scientific conferences. In practice device selection is biased by the secrecy surrounding licensing applications, and by conflicts of interest leading to bias in publication of incomplete and false information about efficacy and safety. My concerns about this have been reinforced by my involvement in clinical trials of medical implants, in one case as the trial principal cardiologist, which made me realise that licensing and use of medical implants is more to do with marketing than science and that the existing regulations for licensing medical implants in Europe is seriously flawed.

I would add that because of my experiences I was asked to write the lead editorial with the title “the regulation of medical devices” for a special issue of the British Medical Journal about medical devices. I concluded that the regulation of medical devices is “unsatisfactory, unscientific and in need of a major overhaul”.¹ I have been asked to speak about my concerns about the regulation of medical devices in the UK (for example at the Royal College of Surgeons) and internationally (e.g. European Society of Cardiology and Irish Cardiac Society).

I wish to provide examples based on an area of my expertise, namely closure of a particular type of hole in the heart, known as a patent foramen ovale (or PFO). I had a significant input into the current NICE guidelines on PFO closure, partly because of

¹ Wilmshurst P. *The regulation of medical devices*. British Medical Journal 2011;342:1093-4.

my role as a Specialist Advisor to NICE and partly because I was one of two doctors asked to provide advice on the subject to NICE on behalf of the British Cardiovascular Intervention Society.

Currently there are about 10 devices with CE Marks available for PFO closure. Many of the early reports of use of these implants came from the cardiologists who invented the implants, who unsurprisingly reported ease of use, efficacy and safety. In some cases the reports came from hospitals that owned the patents of the implants. Some published reports failed to disclose the financial conflicts of interest. To date there has been no “gold standard” randomised clinical trial showing benefit to patient groups from PFO closure. There have been only 2 randomised controlled trials of PFO closure with implants and each showed that outcomes in patients who had PFO closure was no different from those who were in the control groups. Therefore we should consider how it is that many thousands of patients in the UK have had PFO closure with these devices when efficacy is unproven.²

I was an investigator in two multicentre clinical trials in the UK that tested two PFO closure devices made by a US medical device corporation, NMT Medical. NMT has subsequently gone into liquidation and I believe that the events I describe were the result of NMT’s reliance on the results of the clinical research and eventually NMT’s need to present negative results in a favourable way.

I was the principal cardiologist in the Migraine Intervention with STARFlex[®] Technology (MIST) Trial, which randomised patients with migraine with aura and a large PFO to either PFO closure with NMT’s STARFlex[®] implant or a sham procedure. The STARFlex[®] implant consists of two joined discs, rather like a cuff link, with each disc being like an umbrella with radiating metal spokes supporting polyester fabric. The implant is positioned so that the discs sandwich the defect with the aim of sealing it. At the time of the MIST Trial, the STARFlex[®] implant already had a CE Mark for marketing in Europe “for closing atrial-level shunts” despite a relative lack of evidence of clinical benefit in patients. We hoped to demonstrate that a STARFlex[®] implant would seal a PFO and relieve migraine with aura. It had been anticipated that, based on previous observational reports, PFO closure would improve migraine.

I was also asked to be the core echocardiography laboratory in another NMT trial, the BEST Trial, that tested the efficacy of PFO closure with a modified implant called the BioSTAR[®]. The BioSTAR[®] had no CE Mark. It differed from the STARFlex[®] implant in that the polyester fabric was replaced with a porcine collagen membrane. Short duration experiments in sheep had demonstrated that once implanted the collagen membranes of the BioSTAR[®], but obviously not the metal spokes, were replaced by the animals’ own cell to seal the defect. The purpose of the BEST Trial was to obtain evidence that the device would successfully seal a PFO in patients. The core echocardiography laboratory was essential because it would determine whether each PFO had been sealed successfully. There was no attempt to demonstrate clinical benefit from the BioSTAR[®] implant, although obviously it was hoped that patients would benefit. NMT hoped that the BioSTAR[®] would be granted a CE Mark.

