

# Expert Clinical Advice – MHRA Medical Devices

Report of the independent review on MHRA access to clinical advice and engagement with the clinical community in relation to medical devices.

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## Introduction

For medical devices, patient safety is a multi-stakeholder activity with manufacturers, Notified Bodies, regulators, healthcare professionals and patients all playing a role.

The MHRA has played a prominent leadership role in the development and management of the regulatory system in the EU and beyond. The Agency was the first in the world to flag up problems with metal-on-metal hip replacements and to issue guidance on management. Much of the Agency's work on this, breast implants and other high profile stories has been valued and used by regulators around the world.

The medical device landscape is changing with a rapid expansion in both volume and complexity. Hybrid products are being developed which combine medicine with a delivery device (for instance medicated stents) and borders between medicines and devices are becoming more blurred, The boundaries between devices designed for use in a medical setting and those for home consumers is blurring as increasingly sophisticated products are being bought over the counter or on the internet for self-management at home. More and more complex devices are being used by less skilled people.

Medical devices range from products traditionally considered low risk, such as spectacles and bandages, to those acknowledged to have higher potential for harm like heart valves and hip implants. This does not mean that serious harms are confined to high risk products. They can occur during use of 'lower tech' devices such as wheelchairs and hospital beds too.

Heightened awareness of the wide and varied nature of devices used in the care of patients and the need for enhanced vigilance around their deployment suggested the MHRA should consider opportunities to enhance collaborative working with the clinical community.

In addition, high profile events in recent years such as faulty breast implants (PIP)<sup>1,2</sup>, metal-on-metal hips<sup>3</sup> and meshes for repair of vaginal prolapse<sup>4,5</sup> have set new challenges for the Devices Division of the Agency. These, combined with new expectations arising from the Earl Howe review of the performance of the Department of Health for England and the MHRA in relation to the handling of PIP<sup>1,2</sup>; the Keogh Review of Cosmetic Surgery<sup>6</sup>; the reconfiguration of the NHS and creation of NHS England as a national commissioner; and the overhaul of the European regulatory system, made a comprehensive strategic review timely.

This report is that of an Independent Review Group set up under my chairmanship to carry out a strategic and comprehensive review of the MHRA's internal clinical resources and access to relevant external expertise in relation to the regulation of medical devices.

Managing risk in this increasingly diverse and complex landscape demands that rather than simply investigating individual adverse incidents, as might have been the case a decade ago, the MHRA now has to identify potential problems by using larger datasets, with more sophisticated data analysis techniques, as well as via more informal channels from users and patients. In particular, implanted devices constitute

a specific set of challenges associated with durability and with the complexities of effecting remedial action in the case of device failure.

The Agency should work more collaboratively with the healthcare professions and be complementary to activities rather than duplicative.

To ensure that products and procedures are performing as expected, devices have to be fit for purpose and the operators must know how to use them; significant problems can occur even if there are no problems with the device itself, if the user does not know how to use that device. Once in use, incident data needs to be collected and there need to be better processes to 'track and trace' patients who have received/used a device when a problem arises. Clear strategies and channels are needed to inform patients, the public and clinical professionals to help improve safety.

The resources available for the Devices Division within the MHRA have been diminishing over the years due to austerity measures. This has been partly offset by new ways of working, such as shifting to a risk based approach for managing adverse incident reports, but it is proving to be increasingly challenging. It has also been difficult to recruit to vacant clinical posts within the Devices Division.

When a potential safety issue comes to light, the Agency needs to ensure that full, clear and accurate information is made available promptly in a way that is easily accessible and reflects the concerns of patients, carers and healthcare professionals who are affected by doubts over the safety of specific medical devices. The MHRA has to improve the way it manages and co-ordinates communications activity; not just at the point at which a piece of formal advice needs to be issued but in the way it manages a series of communications with diverse audiences.

By working with healthcare professionals, NHS organisations, patient groups, academia and industry, the MHRA can play a pivotal role in minimising risk associated with use of medical technologies whilst facilitating the safe introduction of new and innovative treatments which can have a profound impact on patients' lives and the cost of delivery of healthcare services.

Without some risk, there can never be innovation. Nothing new would ever be tried. Ideally, the risk should be foreseen, measured, monitored and the consequences managed. We need a medical devices regulatory system which encourages the devices industry to develop new technologies which improve the quality of our lives. However, the same system needs to predict risk, detect when harm is occurring and be capable of intervening swiftly to limit adverse events.

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I would like to thank Louise Loughlin for her support in the production of this independent report.

## Summary

The Review Group was aware of the fact that some of the following recommendations are clearly within the remit of the MHRA whilst others require actions from other organisations.

## Key Recommendations

### Organisation of clinical advice input, resources and leadership

- 1 The MHRA must take devices as seriously as medicines: Create a formal mechanism for clinical advice input to MHRA.
- 2 Review the MHRA resources needed.
- 3 Ensure that adequate clinically trained staff are included in the MHRA staff.
- 4 Develop and manage the network of clinical advisors.
- 5 Develop the existing collaboration with EU bodies with similar aims to the UK MHRA.

## Other Recommendations

### Collecting and using device incident data

- 6 Build links with the Clinical Commissioning Groups to help improve the flow of information on safety and performance of devices.
- 7 Improve and simplify the way incidents are reported, aiming to obtain reports on all device incidents.
- 8 Develop means by which devices implanted in patients can be identified by their Unique Device Identifiers, and means by which patients with specific devices can be traced.

### Communications and partnerships

- 9 Improve communication about adverse incidents to patients and the public, clinical staff, clinical scientists, hospital managers and professional bodies.
- 10 Develop improved communications about the MHRA's role in ensuring the safety of devices with clinicians, clinical scientists, hospital managers and the public.
- 11 Develop collaboration with relevant English bodies, including NICE, NHS organisations, Public Health England, with the UK Academy of Medical Royal Colleges and also with devolved administrations.

### Future developments and emerging challenges

- 12 Support the safe introduction of new and innovative technologies into clinical practice.

## Recommendations

### 1. Formal organisation of clinical advice input to MHRA

The field of medical devices is expanding rapidly and there is increasing complexity of both devices and their clinical applications. The MHRA needs to have a high level oversight of devices comparable to that for medicines but designed to reflect the diversity of products, clinical applications and settings, which are more complex than those associated with medicines. A Devices Expert Advisory Committee (DEAC) should be established. The membership of the committee should be limited to the minimum required to cover the broad strategic interests of the Agency whilst being consistent with operating as a cohesive group. The DEAC should be linked to a network of specialist sub-groups and ad hoc groups designed to deliver all specialist advice to the MHRA, as necessary. There should be flexible membership of the sub-groups, depending on the topics.

### 2. Review the MHRA resources needed

The Agency needs to be staffed and configured to maintain strategic and operational relationships with a defined list of clinical organisations (Royal Colleges and specialist societies) in order to maintain a proactive dialogue about patient safety issues and to ensure that the MHRA, industry and the regulatory system are visible and better understood by the professions. It is important that the Agency is configured and resourced to ensure that those providing clinical advice from external bodies are regularly updated regarding changes in regulations and updated on activities related to the Agency's work. The Agency should be explicit to its advisers about the value of their contributions.

### 3. Ensure that adequate clinically trained staff are included in the MHRA staff

It is essential that the Agency has clinical leadership within its Devices Division that is capable of peer-to-peer dialogue with leaders of the professions and has the capability to provide strong strategic leadership both within the Agency, across government and in the broader healthcare community in the United Kingdom, Europe, and beyond. In addition to a strong practical clinical background, the clinical team needs to encompass staff who have broad regulatory expertise and experience including audit training.

The Agency should explore opportunities for fellowships, electives and other forms of secondment with training schemes for clinical staff as a means of both bringing expertise to the Agency, as well as increasing knowledge of the role of the regulator in the broader healthcare system when they return to clinical training within the NHS.

#### **4. Develop and manage the network of clinical advisors**

The MHRA has been reliant on advice on an ad hoc basis from a network of clinical advisors. This network needs to be maintained and systematically renewed and appropriately trained with the help of medical and nursing Royal Colleges and specialist societies in order to ensure that it is quality assured and reflects the range of clinical opinion, including clinical scientists. Consideration should be made to developing a training process for those enrolled into the network, to enhance their ability to provide advice which complements the regulatory role of the Agency.

#### **5. Develop the existing collaboration with EU bodies with similar aims to the UK MHRA**

The MHRA has a strong record of leadership in the EU and must ensure that this is maintained in order to serve the needs of patients and innovative industry in the UK. The absence of clinical capacity within the Agency has resulted in reduced involvement in the development of EU legislation and collaboration over the past year and this critical area must be covered in future. The quality of clinical studies associated with pre-market approval has been variable and is a key area where both legislation and management of the European system needs concentrated effort.

References to the clinical capability and capacity in 3) above are relevant to this recommendation.

#### **6. Build links with the Clinical Commissioning Groups to improve the flow of information on the safety and performance of devices**

MHRA could build links with the Clinical Commissioning Groups to help improve the flow of information on safety and performance of devices.

Although outside the remit of the MHRA, the Group made an observation that the commissioning of clinical services should include mechanisms to measure relevant outcomes in order to ensure that the quality of interventions is measured over the long-term in order that both clinical practice and product development are informed and driving continuous improvement. These mechanisms need to be proportionate, to be costed realistically and paid for. They should include on the part of clinicians obligations to fully participate in quality assurance systems such as registries where they are appropriate and exist and to report adverse incidents in a systematic and complete manner. The cost of such participation should be factored into the commissioning process and appropriate links to procurement mechanisms should be put in place.

#### **7. Improve and simplify the way incidents are reported, aiming to obtain reports on all**

Working with all participants across the healthcare system to improve adverse incident reporting is critical to the early detection and resolution of potential problems. Working with clinicians, in particular, to remove the barriers to reporting adverse incidents and

## device incidents

to ensure that those reporting understand that receiving multiple reports is the driver for intervention will be key to the Agency's ability to take timely regulatory action to minimise risk to patients. The review acknowledges that progress is being made in this area with the publication of updated GMC guidance<sup>7</sup> on reporting for device-related events and the consultation on proposals with NHS England<sup>8</sup> and the devolved administrations on improved adverse incident reporting and accountabilities within Trusts.

Without systematic collection, analysis and transmission of data it is impossible for the MHRA and professional organisations to fulfil their role in managing patient safety issues.

A "one-click" reporting system such as a stand-alone, free MHRA app that sits on all the major 'tablets', smart phones, pads, PCs, etc, would overcome some of the practical barriers to reporting adverse events in real time and is recommended for consideration of introduction. There must be as few mandatory questions as possible – the minimum information is the event; that the device can be identified; and the reporter is contactable.

## 8. Develop means by which devices implanted in patients can be identified by their Unique Device Identifiers, and means by which patients with specific devices can be traced

Access to high quality and reliable data about the performance of devices and clinical interventions over the full life of either the device or patient are critical to making effective clinical and regulatory decisions. This is becoming increasingly important because patients live longer and the number and variety of devices is increasing. The Agency must work with the clinical professions to understand the current distribution of registries and their usefulness and develop a coordinated approach that contributes to the development of rational strategies for tracking the long-term performance of devices, possibly drawing experience from other industrial sectors. A key tool for ensuring that product data are captured and linked to patient records and other databases is the adoption of Unique Device Identifiers (UDI). The Agency must push for the development and adoption of UDI and explore mechanisms for effective market surveillance using tools such as Clinical Practice Research Datalink and the similar system used by NHS Scotland. The NHS number is the obvious unique patient identifier to link to the Unique Device Identifier.

## 9. Improve communications about adverse incidents to patients

It is essential that the information that the Agency and manufacturers hold in relation to adverse incidents should be shared more effectively with professional organisations so that, where appropriate, training and

**and the public, clinical staff, clinical scientists, hospital managers and professional bodies**

education programmes can be developed to mitigate risk to patients. The relationships and architecture described above will be critical to delivery of this recommendation.

**10. Develop improved and more frequent communications with clinicians, clinical scientists, hospital managers and the public**

There is a widespread lack of understanding of the nature of the devices regulatory system and the role of the MHRA. The review recommends a strategic approach to communication with healthcare professionals, showing why and how clinicians should engage with the Agency. This complements recommendations 6) and 7) above. In addition, targeted messages need to be developed by the Agency for patients and the public. The review strongly recommends greater patient and public involvement with the Agency in order to ensure that the quality and effectiveness of communications is enhanced. This is particularly important in light of the shift of often quite complex care and associated devices from acute to homecare settings as well as a substantial increase in self-care and cosmetic interventions which sit in the consumer sector.

**11. Develop collaboration with NICE, NHS, devolved administrations, independent sector**

Patient safety is the concern of all organisations spanning the healthcare system and the MHRA must develop open and constructive relationships with key partners including NICE, the Academy of Medical Royal Colleges, NHS organisations, Public Health England, the devolved administrations and the independent sector.

**12. Support the safe introduction of new and innovative technologies into clinical practice**

The MHRA has a broad role in supporting the safe introduction of new and innovative technologies into clinical practice. To fulfil this role effectively the Agency needs access to networks which are operating at the leading edge of product and clinical innovation in order to ensure that future regulations are fit for purpose and regulation does not act as an unnecessary impediment to the introduction of beneficial new technologies.

The Review Group was mindful of the fact that some of these recommendations are clearly within the remit of the MHRA whilst others require actions from other organisations.

## Context and Terms of Reference (see Appendix B)

### The Medicines and Healthcare Products Regulatory Agency – what it is and what it does

The Medicines and Healthcare Products Regulatory Agency (MHRA) is a UK government agency which is responsible for ensuring that medicines and medical devices work and are acceptably safe. The Medicines and Healthcare products Regulatory Agency was formed in 2003 with the merger of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA). Clinical Practice Research Datalink (CPRD) became part of the organisation in April 2012. In April 2013, the Agency merged with the National Institute for Biological Standards and Control (NIBSC). It is an executive agency of the Department of Health. The MHRA is funded by the Department of Health for the regulation of medical devices, whilst the costs of medicines regulation are met through fees from the pharmaceutical industry. The Agency employs over 1200 people. Approximately 100 are in the Devices Division of whom four are clinically qualified.

The MHRA regulates a wide range of materials from medicines and medical devices to blood and therapeutic products that are derived from tissue engineering.

Medical devices is a subject matter which remains within the powers of the central UK Government for Scotland and Wales, however, for Northern Ireland powers to legislate for medical devices has been handed over to the Northern Ireland Assembly. In practice, MHRA acts on behalf of the whole of the UK on medical devices. This is because the Northern Ireland Health Minister agreed that the Secretary of State acting through the Agency would act for the whole of the UK. Because the Agency works on behalf of the whole UK, it consults the Devolved Administrations (Scotland, Wales and Northern Ireland) on, and keeps them informed of, proposed changes to legislation, policy and practice that affects them as well as giving advance notice of (and the opportunity to observe) any investigations or inspections of manufacturers based in their country.

The regulatory framework for medicines [Fig 1] is relatively longstanding, triggered by the thalidomide disaster of the early sixties. In a bid to prevent a similar occurrence, the Committee on Safety of Drugs was set up in 1963 to examine systematically the triad of safety, quality and efficacy of new medicines. This subsequently became the Committee on Safety of Medicines (CSM) under the terms of the Medicines Act of 1968, which provided the legal framework for the control of medicines in the UK. In 2005 this committee became the Commission on Human Medicines (CHM) which again has a statutory basis. The Act required medicines to be licensed before being allowed onto the UK market. All medicines were directly approved by the MHRA which issued a 'marketing authorisation', or licence. Manufacturers and wholesale dealers are also licensed directly by MHRA. Many of the provisions of the Act were superseded by regulations implementing European legislation on medicines. Those were recently consolidated under the Human Medicines Regulations 2012.

In contrast, and not least because of their heterogeneity compared to pharmacological molecules, the regulation of medical devices [Fig 2] has developed in a more ad hoc manner. Unlike the CHM, the Committee on Safety of Devices is advisory and has no statutory basis. Clinical input into the devices work of the Agency relies on a loose pool of 400 experts who are not reimbursed for their input.

The main difference between medicines and medical devices in terms of how they are regulated lies in how a product obtains market approval. Unlike drugs, which must be licensed prospectively by the MHRA (or its European counterpart), medical devices are approved by private sector organisations called 'Notified Bodies'. Once approved by a Notified Body a CE mark can be granted for a device. Notified Bodies have no involvement in the approval of low risk (Class I) devices, where self-certification by the manufacturer is sufficient and the products are simply registered with the MHRA. The MHRA audits the performance of Notified Bodies, five of which are based in the UK. A device approved by a Notifying Body in one EU country can then be marketed across the whole of the EU.

Hence, the MHRA generally becomes involved in detailed scrutiny of devices only after a problem arises. In keeping with this, 80% of the Device Division's work is on 'post-marketing' incidents; the other 20% is monitoring the UK's five Notified Bodies.

However, when a product is on the market and in use, there are more similarities than differences in the ways medicines and devices are currently regulated. There are similar systems for receiving reports of problems with products and similar ways of issuing warnings if issues are confirmed after investigation. There are also similar systems for inspection of manufacture to ensure that companies are complying with regulations, and similar ways of enforcing the law if that proves necessary.