² Wilmshurst P. *CLOSURE 1 seen through the MIST*. British Medical Journal 2012;344:51.

In the MIST Trial we found that implantation of a STARFlex[®] implant did not lead to cessation of migraine more frequently than a sham procedure. In the implant arm 3 out of 74 patients were free of migraine during the analysis period compared with 3 out of 73 patients in the sham procedure (control) group.³ One possible explanation for the lack of clinical efficacy might be inadequate sealing of the cardiac defect by the STARFlex[®] implant as some of our observations suggested. I was keen for full disclosure of all the findings, but NMT objected to full reporting of those findings. As a result the final version of the paper omitted disputed findings about efficacy of PFO closure with NMT's STARFlex[®] implant and also omitted mention of some potentially life-threatening complications experienced, such as the fact that in some patients the implants fell out of the PFO to lie free in the heart or to be carried by blood flow to a pulmonary artery. Those patients need additional procedures to remove the dislodged devices in order to prevent life-threatening complications. So the original version of the paper published in the most prestigious cardiology journal, Circulation did not provide readers with full information about efficacy or safety.

One other doctor on the trial steering committee and I refused to be authors of the paper because it contained statements which were false and misleading. In addition there was inadequate declaration of financial conflicts of interest, including the fact that a vice-president of NMT wrote part of the paper and that the first author of the paper, the principal headache specialist, owned NMT shares during the trial. At the start of the trial that doctor had declared to the West Midlands Multicentre Research Ethics Committee, which approved the trial, that no investigator owned NMT shares. After considerable efforts and 18 months delay after the original publication I managed to get Circulation to publish a new version of the paper with a correction of 700 words and a data supplement of 4 pages.⁴⁵⁶

In the meantime, NMT started three defamation claims against me in the UK; each time for both libel and slander. Two claims were because I expressed concerns about inaccuracies in data presentation at a cardiology meeting in the USA and my comments were published by an American on-line cardiology website. The other claim was after I spoke about the defamation claims on the Today Programme on BBC Radio 4. The US website, the website's reporter and the BBC were not sued. The claims against me went on for nearly 4 years. NMT also asked their lawyers to bring claims against the other doctor on the steering committee who had refused to be an author of the paper and against my hospital. Those claims were not served. Other threats were made to try to prevent clinicians discussing any version of the trial results that NMT did not want disseminated.

While NMT was trying to silence me and other doctors, NMT's website and annual reports contained misleading testimonials from the three patients who had a STARFlex[®] implant and who were migraine free during the analysis period.⁷ Their

³ Dowson A, Mullen MJ, Peatfield R, Muir K, Khan AA, Wells C, Lipscombe SL, Rees T, De Giovanni JV, Morrison WL, Hildick-Smith D, Elrington G, Hillis WS, Malik IS, Rickards A. Migraine intervention with STARFlex Technology (MIST) Trial: a prospective, multicenter, double-blind, sham-controlled trial to evaluate the effectiveness of patent foramen ovale closure with STARFlex septal repair implant to resolve refractory migraine headache. Circulation 2008;117:1397-1404.

⁴ <http://circ.ahajournals.org/cgi/content/full/circulationaha;120/9/e71>

⁵ <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.107.727271/DC1>

⁶ <http://circ.ahajournals.org/cgi/content/full/117/11/1397>

⁷ <http://www.badscience.net/2010/12/nmt-are-suing-dr-wilmshurst-so-how-trustworthy-are-they/>

testimonials and the website suggested that the procedure had cured their migraine, but an equal small number of patients in the control group were also migraine free. NMT, as the sponsor, should not have been able to identify or contact the patients. Also of concern was the fact that the NHS website of the Royal Brompton Hospital in London carried similar information and a testimonial from one of the three patients suggesting that a STARFlex[®] implant could cure migraine. The web page was put up sometime in 2006 (presumably after the results of the trial were first presented in March 2006) and remained on the Royal Brompton Hospital's website until 28 November 2010. The Royal Brompton Hospital removed it only after Dr Ben Goldacre asked the hospital to comment before he wrote about it in his "Bad Science" column in the Guardian newspaper.⁸

The Royal Brompton Hospital's website were headed: "Heart trial offers relief for migraine sufferers." This is surprising because the MIST Trial showed that a STARFlex[®] implant did not help migraine. The web page included the following statements about the MIST Trial:

"Our researchers investigated the relationship between migraine headaches and holes in the heart. Their study indicates that as many as 40 percent of patients could have their migraine symptoms significantly relieved through intervention to close the holes in their hearts."