# Medicines Development Pathway

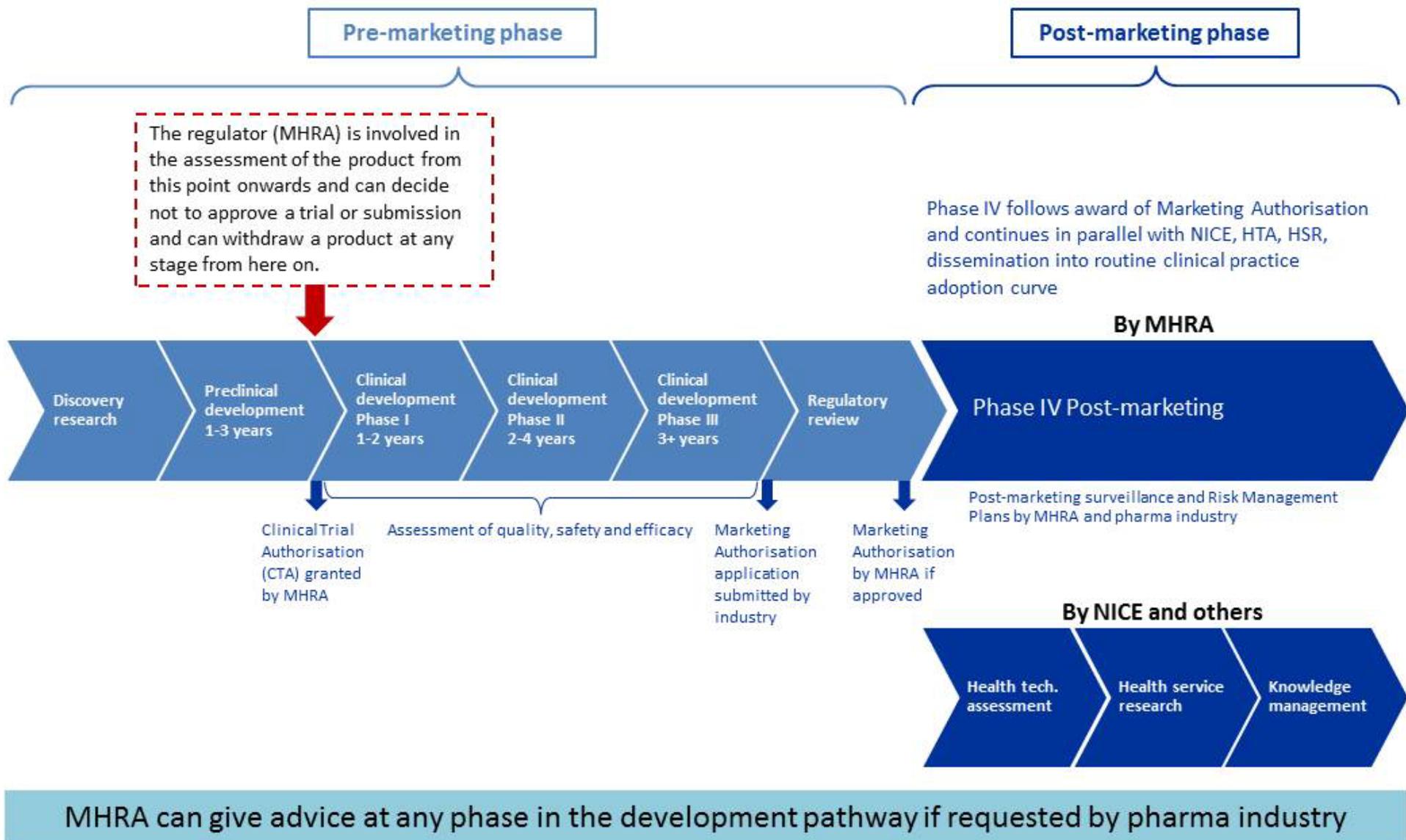


Figure 1 Overview of key stages in the medicines regulation process

# Medical Device Development Pathway

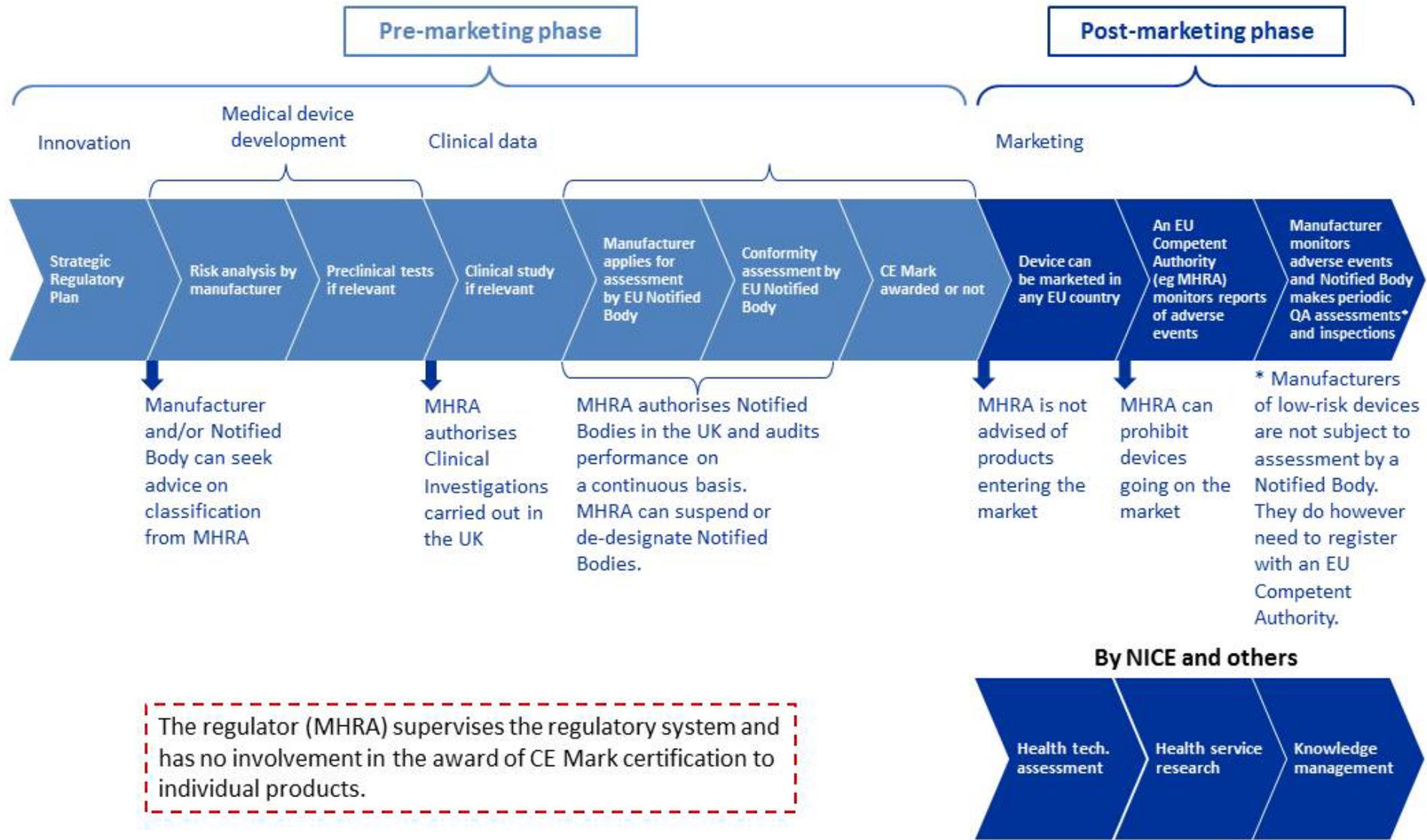


Figure 2 Overview of key stages in the device regulation process

## Examples of what Devices division does well

The MHRA and its precursors, the Medical Devices Agency and Department of Health Scientific and Technical Branch, have been at the forefront of developing medical device regulation on a global scale. The current European legislation introduced in the early 1990's was the first formal system to operate in Europe and the UK was a leader in both the design and implementation of those regulations. International collaboration at a European level has been enhanced by the formation of the Notified Bodies Operations Group (NBOG) and the Compliance and Enforcement Network (COEN), both of which were created in response to proposals from the UK.

The MHRA continues to play a leading role in the development of the system within the EU: the Agency proposed vigilance conference calls involving Member States and the European Commission which now take place on a monthly basis. The Agency held the chair of a task force which has proposed fundamental changes to the organisation and governance of mechanisms designed to enhance both strategic and operational collaboration across the European network. The MHRA also pressed for the introduction of a system of multi-country/agency audit of Notified Bodies and this has subsequently been given a legal basis as a result of implementing legislation introduced in September of 2013. The Agency participated in the first joint audit of a Notified Body which took place in January 2013: it has provided training to European officials supporting these audits whilst supplying expert staff to support audits in other Member States. The MHRA also leads, on behalf of fellow EU member states, in the area of counterfeit devices under the auspices of the Council of Europe.

On the global landscape, the MHRA led the Global Harmonisation Task Force (GHTF) working group on clinical investigations for many years. More recently, the Agency has represented European interests in the International Medical Device Regulators Forum (IMDRF) working group developing a Medical Devices Single Audit Programme (MDSAP) designed to bring greater consistency to the audit of manufacturers in increasingly global supply chains.

The National Joint Register of England, Wales and Northern Ireland was established as an outcome of the Agency's work in the early part of the millennium and provided the data which allowed the MHRA to take the first regulatory action in the world in relation to metal-on-metal hip implants. The Agency's guidance and leadership in this area has been used by regulators across the world. The Agency commissioned a literature review of reported outcomes and complications in relation to meshes and tapes for pelvic organ prolapse repair and stress urinary incontinence treatment<sup>5</sup> in 2012 which has served as a reference for regulators across the world. The MHRA has been part of a network including professional organisations which has looked to enhance the safe use of these devices in clinical practice.

More recently the MHRA has been working with NHS England and the Devolved Administrations to improve both the level of adverse incident reporting and the governance of that process, which culminated in the joint publication of a consultation with NHS England on proposals<sup>8</sup> in October of 2013. This follows on from work with the General Medical Council to clarify obligations on clinicians for reporting of

adverse incidents which were incorporated in a revision of GMC guidance<sup>7</sup> published in 2013.

## Background – the case for change

High-profile events involving the fraudulent use of unauthorised industrial grade silicon in the PIP breast implants and the withdrawal of many categories of metal-on-metal hip replacements from the market have raised questions both about the regulatory system and the role of the MHRA in managing that system. These have had the effect of raising awareness about medical devices amongst the general public and, to an extent, undermined confidence in the regulatory system. In particular, the accumulated experience of the metal-on-metal exercise had the effect of not only diminishing confidence in regulation and the regulator but also in manufacturers and orthopaedic surgeons.

Subsequently, issues around the safety and appropriate use of meshes and tapes for vaginal prolapse repair and stress incontinence have raised concerns and have been a major area of collaborative effort between the Agency and healthcare professionals.

These device problems, and the subsequent reviews by Earl Howe of the performance of DH and the MHRA in relation to the handling of PIP and by Sir Bruce Keogh of cosmetic surgery, have raised serious questions:

- How to define device ‘failure’ as opposed to ‘acceptable’ risk? Just as all medicines have a risk of adverse events, few devices work for ever in every patient. NICE suggests that a 10% revision rate for hip implants over 10 years is acceptable. However, there are approximately 14,000 hips revised each year but few reported to the MHRA.
- Should there be compulsory reporting of all individual device ‘failures’, even if the overall performance of the device and the clinical team is within the ‘acceptable’ range? If not, how does this sit with a ‘duty of candour’ as described by the Francis Inquiry<sup>9</sup>?
- As with cardiac surgery over the last decade, should the number of procedures and ‘failure’ rate be published openly – and if so, by device, or by clinician or by unit?
- How should poor performance be detected? Quality assurance in industry has developed QSUM, 6-sigma and ‘lean’ philosophies. Should the ‘production line’ stop when there is one serious event, as in the car and aircraft industries? If so, there will be consequences for patients who do not receive a device they need.
- Should every device have a unique identifier, matched to the NHS number of the recipient (a unique identifier for patients)? This would allow data linkage to outcome databases.
- What are the benefits of closer working between the MHRA as regulator, NHS procurement functions which purchase approximately 150 different types of hip implants, and NICE who advise on the efficacy and safety of procedures, but whose Interventional Procedures guidance does not consider the cost of the devices?

- Do we need other device registers? The National Joint Register costs the purchasers of hip replacements, largely the NHS, roughly £3m per year to run; it did not initially detect the problems with metal-on-metal hip replacements. Problems with small numbers of niche products can be missed, amid the larger number of routine procedures, because the hospital or clinician may not be an outlier from the overall data.
- Should submission of data to registers be compulsory, with sanctions for those who do not comply, such as reduced re-imburement through the tariff?

The Howe and Keogh reviews also raised the need for more and clearer information for the public, better and auditable training for professionals, routine incident reporting, and the need for ready access to professional, quality assured advice.

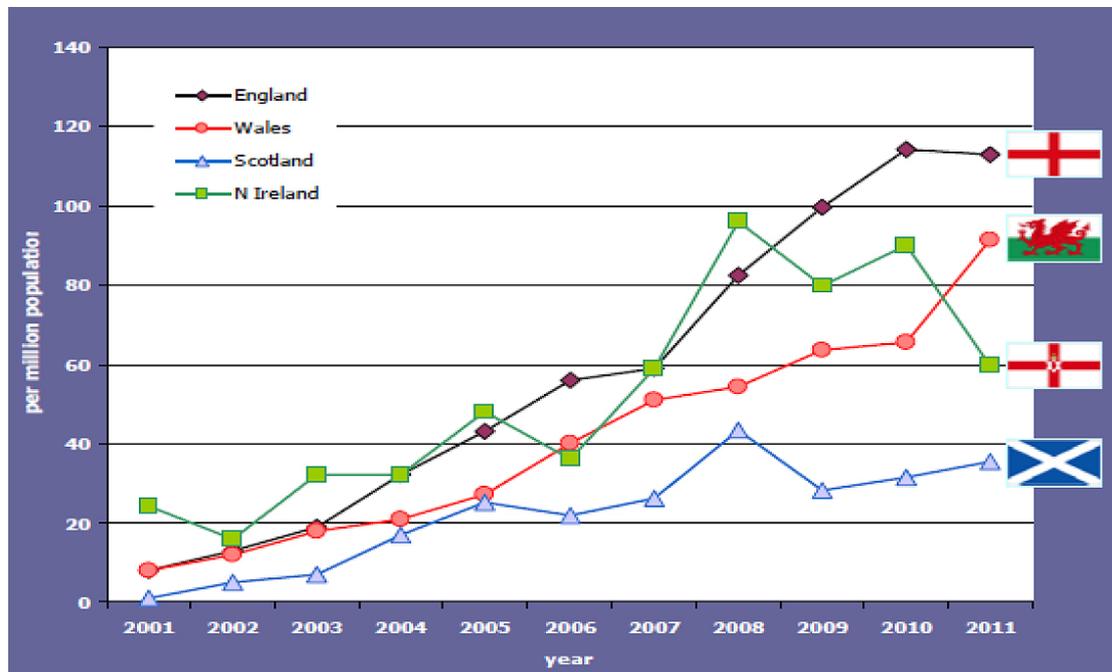
Recent emphasis on clinical governance and outcome measurement will undoubtedly increase the need for joint work between the MHRA and professional organisations in cases where medical devices are a key component of the care pathway. There have also been radical changes to the architecture of the health system in England and the establishment of new organisations focused on patient safety. This combination of developments indicates a need for the establishment of a coherent network of sustainable linkages between the MHRA and commissioners, providers and professional bodies, in order to ensure that concerns relating to medical devices are communicated and addressed in a timely and satisfactory manner.

The experience of handling the recent high-profile cases involving PIP breast implants, metal-on-metal hips and meshes and tapes for management of vaginal prolapse and stress incontinence has highlighted that when there are failures, or perceptions of failures, the reputations of industry, clinicians and regulators all suffer. There is a shared interest therefore in resolving the problems, preventing future problems and building confidence in both the products and procedures used to treat patients. This touches on the interface between product regulation and the role of training in helping to ensure successful outcomes.

Thus the MHRA faces a rapidly evolving environment where new demands are emerging in several domains. The key operational drivers are:

- Demographics – an increasingly elderly population driving up demand for devices which improve health
- Increasing range and complexity of devices and combination products (such as drug eluting vascular stents which contain a medicinal component).
- Rapid increase in the number and range of implants on the market
- Steady increase in adverse incident reports
- Increasingly complex legal environment (more litigious)
- Increased use of devices which are self-prescribed, rather than clinician prescribed and sourcing via channels outside of the control of healthcare professionals such as over the internet

There has been an accelerating growth in both innovation and application of evolving complex technologies in the UK and beyond. This is illustrated, for instance, by a six-fold increase in use of pacemakers and implantable defibrillators over the ten years 2001-2011 (Fig 3).

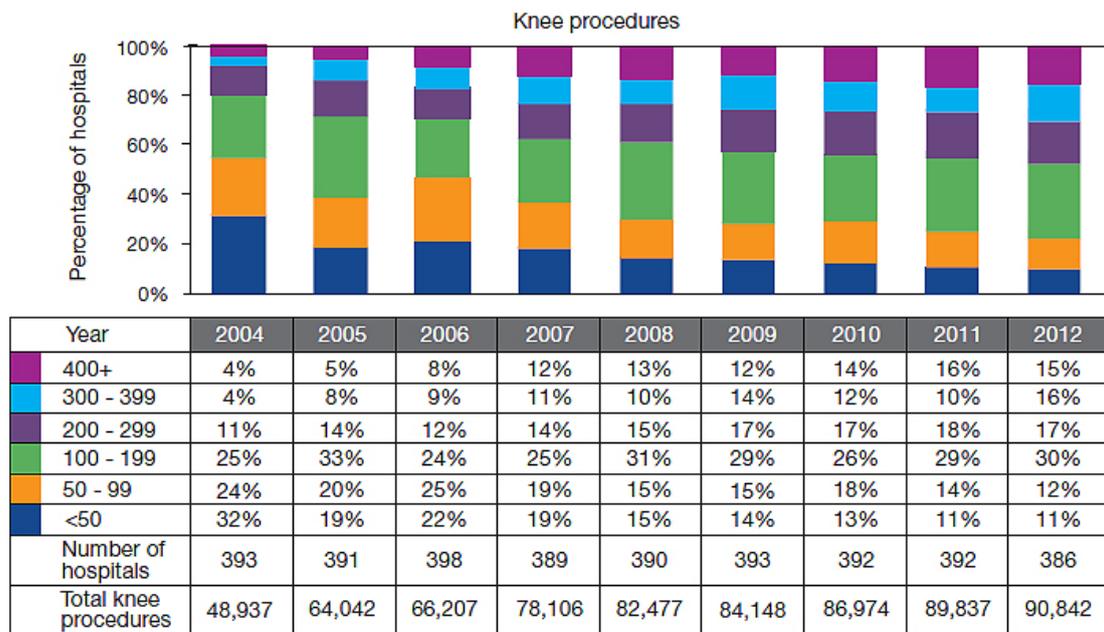
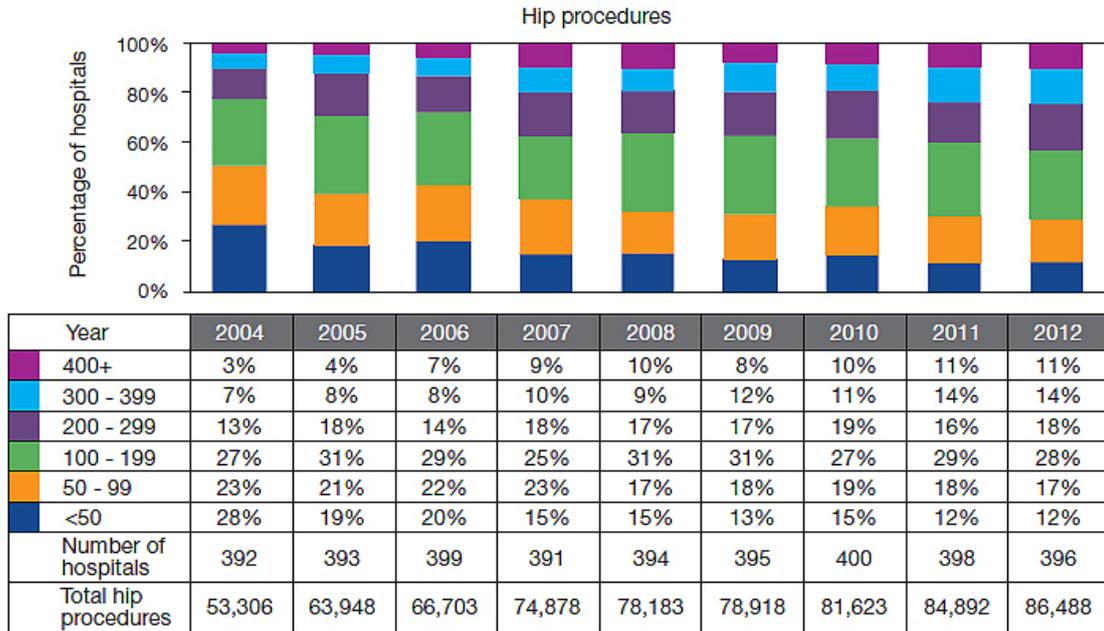


**Figure 3 Implantation of pacemakers and defibrillators in UK (Heart Rhythm UK 2012)**

It is also reflected by near doubling in the numbers of hip and knee implants (Fig 4) and a similar growth in the number of angioplasty procedures (Fig 5).

Whilst these data reflect very visible and rapid growth of activity in the acute sector, similar trends are occurring in some less invasive but often risky settings; wheelchair and hoist accidents being obvious examples, whilst a shift from gravity to pump managed infusions has seen a significant rise in reported Adverse Incidents involving infusion systems<sup>10</sup>.

Percentage of participating hospitals by number of procedures per annum, 2004 to 2012.



**Figure 4 Hip and knee implant procedures reported to National Joint Registry (2013)**

# Angiography In PCI and Angio only centres

BCIS  
2012 data: Ludman

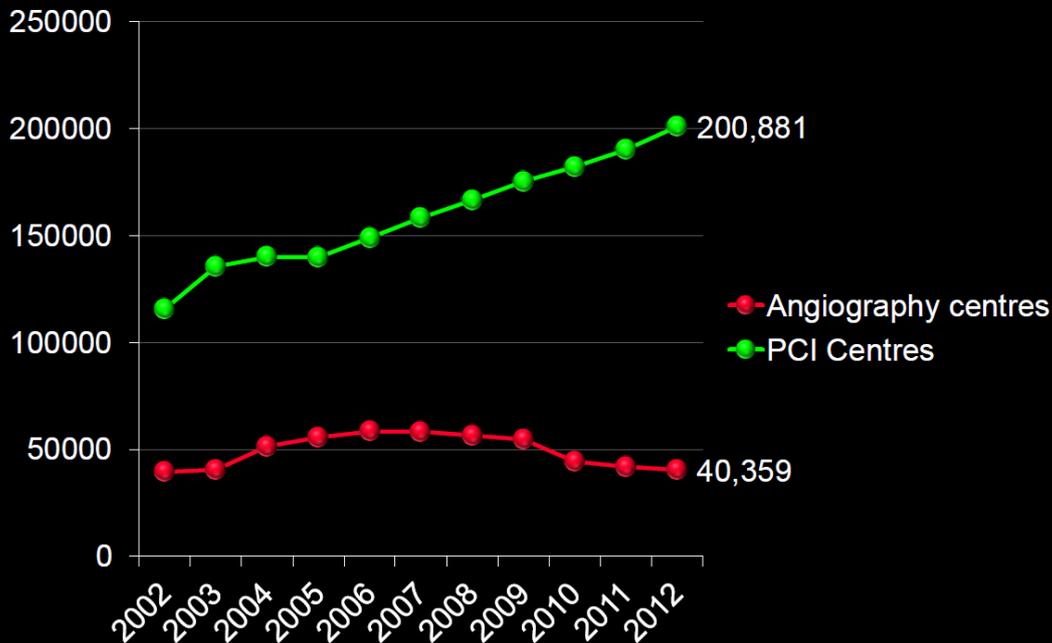


Figure 5 Angioplasty procedures in the UK (BCIS 2012) \*PCI = Percutaneous Coronary Intervention

## Strategic drivers for change

The strategic drivers for reform can be divided into three broad categories:

### Stakeholder expectations

- Patients 'live' with devices day-by-day and often for long periods: they are becoming increasingly aware, informed and assertive
- There is increased blurring of expectations around 'cosmetic' devices and potential for a substantial increase in the number and nature of procedures
- There is increased 'consumerisation' of the medical device markets (Over The Counter, cosmetic, on-line, software apps)
- There has been considerable expansion of access to information (both reliable and unreliable) via the internet, promoting patient choice
- There is a need for better Public/Patient understanding of the role, mechanisms and importance of regulation
- Technology is increasingly at the centre of health service transformation
- Transformed expectations of the clinical community – the demand for clearer guidance
- Government stakeholders are increasingly aware and have enhanced expectations of the MHRA in leading analysis and providing high quality policy advice

## **Technology**

- Increasing convergence of devices, IT and pharmaceuticals are driving ever more complex borderline issues
- Both embedded and free-standing software creating regulatory challenges for all players as well as expanding scope of device regulation
- Accelerating pace of 'new-materials' introduction (including nanotechnology and regenerative medicine) increases need for toxicology expertise and collaboration with colleagues in the medicines divisions of the MHRA
- Personalised/stratified medicine bringing new challenges to in vitro diagnostics (IVD) and potential disconnects between legislative streams
- Increasing use of technology to deliver care in the community (eg telemedicine) will create new regulatory demands and a wider stakeholder audience

## **Policy**

- Revision of EU Legislation will increase both obligations and expectations of competent authorities
- Recent 'alerts' have emphasised the need for increased collaboration amongst EU competent authorities if legislation is to be effectively and consistently implemented
- There is an increasing expectation of the EU Member States to play a key role in device vigilance
- Given the nature of the global supply chains and global markets, global regulatory harmonisation is essential if UK citizens are to be protected against failure of foreign sourced devices
- The development of the UK life sciences industries will support both patient care and the economy in the UK. A balanced and predictable regulatory environment supported by a well informed and forward thinking regulator will help to increase the attractiveness of the UK as a location for investment
- There will be a need for increased dissemination, explanation and communication of information relating to device performance with the evolving transparency agenda and forthcoming changes to the legislation.

It was recommended in the Howe Report<sup>1</sup> that the MHRA should review and further develop its communications capability to ensure that the Agency can rapidly establish and provide centralised communications regarding device alerts and related issues on an ongoing basis. This should be a proactive capability serving the needs of patients, professionals, media and public. The Agency should regularly update interested parties about progress and current information on specific safety concerns, anticipating areas of anxiety or uncertainty and managing the information and misinformation that can circulate around safety concerns. It should also constitute an easy-to-access source of data for concerned individuals. Information should always be given in as simple and understandable terms as possible.

The Howe Report also made the following recommendation; 'All parties - healthcare professionals, providers and patients, as well as industry - must be involved in the vigilance system as equal partners with the single aim of reducing the risk of harm to patients from medical device incidents. MHRA should therefore continuously review its activities to ensure that everything it does is consistent with this aim, and that it promotes this shared aim amongst all those involved in medical device vigilance.'

## Scope of the review and methods of working

The Terms of Reference of the Independent Review Group can be found at Appendix B.

The review covered both the access to suitable expertise to support the Agency's regulatory role as well as the increasingly important aspect of influencing clinical practice (for example, through sharing information, etc). In particular, the Group looked at the needs of the MHRA in the following areas:

- Linkages to professional bodies and other major stakeholders, especially in the context of outcome audits, and the implications of such audits for the professions, other stakeholders and the Agency.
- The network of accessible clinical experts, including those used to provide advice as well as those who review clinical investigation protocols.
- The role of external experts in supporting the Agency's work. The mechanism for providing for "in-depth" and strategic authoritative advice to the Agency over and above that of the individual, immediately available advisor.
- Linkages to NHS England, Public Health England, the devolved administrations, the NHS, patients and public, developers and manufacturers of devices and private sector providers. Also, interfaces with the National Institute for Health Research, National Institute for Health and Care Excellence and other bodies relevant to the MHRA's role in protecting the public health.
- The development of broader Agency capabilities for informing education and training about medical device safety and what the Devices Division needs in order to manage its network of clinical contacts.
- How the MHRA can work with clinicians through their Royal Colleges and specialist societies to facilitate registration and prospective audit of all implanted materials/devices.
- How the MHRA works with scientists, academia and industry to horizon scan.
- The leadership role of the Agency in creating an EU framework for sharing of data and using international links.

The Group met four times between September and November 2013 and sought qualitative input from major stakeholders including professional bodies (Royal Colleges and specialist societies), NHS England and the broader NHS, industry, the Committee on the Safety of Devices, Notified Bodies, National Institute for Health and Care Excellence (NICE) and the Technology Strategy Board (TSB).