"Dr Mullen said "This is significant news for migraine sufferers. For the first time this study has shown that closing a PFO can have a substantial effect in reducing the symptoms for patients with severe migraine."

"Zoe Willows, a patient involved in the trial, suffered migraines with acute aura for over 22 years. "My doctors just kept on prescribing different pills and medications but nothing ever worked", she said. I've now been completely cured and can live my life as a normal person.".... "I encourage other migraine sufferers like me to go to their GPs and insist they refer them to a specialist to test whether they too have a hole in their heart."

Dr Mullen, who worked at the Royal Brompton Hospital as an NHS consultant, was a member of the MIST Trial steering committee. While on the steering committee and during the clinical trial he owned NMT shares and received payments from NMT for consultancy work and teaching. The Royal Brompton Hospital's website also had a photograph of Zoe Willows. Beneath her testimonial on the Royal Brompton Hospital's website was a statement saying "Read more about the study on the MIST website" with a link to NMT's website.

So at a time when NMT were misrepresenting the results of the MIST Trial in the scientific literature and on the corporation's website, they were also able to use an NHS website to misrepresent the results of this clinical trial and were using the English defamation laws and threats of libel action to silence those researchers who were concerned about the accuracy of their reports.

As stated above, my role in the BEST Trial was to be as the core laboratory for the echocardiography studies in the Trial to determine whether implanting a BioSTAR[®] implant successfully sealed a PFO in each patient. Once I started to question the

⁸ <http://www.badscience.net/2010/12/nmt-are-suing-dr-wilmshurst-so-how-trustworthy-are-they/>

efficacy of PFO closure with the STARFlex[®] implant in the MIST Trial I was dropped from my role in the BEST Trial. The BEST paper was also published in Circulation.⁹ Circulation sold reprints of the paper to NMT for distribution to cardiologists. Such reprint sales to industry by major journals may bring the largest journals as much as \$500,000 for a single article. There is a suggestion that the income from reprint sales influences the conduct of those journals in allowing trials to be presented in the most “positive” manner, because sponsors will not buy reprints for distribution if the article says that their product is ineffective or unsafe.

In the BEST Trial only 57 patients had a BioSTAR implant. The trial reported high rates of successful PFO closure with the BioSTAR[®] implant, but the decision by NMT to drop me from acting as the core echocardiography laboratory and my experience in the MIST Trial raise questions in my mind about the accuracy of the reported rate. In the patients the follow-up was for only 6 months. On the basis of this slim evidence, the BioSTAR[®] implant was granted a CE Mark.

The award of a CE Mark in June 2007 was rapidly followed by comments by investigators on BBC television and in the press about the BioSTAR[®] implant. A public relations company employed by NMT arranged the interviews. The media were not informed that the two investigators put up to speak to them were conflicted because they also owned NMT shares. The published reports contained the quotation from one of them that “PFO appears to allow blod(sic) clots and other debris to clog up arteries in patients, which not only causes strokes but other problems. Using the bioabsorbable device is a radical rethink of a treatment option for migraine but it seems to have shown some very positive results. For a proportion of sufferers, this could end up as a cure for them.” This claim was unjustified because the BEST Trial had not investigated the effect of the BioSTAR[®] implant on migraine and in the MIST Trial PFO closure with the STARFlex[®] implant had not helped migraine.