Written views were sought from a wide group of interested parties and a range of stakeholders were invited to the meetings to present their views, providing an opportunity for discussion to help inform the Group's considerations. A list of those who gave their views to the Review Group can be found at Appendix C.

Observers from the Departments of Health and Business, Innovation and Skills and the Devolved Administrations were invited to attend the meetings.

### **In scope and out of scope**

Details on the regulatory and legal framework for devices, which provides additional background and context to the discussion, can be found at Appendix F.

A number of themes and key areas were considered by the Group: some issues were considered to be important, but peripheral to the scope of the review. A table of the issues within scope and outside scope of the Terms of Reference, but which are important, can be found at Appendix D.

# What we learned and heard – the basis for the recommendations

## Section 1 Organisation of clinical advice input, resources and leadership

### Create formal organisation of clinical advice input to MHRA

The structure of the existing Committee on Safety of Devices (CSD) is built around three committee meetings per year where a relatively large number of people (approximately 40) gather for a short time. If there has been a crisis, then the Agency, has already started to deal with it, through its direct contacts, and simply reports back to the CSD. So the idea of the CSD being able to bring a wealth of expertise to the Agency in the most helpful way really does not fit with the current structure. There needs to be a more flexible and responsive structure for working. There is a need to ensure that specialist advice meets requirements of individual situations. Individuals also need the ability to network effectively from national to personal level.

A structure is required which responds to this need, from achieving contact at the highest strategic level through to day to day operational contacts which involve the right people without delay. One possible way to achieve this is outlined below:

- At the most strategic level partnerships with other bodies, including professional, regulatory, industry, academia, procurement, monitoring and clinical safety, and with the devolved nations need to be at the highest level so that core and strategic issues can be prioritised and funded.
- To ensure immediate, flexible and effective contact with the right person at the right time as queries and actions arise, there must be links with clinical and scientific bodies and individual experts. This could be achieved through 'Speciality Hubs', each led by a clinical expert linked to a senior member of Devices Division staff in the MHRA, and with appropriate scientific and wider membership. This Hub would take ownership of horizon scanning, emerging issues, an up to date list of specialist advisors, managing operational aspects of device issues in their area of practice and monitoring safety. Such an arrangement would be much closer to day to day practice and patient contact and be identifiable and responsive. Activity would be driven by clinical need and much work could be done by sub-groups online or by teleconference, ensuring the system is both flexible and responsive. To illustrate the merits of this proposal, consider two potential 'Hubs' – Orthopaedic Implants and Interventional Cardiovascular Devices. The first involves expertise in materials science and the advice of orthopaedic surgeons. The second includes programmable electronic devices with both hardware and software elements which are used by cardiologists. For such different technologies to be assessed by one committee represents huge redundancy in time and expertise. Some experts might contribute to only a single agenda item.

- To ensure overarching clinical advice the chairs of speciality Hubs (by rotation), would come together with scientific and relevant non-clinical experts and Devices Division Agency staff as the Devices Expert Advisory Committee (DEAC). The DEAC would consider wider, more generic issues than the Hubs, assist with areas of significant change/difficulty/significant challenge and set annual strategy with Partners. This model would ideally result in a DEAC of approximately 10-15 members. The DEAC would have the capacity to respond to critical issues and create task groups when required to deal with particular issues that arise if needed and support speciality Hubs. Critically it would function at a level of direct engagement with partners to respond to strategic imperatives, set agreed objectives and report back to them.

### **Recommendation 1 – Create formal organisation of clinical advice input to MHRA**

The field of medical devices is expanding rapidly and there is increasing complexity of both devices and their clinical applications. The MHRA needs to have a high level oversight of devices comparable to that for medicines but designed to reflect the diversity of products, clinical applications and settings, which are more complex than those associated with medicines. A Devices Expert Advisory Committee (DEAC) should be established. The membership of the committee should be limited to the minimum required to cover the broad strategic interests of the Agency whilst being consistent with operating as a cohesive group. The DEAC should be linked to a network of specialist sub-groups and ad hoc groups designed to deliver all specialist advice to the MHRA, as necessary. There should be flexible membership of the sub-groups, depending on the topics.

### **MHRA resources**

The Devices Division has a wide range of expertise that includes biotechnology, medicine, engineering and nursing. Many members of staff have worked in academia, the healthcare sector or the medical device industry and the division deals with the whole spectrum of medical devices and equipment.

There are about 100 posts in the Devices Division and of these, four are clinical posts. The Agency as a whole has a total of approximately 65 medically qualified staff. Three of the clinical positions in the Devices Division are currently unfilled and it has been very difficult to recruit staff in this area, due to career paths and civil service pay rates, which are becoming more disconnected with NHS salaries.

Several of the interested parties who fed into the Review commented that the Devices Division seemed significantly under-resourced. Managing limited resources well and correctly allocating staff to appropriate tasks are extremely important.

It is vital to have clinicians within the MHRA Devices Division. Senior clinicians with a broad depth of knowledge who are respected within the clinical community are key. The job title of the key clinical position is also an important factor in terms of credibility and understanding externally and internally; the person in this senior role needs to be able to speak to senior clinicians in Royal Colleges and specialist societies as a respected peer.

Healthcare practitioners who are nearing the end of their clinical careers might be a useful pool of resource for the MHRA to explore. Promising younger clinicians might well be identified through secondments into the Agency and by further MHRA contributions to external MSc courses or through running an MSc course (see later).

Career development and succession planning issues need to be addressed and the steep learning curve that new joiners face should also be acknowledged. The level of competence required to carry out regulatory duties, including Audits of Notified Bodies, needs to be maintained and developed. All these considerations are challenging when set against the reduction in manpower arising out of austerity measures.

Staff are required to deal with difficult and often complex problems with specific devices, maintaining a balance between safety and the potential need to withdraw devices when withdrawal may cause greater risk. Multidisciplinary input to such decisions, including well informed clinical input, needs to be readily available as and when required.

In terms of new hybrid devices between medicines and devices, devices staff will need to work much more closely with colleagues in medicine. The benefits from synergies between the Devices Division and other parts of the Agency need to be maximised, particularly with borders blurring between what constitutes as a device or a medicine. The traditional model of medications being delivered by simple means is outdated – the ability of a device to deliver the correct volume and dose, to the correct area at the correct rate is now often the most important and complex component of a 'hybrid' system. This trend needs to be recognised through strong and harmonious partnerships between the different parts of the Agency. Recently, clinicians from the medicines side of the Agency have been assisting with the Devices Division clinical work – this has been both beneficial to the individuals and to the Devices Division and this is a model that should be built upon further. It should also be noted that new pharmacovigilance legislation adds responsibility for medication errors to the Agency and this, too, will necessitate closer collaborative working between staff involved with devices and medicines vigilance.

Device activity is increasing in volume, complexity, innovation and in parallel, inevitably, risk. The lack of investment limits the ability of the Devices Division to look beyond its essential regulatory tasks, as this Review suggests that it should. Working in partnership, much more can be achieved in horizon scanning and risk mitigation but this would need to be properly resourced.

At an operational level, clinical, scientific and non-clinical expert members need to be given time to undertake this work of significant national importance. This is a major issue for NHS employers in both primary and secondary care and consideration needs to be given regarding ways to increase employer permission. This is a central and more general issue shared with the Medical Royal Colleges and other organisations. Arrangements must be structured such that lay members can be encouraged to join and receive appropriate support.

There is a current national focus on patient safety and the current creation of new committees by Royal Colleges and others (possibly safety committees in every CCG and Trust) gives the Agency the opportunity to build national partnerships. Agency representation at specialist society safety meetings has worked well. Having a key contact for each has allowed good joint working because the Agency does not have the resources to attend all of these meetings. Bringing the key players together to discuss what needs to be achieved in terms of patient safety and devices in the next year and funding for this is an important aspect.

Within NHS England, patient safety is one the five key domains by which performance will be monitored. Since its inception in April 2013, NHS England has also absorbed the previous separate functions of the National Patient Safety Agency (NPSA), the National Reporting and Learning System (NRLS) and the National Research Ethics Service (NRES), all of which are potentially very relevant to device safety. In addition, Healthcare Quality Improvement Partnership (HQIP) has responsibility for national audits which often address safety issues. Finally, a Quality & Clinical Risk Committee reports to the Board of NHS England. The MHRA in general, and the Devices division in particular, need to engage with these different facets of a burgeoning NHS safety culture post-Francis.

#### **Recommendation 2 – Review the MHRA resources needed**

The Agency needs to be staffed and configured to maintain strategic and operational relationships with a defined list of clinical organisations (Royal Colleges and specialist societies) in order to maintain a proactive dialogue about patient safety issues and to ensure that the MHRA, industry and the regulatory system are visible and better understood by the professions.

It is important that the Agency is configured and resourced to ensure that those providing clinical advice from external bodies are regularly updated regarding changes in regulations and updated on activities related to the Agency's work. The Agency should be explicit to its advisers about the value of their contributions.

The FDA is putting considerable money into regulatory science and the MHRA could perhaps be doing more in this area, building on existing academic partnerships. In particular, an MSc in this area could be developed which includes a rotation through MHRA. The Foundation and Specialty Training programmes for trainee doctors could include a small number of options for a rotation into regulation which could be helpful for future recruitment and awareness.

Bringing public health trainees into the Devices Division on a placement would be beneficial to both parties. Working with the MRC<sup>11</sup>/Wellcome Trust<sup>12</sup> and other bodies might be another route to bringing Fellows/seconded into the Agency. The FDA runs a Regulatory Pharmaceutical Fellowship<sup>13</sup>, which is a jointly funded programme that maintains and enhances scientific links among the FDA, academia and the pharmaceutical industry. Having key set work or projects for the secondees rather than merely a shadowing role is important. These fellows can go back to their clinical practice better informed and be good ambassadors for the work of the Agency. Additionally, this could help with the Agency's academic capacity to publish more of its work into peer reviewed literature.

Having trainees or fellows might have the secondary benefit for future recruitment into clinical posts.

### **Recommendation 3 – Ensure that adequate clinically trained staff are included in the MHRA staff**

It is essential that the Agency has clinical leadership within its Devices Division that is capable of peer-to-peer dialogue with leaders of the professions and has the capability to provide strong strategic leadership both within the Agency, across government and in the broader healthcare community in the United Kingdom, Europe, and beyond. In addition to a strong practical clinical background, the clinical team needs to encompass staff who have broad regulatory expertise and experience including audit training.

The Agency should explore opportunities for fellowships, electives and other forms of secondment with training schemes for clinical staff as a means of both bringing expertise to the Agency, as well as increasing knowledge of the role of the regulator in the broader healthcare system when they return to clinical training within the NHS.

### **Develop and manage the network of clinical advisors**

With the metal-on-metal hip replacement issue, the UK was the first country to issue guidance and bringing together the Agency and the relevant clinicians, scientists and industry resulted in the MHRA playing the leading global role; this underlines that there can be good professional, multidisciplinary relations. The MHRA also needs to work constructively and proactively with a range of other major partners in industry, healthcare, regulatory, procurement and government to continue to develop and lead standards in the field of device regulation.

The MHRA maintains a register recording the special interests and skills of a wide variety of professionals that it can consult on an ad hoc basis. Whilst these are excellent contacts, the network needs to be built on a more secure footing in the future. Work needs to continue to establish and maintain personal contact with named, dedicated and quality assured experts who can bring expertise to clinical or scientific queries and problems in specific areas. This network needs to be dynamic to reflect both changes in technologies and clinical practice.

Comparison was also made between MHRA and NICE requests for expert advice<sup>14</sup>. It was thought that MHRA could be more persistent, as we heard NICE is, in its pursuit of specialist societies and their nominated advisers. The short timeframes for responding to MHRA requests for advice are, however, often difficult for experts to meet.

Rapid Response processes have been used previously for implantable devices in the area of cardiology where the Agency had a guarantee that a response from at least two experts would be provided within 48 hours. This might be an example of where the specialist societies could help ensure appropriate training of their members and the provision of advice.

There is an increasingly challenging environment with regards to the availability of clinicians to work in support of the Agency. Many Trusts are less willing than previously to release staff from frontline duties in order to provide support to the system as a whole.

In terms of non-monetary reward, feedback and thanks for the advice provided, which clinicians can then use as a reference and evidence for revalidation purposes, is an option. Researchfish (MRC) has a mechanism for researchers to record when they have been involved in providing clinical advice and this does include devices. Additional ways to recognise the contribution made by experts might be considered by Royal Colleges and other clinical professional bodies.

Many clinicians know little about the MHRA, particularly the Devices Division. Therefore there is less motivation for clinicians in helping MHRA than some other organisations (such as the Department of Health, Royal Colleges or NICE). If MHRA can raise its standing with clinicians this could improve the response they receive from clinicians.

Accreditation/credentialing for experts is a possibility that could be explored further.

#### **Recommendation 4 – Develop and manage the network of clinical advisors**

The MHRA has been reliant on advice on an ad hoc basis from a network of clinical advisors. This network needs to be maintained and systematically renewed and appropriately trained with the help of medical and nursing Royal Colleges and specialist societies in order to ensure that it is quality assured and reflects the range of clinical opinion, including clinical scientists. Consideration should be made to developing a training process for those enrolled into the network, to enhance their ability to provide advice which complements the regulatory role of the Agency.

### **EU and International role**

The MHRA has an important role in building relationships, especially with the EU. It should show leadership in current policy initiatives to address areas of concern and to improve patient safety. The Agency should continue to develop contacts and help to increase sharing of knowledge and good practice globally: routine teleconferences form part of this activity.

With regard to international advice, the Agency has good, candid communications with its European, American and Australian counterparts: they rely on one another for efficient exchange of relevant information.

The Howe Report commented that *'it is clear that there is also scope for all EU countries to work more closely together and get better at sharing information on devices, and this can and should be done within the existing regulatory framework. We must in addition work to ensure that the ongoing revision of the European regulation of devices ensures the system works robustly and that information sharing across international boundaries is comprehensive, timely and accurate.'*

As recommended in the Howe report, *The MHRA should fully support effort initiated by the European Commission to improve the operation of the regulatory system, with particular regard to higher risk devices, within the current legal framework and in advance of any specific legislative proposals the Commission brings forward.*

The MHRA should continue to collaborate and demonstrate leadership, particularly in the areas of joint inspections.

### **Pre-marketing activities and role of the Notified Bodies**

A key element of ensuring that products are placed on the market only after suitable scrutiny lies in the role of the MHRA in supervising Notified Bodies. The process by which the MHRA monitors the Notified Bodies for designation purposes is generally working well. The Review Group was informed that Notified Bodies are clear about what is expected of them in terms of audits and responses to audit findings when these are presented to them by the MHRA. The MHRA tends to give a frame of reference in terms of what the current state of thinking is regarding what they expect as a Competent Authority from Notified Bodies and manufacturers.

The regulatory environment is changing rapidly and the MHRA is closely involved in relevant arenas in Europe and internationally: it was suggested that the Agency could provide more clarity to the Notified Bodies on its understanding and expectations related to these significant changes, for example, providing guidance to coincide with publication of Commission Recommendations.

UK Notified Bodies are reliant on the MHRA to help ensure a level playing field across EU and the MHRA must therefore ensure that its input into the various European fora is not diluted. Stakeholder input into UK positioning for the European Council workgroups in light of revision of the legislation is open and transparent.

Notified Bodies and the MHRA act as “co-regulators” of medical devices. In that context it was suggested to the Review Group that the MHRA could work more in collaboration with Notified Bodies. Having a mutual understanding of expectations would improve the overall quality of design examinations and therefore result in improved patient safety.

Concerns were brought to the attention of the Review Group that declining resources at the MHRA might lead to a dilution in the capability of the Agency to perform effective audits of the activities of Notified Bodies and when necessary, individual companies.

Although outside of the scope of the Review, the Group considered that there are too many Notified Bodies, with approximately 80 across Europe. Differences in the performance of Notified Bodies across Europe may be perceived as a potential weakness in the European regulatory system.

Joint Audits (involving staff from the responsible Member State as well as other Member States and the European Commission) across Europe may help with consistency in approach for Notified Bodies and help to ensure that common standards are enforced. The MHRA should continue to play a leading role in this area

as a key component of protecting patients. Good quality clinical input into these processes is essential to the working of the system but the issue of whether Notified Bodies should employ full-time clinical staff remains an open question.

**Recommendation 5 – Develop the existing collaboration with EU bodies with similar aims to the UK MHRA**

The MHRA has a strong record of leadership in the EU and must ensure that this is maintained in order to serve the needs of patients and innovative industry in the UK. The absence of clinical capacity within the Agency has resulted in reduced involvement in the development of EU legislation and collaboration over the past year and this critical area must be covered in future. The quality of clinical studies associated with pre-market approval has been variable and is a key area where both legislation and management of the European system needs concentrated effort.

References to the clinical capability and capacity in 3) above are relevant to this recommendation.

## Section 2 Collecting and using device incident data

### Quality of products and post marketing activities

There is a huge number of products of varying quality on the market. Users should be better able to differentiate between them and to choose which ones are best to use.

Unlike medicines, medical devices require a variety of potential sources of clinical evidence to demonstrate safety and performance. In some cases blinded randomised controlled trials can be used but in many cases these are not possible to construct or they would be disproportionately expensive to conduct, without adding sufficient extra value to base decisions upon.

The issue of when an incremental improvement in a device makes it a “new device” is currently being debated in the EU. This is a matter of judgement: some changes to devices (and their intended use) make a modification high risk while others may be judged low risk (or add no additional risk). There is also the expanding area of software updates for complex electronic devices. Risk assessment is required to ascertain whether changes are minor or whether they are so radical as to constitute a ‘new device’, even if the hardware is unchanged.

The MHRA does not receive enough reports from clinicians about revisions. Hospital data collection could be improved to ensure that all revisions are captured. Significant sanctions if data on Adverse Events are not entered should be explored further, working with CQC and commissioners as appropriate.

Monitoring of implanted devices is particularly important. Once an implant has been inserted it can be difficult to remove or replace, unlike a medicine where once a

safety issue has been identified there is the option to stop taking the medication. Ongoing safety monitoring is vital for implants. It is important to appreciate that if a device fails for one person in one hundred, it is perfectly possible that it is working well for 99 out of one hundred, and that these people might suffer significant harms if their device were to be removed.

The roles of MHRA, NICE and the NHS Supply Chain could be more joined up in terms of making sure the most appropriate products are being used, with NICE looking at cost-effectiveness, the NHS Supply Chain procuring the products and the MHRA focussing on safety and placing products safely on the market.

Procurement needs to be founded on principles of patient safety and device effectiveness and not driven by cost alone. Procurement is not within the Agency's remit, but there should be sharing of device performance related information between MHRA and the NHS within commercially allowed boundaries.

Much of the post-market surveillance data collection has been initiated by industry (pacemakers in cardiology is an example) with independent clinical audits having the potential to support safety and outcomes research. To do this across the system as a whole, the use of Unique Device Identifiers (see later) would be essential. Registries which report outcomes require effective clinical oversight. In Scotland there is a group reviewing clinical quality and outcomes, which may provide further insight into developments in this area.

There is a clear opportunity to use commissioning and procurement as levers to facilitate enhanced involvement in registries and other means of outcome measurement.

**Recommendation 6 – Build links with the Clinical Commissioning Groups to improve the flow of information on the safety and performance of devices**

MHRA could build links with the Clinical Commissioning Groups to help improve the flow of information on safety and performance of devices.

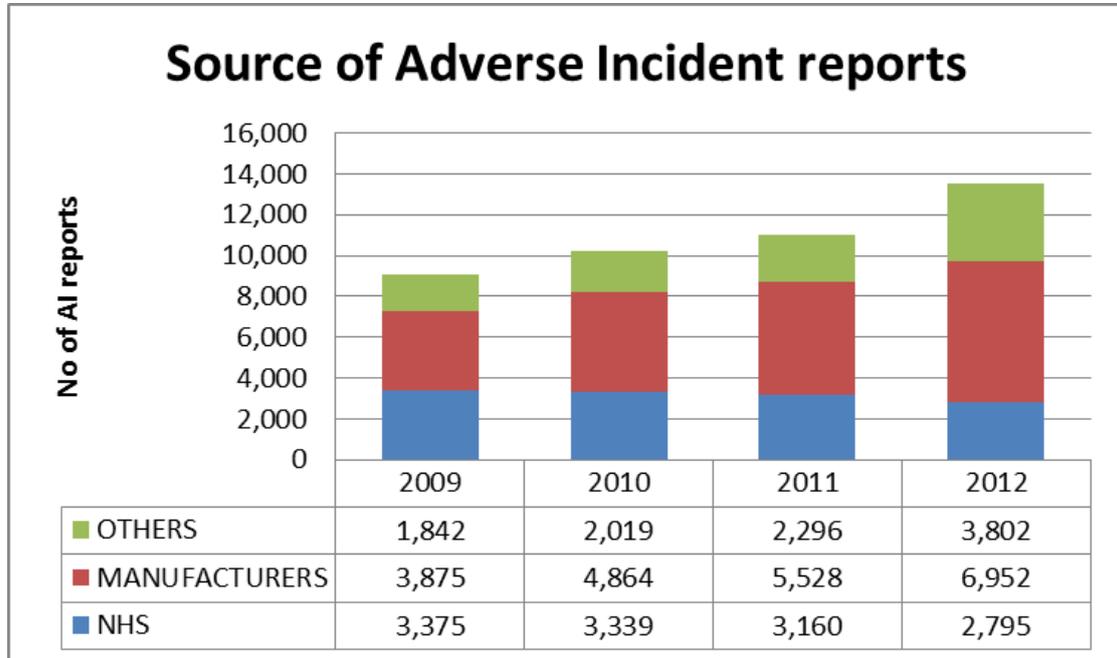
Although outside the remit of the MHRA, the Group made an observation that the commissioning of clinical services should include mechanisms to measure relevant outcomes in order to ensure that the quality of interventions is measured over the long-term in order that both clinical practice and product development are informed and driving continuous improvement. These mechanisms need to be proportionate, to be costed realistically and paid for. They should include on the part of clinicians obligations to fully participate in quality assurance systems such as registries where they are appropriate and exist and to report adverse incidents in a systematic and complete manner. The cost of such participation should be factored into the commissioning process and appropriate links to procurement mechanisms should be put in place.

## **Adverse Incident Reporting**

Adverse Incident reporting is an inherently imperfect way of collecting data. It relies upon all those involved in delivering care - clinicians, cosmetic surgery providers, and

manufacturers - playing their part in full and acknowledging the importance of adverse incident reporting in protecting patient safety. All those involved must be persuaded to redouble their efforts to improve reporting of incidents and ensure that information is shared with the MHRA. Even then, reporting will never reflect 100% of the experience with a device and this means other information must be generated and used. Adverse Incident reporting (the numerator) can only be a 'signal', not a definitive answer: unless there is a register of every device used, the denominator is unclear. It is important that the Agency continues to explore opportunities to track the number of products used in order that proportionate responses are made relative to risk to patients.