Other published quotations, such as “this treatment (BioSTAR) does the repair job and then disappears in a natural way” suggested that the BioSTAR[®] implant entirely disappears once replaced by the patient’s own tissue. In fact only the collagen disappears, leaving behind a series of metal spokes inside the heart. There is of course nothing “natural” about having animal collagen implanted, as indicated by allergic reactions subsequently reported in patients given the implant. Furthermore, the evidence now suggests that, in distinction to what happens in sheep, in some patients the porcine collagen disappears without being replaced by the patient’s tissue. That results in return of the hole in the heart more than 6 months after implantation. So the follow up period in the BEST Trial had been too short. In fact, because the hole was then splinted open by the metal framework of the BioSTAR[®] implant, the amount of blood crossing the defect can be greater after the implant than before. In addition the metal spokes are no longer restrained by the collagen sheets that were present when the BioSTAR[®] was first implanted or by the polyester fabric in the STARFlex[®] implant. Relative to the number of implants there has been a high rate of cardiac perforations resulting from the metal spokes of the BioSTAR[®] implant moving and perforating the cardiac chambers compared with the rates seen with other devices

⁹ Mullen MJ, Hildick-Smith D, De Giovanni JV, Duke Christopher, Hillis WS, Morrison L. BioSTAR Evaluation Study (BEST). A prospective, multicenter, phase 1 clinical trial to evaluate the feasibility, efficacy, and safety of the BioSTAR Bioabsorbable Septal Repair Implant for the closure of atrial-level shunts. Circulation 2006;114:1962-7.

used for PFO closure. These perforations occur later than the 6 months after implantation.

NMT went into liquidation in April 2011. Had they still been trading, NMT would probably have refused to reveal details of their device sales for commercial reasons, but the accountants who dissolved the company informed MHRA that 505 BioSTAR® implants had been sold in the UK. We do not know whether all 505 had been implanted but we do know that there were at least 2 cases of cardiac perforation requiring emergency cardiac surgery and many recurrent atrial-shunts in the UK. In Europe 1500 BioSTAR® implants were sold and there have been at least 3 cardiac perforations, one of which was fatal, and 2 others required emergency cardiac surgery. The true rates may be higher because there has been no vigilance of complications with the device. MHRA do not know all the centres in the UK that used the BioSTAR® implant or how many they used or what complications they experienced.

In the UK we have a registry of interventional cardiac procedures, but at present there is no record of the type, lot number or serial number of devices implanted. There is also very poor late reporting of complications with devices in the UK, because many complications that I have heard about do not seem to have been reported to MHRA. I have expressed my concerns to MHRA about the problems with BioSTAR® implant for 2 years because it seemed clear to me that the complications with this device are 50-100 times greater than with other PFO implants. I am unclear whether MHRA lacks the power or will to take effective action to investigate concerns or provide guidance to protect patients when there are concerns about medical implants.

I am concerned that my experiences with medical implants in my area of expertise are mirrored in other areas with ineffective and unsafe devices being CE Marked on the basis of inadequate evidence, poor science and misreporting as a result of conflicts of interest.

I believe that we need greater transparency and scrutiny of evidence used for approving medical implants. Commercial interests in confidentiality should not be allowed to take precedent over patient safety. Therefore the evidence used to obtain a CE Mark should be made public and the reasons why approval was granted should be stated. We should have a registry of all devices implanted, so that when problems are encountered the patients with that device or lot number of the device can be contacted if appropriate. We should require stricter vigilance.

June 2012

Written evidence submitted by Professor Stephen Westaby (MI 20)

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 (PMI21)

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.
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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.¹

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

¹ Not printed

versions which are currently subject to stakeholder consultation and are therefore not confidential.

Enclosure:²

- 1 . Selected draft provisions from the proposal for a Regulation on medical devices
2. Draft Commission Regulation on the designation and the supervision of notified bodies under Directives 90/385/EEC on active implantable medical devices and 93/42/EEC on medical devices
3. Draft Commission Recommendation on the audits performed by notified bodies in the field of medical devices

² Not printed