The Devices Division depends on the Adverse Incident reports it receives and the majority of these are from manufacturers, who have a legal obligation to report incidents that have happened in the UK to the MHRA. Very few reports are received from members of the public or from private healthcare providers and reports from clinicians and other healthcare professionals in the NHS have been declining over recent years despite the increase in the number and complexity of devices in use and there is no legal obligation for the NHS and private healthcare providers to report. The MHRA is working with NHS England<sup>8</sup> to try to reverse this trend. Clarity of what constitutes an Adverse Event needs to complement greater awareness of the value and role of reporting. Some specialist societies have links to the relevant section of the MHRA website on their websites in order to improve understanding of the importance of and facilitate reporting. Figure 6 shows the trends for Adverse Incident (AI) reporting for 2009 to 2012.



**FIGURE 6 Trends for Adverse Incident (AI) reporting for 2009 to 2012**

There can be reluctance amongst clinicians to report issues to the MHRA and also some confusion about whose responsibility it is to report, a situation best summed up as everyone thinks someone else is doing it. Additionally, healthcare professionals

may not report adverse incidents because they assume what has occurred is well recognised and not worthy of report. However, the MHRA relies on the number of reports it receives to generate a signal that a problem may exist, so it is most important that people continue to keep reporting, even when a problem is thought to be well known. Current hospital reporting systems are perceived to be overly complicated and need to be simplified. In some case reporters have to send multiple reports to different recipients which is inefficient and time consuming.

The information used by the manufacturers is only as good as the information it receives from the users; so this process needs to be tightened. The NHS needs to become better at providing information and there needs to be some obligation on Trusts similar to the duty of candour. There are so many people involved with a product in hospitals that nobody is sure if it is their responsibility to do the reporting. There may also be fear from employees that if they report centrally to the MHRA, it may compromise their position with their employer or precipitate unwarranted litigation.

In November 2013, in his response in Parliament to the Francis Inquiry<sup>9</sup>, the Secretary of State for Health for England said “The response gives stronger professional responsibility also, making clear the need to be open about mistakes and candid about ‘near misses’, following the example of the airline industry in building an open culture that learns from errors and corrects them.”

The Government response to the Francis Inquiry also stated:

**A new national patient safety programme across England will spread best practice and build safety skills across the country. NHS England will start the programme in April 2014 and will bring together frontline teams, experts, patients, commissioners and others to tackle specific patient safety problems, develop and test solutions, and learn from each other to improve safety. Five thousand patient safety fellows will be trained and appointed by NHS England within five years, to be champions, experts, leaders and motivators in patient safety. The fellows could be anyone, from a frontline nurse to a senior manager, who has demonstrated a commitment to and success in delivering quality improvement.**

**Better reporting of safety incidents: Experts will be asked to advise the Government on how to improve reporting of safety incidents, including whether the statutory duty of candour on organisations should cover incidents of death and severe harm, or death, severe and moderate harm.**

**To shift this reporting culture, it may help to move towards reporting via the ‘risk/safety’ staff within Trusts. Barriers to Trusts, private hospitals, GPs and care homes reporting incidents should be investigated.**

There is compulsory reporting of device incidents in France. However, despite this (or because of it) they receive no more reports per capita than the UK.

Anonymised reporting has not worked for the MHRA previously because most of the reports did not specify the products used and therefore these reports could not be followed up. There have been similar criticisms of the National Reporting and Learning System (NRLS) established by the National Patient Safety (NPSA) following the Organisation with a Memory (OWAM) Report.

Emphasising that there is a paucity of evidence and that an opportunity exists for clinicians to contribute to the evidence should be an important driver to an increase in reporting rates. The General Medical Council has updated its Good Medical Practice guidance in relation to reporting adverse incidents involving medical devices. Improving feedback to clinicians on reports to help them make better clinical decisions is important. Pre-operative checklists and procedural or operation notes could include a reminder for clinicians about whether anything should be reported; this could be a simple tick box for every device used to indicate whether there were any device issues or not. In the USA, Michigan has been a leader in patient safety – every clinical meeting or ward round starts with the question “Have we harmed a patient today?” Additionally, appraisals could present an opportunity to question clinicians about their reporting. Off-label use of devices is another area where lack of reporting needs to be explored.

With adverse events there is often a presumption that it is a device failure rather than human error, until proven otherwise. The absence of a no-blame reporting culture may act as an impediment to reporting unless there is absolute certainty that it was an issue with the device rather than user; this would be particularly relevant in the case of off-label use of devices. Improving performance and reducing adverse events is ultimately best served by an open and co-operative relationship between clinicians and industry. This will facilitate both design improvements and changes in clinical practice aimed at improving outcomes.

Reporting of incidents needs to be made as simple as possible. Data entry can take longer to complete than the procedure during which a device was inserted or used. There will be an increasing number of home device users who will also want to report a fault or problem. Setting up a very simple internet application, or mobile phone app, which could be used for reporting device problems and adverse incidents should be explored. This should be quick and easy to use, taking less than a minute or two: capable of being used by both the public and healthcare professionals. For example an app where the reporter can take a photo with a smart phone or tablet of the device/barcode with tick boxes to indicate mild, severe etc. and an optional free text box would help to provide an indication if a problem is building up through aggregated data. This would also potentially help to identify operator errors as opposed to device faults. Not everyone uses apps and not everyone is equally comfortable with this kind of modern technology but the proportion of people who are will increase over time. Carers could report on behalf of those unable to do so themselves.

The MHRA would need to continue to develop algorithms to sort and sift reports and there should be a system for risk-based investigation of adverse incidents, accompanied by careful management of expectations and good communication.

There would need to be continuing development of 'trending' to identify areas requiring increased levels of scrutiny.

The MHRA has a network of Medical Device Liaison Officers (MDLO), whose primary roles are to encourage reporting of adverse incidents, to provide feedback as required to the reporter regarding ongoing investigations, and to ensure dissemination of Medical Device Alerts to the appropriate target audiences. The MDLO system has had mixed success: part of the difficulty has been that people appointed to these posts may have been too junior to make an impact. However, the concept of having 'eyes on the ground' has been beneficial and the MHRA is working with NHS England. Experience from this exercise will be shared with the Devolved Administrations so as to establish appropriate processes to match their needs. To define the roles and responsibilities of the MDLO to obtain the best results. At Clinical Commissioning Group and Trust level, there is a need for device vigilance at senior (i.e. Board) level, to meet the collective responsibility to manage devices safely for and with patients. There should be a member of each Board (Trust, CCG, NHSE) with designated responsibility for patient safety.

One promising initiative is 'Beyond Compliance'<sup>15</sup>, a collaboration between orthopaedic surgeons, industry and others to support the safe introduction of new products.

There are three main processes that 'Beyond Compliance' has sought to address, all of which aim to improve the quality and safety of care given to patients:

1. Improving the rigour of processes around CE marking before an implant is sold by offering good quality advice.
2. Providing guidance and support for the safe and managed introduction of innovations.
3. Providing high quality surveillance and a decision-making process to identify failures at the earliest point and to suggest appropriate actions.

Surgeons need to know what failed, for what reasons, how failure was identified and whether failure could have been identified even earlier. The 'Beyond Compliance' project therefore has the potential to help surgeons practise safer surgery by ensuring that the anticipated benefits of new and innovative products are realised or else that the product is withdrawn at an early stage if they are not.

#### **Recommendation 7 – Improving Reporting across the health system**

Working with all participants across the healthcare system to improve adverse incident reporting is critical to the early detection and resolution of potential problems. Working with clinicians, in particular, to remove the barriers to reporting adverse incidents and to ensure that those reporting understand that receiving multiple reports is the driver for intervention will be key to the Agency's ability to take timely regulatory action to minimise risk to patients. The review acknowledges that progress is being made in this area with the publication of updated GMC guidance<sup>7</sup> on reporting for device-related events and the consultation on proposals

with NHS England<sup>8</sup> and the devolved administrations on improved adverse incident reporting and accountabilities within Trusts.

Without systematic collection, analysis and transmission of data it is impossible for the MHRA and professional organisations to fulfil their role in managing patient safety issues.

A “one-click” reporting system such as a stand-alone, free MHRA app that sits on all the major ‘tablets’, smart phones, pads, PCs, etc, would overcome some of the practical barriers to reporting adverse events in real time and is recommended for consideration of introduction. There must be as few mandatory questions as possible – the minimum information is the event; that the device can be identified; and the reporter is contactable.

## Registries and Unique Device Identifiers

The MHRA must be able to obtain evidence from a wider and more detailed set of sources, including robust outcomes data from clinicians. It needs to be at the forefront of using more sophisticated and rich sources of data to determine if there are problems with a device. It must have the ability to review routinely the sum total of the information about specific higher-risk devices, to ensure that the need for any further action is identified promptly. The Agency needs to investigate how to obtain data on the total number of implants and other devices in use in the range of clinical and non-clinical settings. Providing this information to clinicians and the public might also facilitate reporting and better inform selection of products.

The ability to identify which patient has received every individual device would be the ideal and steps in this direction are being taken but there will always be difficulties in achieving this. Registries are useful tools but they are not a panacea.

The National Joint Registry (NJR) has a 93% compliance rate for data entry. Other registries have lower compliance rates and there are on-going discussions about tariffs as a lever to encourage higher compliance but at the moment data entry is voluntary and there are no financial penalties if data are not submitted. Patient consent can be another obstacle to comprehensive reporting.

Another important example is the register for paediatric cardiac surgery (part of the National Institute for Cardiovascular Outcomes Research (NICOR)). There is now a mandatory requirement for paediatric cardiac surgery data to be entered, with links though evaluation and Trusts not being paid until the data have been submitted. Additionally, with NICOR, all data is entered with appropriate encryption so that patient consent is not required, but these national cardiovascular audits are designed primarily for clinical purposes not specifically for device monitoring. Nevertheless, national audits and registries can provide useful information to inform device performance and post market surveillance.

The Group heard that it has been demonstrated in Europe that transparency of performance data contained within registries has reduced the number of revision hip implant procedures in Sweden and UK. The Blue Book<sup>16</sup> provides quality improvement information for cardiac surgery.

There is now an expectation as part of revalidation for doctors to demonstrate that they are contributing their data to relevant national audits.

Good systems for data analysis are essential. Device related concerns within registries can be difficult to detect where there may be multiple factors affecting outcome. Extensive data analysis is required to establish the causality of data outliers. Where registries are developed primarily from a clinical standpoint, confounding factors may make it impossible to detect a relatively small device related effect.

The introduction of Unique Device Identifiers (UDI) will allow the linkage of devices to patients, which will enable better monitoring of devices over their life span and active follow up, for example through using the Clinical Practice Research Datalink (CPRD). The Agency should explore how to make even better use of CPRD as a tool for devices vigilance.

Clinical audits, if funded adequately, could do a lot to support device location, follow-up and post-market safety/outcome surveillance, but this is beyond the scope of this Review and would require the introduction of a Unique Device Identifier.

Currently, it is possible for national registries to link to outcome data for mortality through the Office of National Statistics (ONS). At a national level this can be encrypted/anonymised. However, individual hospitals, providing the data, would be able to identify patients if a specific device problem was encountered, provided the relevant device information and Unique Device Identifier information was available. The requirement to provide national data can be linked to commissioning as a requirement for payment of services and ultimately a service could be decommissioned if data were not being uploaded. This concept to ensure that there are mandatory mechanisms to upload data has already been instituted for a small number of new procedures at the National Specialist Commissioning level.

'Track and trace' of medical devices to allow identification of patients who have had a device implanted will be useful and work will need to continue to develop this process, with clear endpoints and as little IT cost as possible. The provision of a device information card to patients receiving an implant, such as occurs in cardiac pacing, would be beneficial and this is proposed under new legislation.

Increasing new methods of device "labelling", such as radio-frequency identification (RFID), near field communication (smart phone linkage), barcodes and digital watermarking raise the issue of cyber security and linkages.

**Recommendation 8 – Develop means by which devices implanted in patients can be identified by their Unique Device Identifiers, and means by which patients with specific devices can be traced**

Access to high quality and reliable data about the performance of devices and clinical interventions over the full life of either the device or patient are critical to making effective clinical and regulatory decisions. This is becoming increasingly important because patients live longer and the number and variety of devices is

increasing. The Agency must work with the clinical professions to understand the current distribution of registries and their usefulness and develop a coordinated approach that contributes to the development of rational strategies for tracking the long-term performance of devices, possibly drawing experience from other industrial sectors. A key tool for ensuring that product data are captured and linked to patient records and other databases is the adoption of Unique Device Identifiers (UDI). The Agency must push for the development and adoption of UDI and explore mechanisms for effective market surveillance using tools such as Clinical Practice Research Datalink and the similar system used by NHS Scotland. The NHS number is the obvious unique patient identifier to link to the Unique Device Identifier.

## **Section 3 Communications and partnerships**

### **Improve communication of adverse incidents to clinical staff, clinical scientists, hospital managers and professional bodies**

When clinical advice is given, there is a need to report back to clinical advisers on actions taken and when closure has been achieved, in order to ensure no clinically important advice or actions remain outstanding. To do less than this means that those with a formal duty of care cannot be assured that this has been fully achieved.

Medical Device Alerts are targeted to particular audiences, with active decisions on when the public needs to be told about issues using the Press Office. In terms of product recalls, the vast majority are voluntary. If there is a remedial problem then a programme for dealing with the remediation will be agreed with the manufacturers and the Agency will monitor progress. This may include the use of diverse media channels should the message be targeted at members of the public, such as in the case of failures of devices used widely in the community.

### **Recommendation 9 – Improve communications about adverse incidents to patients and the public, clinical staff, clinical scientists, hospital managers and professional bodies**

It is essential that the information that the Agency and manufacturers hold in relation to adverse incidents should be shared more effectively with professional organisations so that, where appropriate, training and education programmes can be developed to mitigate risk to patients. The relationships and architecture described earlier will be critical to delivery of this recommendation.

### **Communications and networks**

There is a general lack of awareness amongst clinicians about the role and responsibilities of the MHRA. Its public profile needs to be raised, highlighting the important work done by the Agency. The Devices Division within MHRA needs to re-establish its visibility with the external community. This must be addressed through the MHRA Communications Strategy which should recognise the importance of devices as a growing area.

The MHRA should embrace social media (especially LinkedIn and Twitter) as potential tools to monitor activity, educate, rapidly reassure and provide proactive and reactive information to stakeholders, especially the public.

Inappropriate use of devices can lead to serious injury, or even death, and there is a need for all to be aware of and educated in the safe use of devices. The sector needs to be responsive to changes in practice, such as increased home use of devices, through medical provision or over-the counter or internet purchase. Patients and the public need to know what to do if there is a safety problem with the device they are using. Channels of communication and education directly to patients and home users need to be significantly strengthened, through partnerships with NHS England, NICE, the new Clinical Commissioning Groups and Trusts. Further patient involvement within the MHRA's lay members' forum (which has representation from various committees and the Expert Advisory Groups from the medicines side but only one representative on the devices side from the CSD) is recommended.

Transparency of information relating to device performance can significantly improve the safety of devices by empowering patients and healthcare professionals, increasing scrutiny on industry and regulators and ensuring market surveillance information is better shared between Member States and more quickly acted upon. Transparency about the mechanisms for sourcing expert advice is also important. Current legislation places significant obligations on regulators in terms of what information may be disclosed with regard to devices in the market. Proposals for new legislation promise to remove many of the existing barriers to disclosure where intellectual property issues are not an overriding concern.

The Committee on Safety of Devices (CSD) considered that the two key problems in working with the MHRA have been in sharing information and in communication between the Agency and the CSD. It was felt this hindered the ability of the CSD to provide advice and support to the Agency in a timely way and to bring the substantial expertise of the CSD together to safeguard patient safety. Beyond the advice they give in the CSD itself, its members have a substantial network of clinical and academic links which could be used much more effectively. The CSD highlighted that it needs to be asked clinically relevant questions, rather than be presented only with specific areas of current concern. The CSD also highlighted that there is clear potential to use the 'collective talent' to much greater effect.

There is a lack of core information at central level, which could support the work of the MHRA. What is the size of the UK devices sector? Where are the areas of growth and innovation – the place of future opportunity and also the places where the MHRA needs to think about and mitigate risk? Where are the devices that cause harm to patients? What is the cost of that harm, to people and to the economy - to the NHS? How are these patterns changing? The lack of such information and the sharing of these important questions has led to a focus on specific areas (eg metal-on-metal hip replacements, breast implants) and discussion has taken place only after a problem has been identified and often after key actions have already been taken. This core information and consideration of trends is essential if strategic clinical questions are to be considered and problems identified so that the Agency and experts can work

together in order to trouble-shoot issues as soon as they are identified in order to minimise detrimental impact to patients.

## Education and training

The MHRA has the desire and the expertise to engage with healthcare and patient groups in education and safety issues. MHRA can give advice and information that can help with training, but the provision of the advice is done by others; MHRA does not have the resources to develop or deliver extensive training.

The MHRA only regulates the device, not the users of the devices. Bodies such as the GMC are responsible for professional regulation and the Agency could work with these organisations in terms of training requirements.

There is a concern that there are significant numbers of clinicians performing procedures involving implants without the appropriate training (particularly in dentistry) although this situation is slowly improving with annual appraisals and revalidation. There should be mandatory training for use of some devices, with users demonstrating competence. Although, MHRA will not be directly providing training, it should be working in partnership with the Royal Colleges and bodies such as Health Education England to enhance training for the benefit of patient safety. In some areas where there is a fast pace of innovation it will be particularly challenging to maintain accreditation.

### **Recommendation 10 – Develop improved and more frequent communications with clinicians, clinical scientists, hospital managers and the public**

There is a widespread lack of understanding of the nature of the devices regulatory system and the role of the MHRA. The review recommends a strategic approach to communication with healthcare professionals, showing why and how clinicians should engage with the Agency. This complements recommendations 6) and 7) above. In addition, targeted messages need to be developed by the Agency for patients and the public. The review strongly recommends greater patient and public involvement with the Agency in order to ensure that the quality and effectiveness of communications is enhanced. This is particularly important in light of the shift of often quite complex care and associated devices from acute to homecare settings as well as a substantial increase in self-care and cosmetic interventions which sit in the consumer sector.

The MHRA operates in conjunction with a number of other Government bodies, each with their own specific remit and there are areas that are interlinked. Whilst the MHRA focuses on the safety of devices on the market and ensuring safe entry into the market, NICE develops guidelines based on best evidence to help improve standards for high quality healthcare and, acting as an agent, NHS Supply Chain procures medical devices for NHS England, with equivalent organisations in the Devolved Administrations. There could be better working between these organisations in terms of sharing information to help improve device safety and ensure that the best products are being used.

Joined-up working between the MHRA and NICE is very important. Senior members of MHRA on NICE committees can be extremely useful and vice versa. In terms of improvements, it would be helpful to increase team level contact between technical staff in the two organisations, although current rules of confidentiality limit the amount of information the MHRA can release.

The MHRA's role in the pre-market process is limited to supervising the UK Notified Bodies. The Agency does not scrutinise individual products before they enter onto the market and has little or no visibility of devices coming into the UK. This limits the scope for MHRA and NICE working more in tandem in the pre-market process. The MHRA does, however, approve all clinical investigations carried out in the UK for the purposes of supporting regulatory approval to ensure that they are appropriately safe and will deliver the necessary level of evidence.

Once a device has a CE mark, a company can promote its use. However, this does not ensure that the device, when used by "experts" in the country where it was developed, can be safely used by "non-experts" in another EU country. The commissioning through evaluation (CtE) commissioning process that specialised commissioners are piloting may help reduce the likelihood of occasional and inexpert use, but at the moment it is only NICE, through its Interventional Procedures programme or Technology Appraisal guidance that helps ensure appropriate and safe introduction of new devices/technologies. The MHRA could be more "joined in" to NICE and commissioning prospectively to improve this.

**Recommendation 11 – Develop collaboration with NICE, NHS, devolved administrations, independent sector**

Patient safety is the concern of all organisations spanning the healthcare system and the MHRA must develop open and constructive relationships with key partners including NICE, the Academy of Medical Royal Colleges, NHS organisations, Public Health England, the devolved administrations and the independent sector.

## **Section 4 Future developments and emerging challenges**

### **Nurturing the innovator and protecting the patient**

In order to adopt better and safer models of healthcare for the UK population, we need innovation, especially the ability to develop good ideas and adopt them effectively and sustainably. Radical innovation will be needed to meet the emerging health challenges of an ageing population, often with several co-morbidities, and the financial pressure to provide the best care possible as close to home as possible.

However, innovation cannot occur without some risk. Without acceptance of a degree of risk nothing new would ever be tried. Ideally, the risk should be foreseen, measured, monitored and the consequences managed. We need a regulatory system which encourages the devices industry to develop new technologies which

improve the quality of our lives. However, the same system must detect when harm is occurring and be capable of intervening swiftly to limit adverse events.

Broadly, innovation is likely to include four main sources of new devices:

1. Modification of existing 'platforms' eg Miniaturisation of ultrasound scanners for more routine use by non-radiologists at the bedside and in the community. An ultrasound probe which can be used by midwives has been developed which plugs into a smart phone and displays the scan on the phone screen.
2. IT to improve productivity and reduce costs - "doing more for less cost".
3. Stratified medicine and the need for companion diagnostics/diagnostic devices.
4. Greater convergence of other therapeutic platform technologies (eg small molecule drugs, biologics, cell therapy and gene therapy) with devices.

All innovations can carry a finite risk of harm and those with significant risks must be evaluated once in use in patients. The IDEAL system<sup>17</sup> has been proposed as a model for reporting on the use and outcomes of new procedures (which often involve devices) from their first use in man, through their development and clinical study, to monitoring in the long term.

## No surgical innovation without evaluation: the IDEAL recommendations

*Peter McCulloch, Douglas G Altman, W Bruce Campbell, David R Flum, Paul Glasziou, John C Marshall, Jon Nicholl, for the Balliol Collaboration\**

Surgery and other invasive therapies are complex interventions, the assessment of which is challenged by factors that depend on operator, team, and setting, such as learning curves, quality variations, and perception of equipoise. We propose recommendations for the assessment of surgery based on a five-stage description of the surgical development process. We also encourage the widespread use of prospective databases and registries. Reports of new techniques should be registered as a professional duty, anonymously if necessary when outcomes are adverse. Case series studies should be replaced by prospective development studies for early technical modifications and by prospective research databases for later pre-trial evaluation. Protocols for these studies should be registered publicly. Statistical process control techniques can be useful in both early and late assessment. Randomised trials should be used whenever

*Lancet 2009; 374: 1105-12*

*See Editorial page 1037*

*See Comment page 1039*

*This is the third in a Series of three papers on surgical innovation and evaluation*

*\*For members see Lancet 2009; 374: 1089-96*

## Horizon scanning

The MHRA needs to improve its ability to horizon scan, in order to adapt to the increase in size and complexity of the devices sector, and to mitigate risk as new technologies appear. Clinical input into strategy development and informing policy is important.

Free-standing software is now classed as a medical device. However, there is a blurred line between those types of software with a medical purpose and those with primarily "lifestyle" applications. An example of this would be devices that aim to help prevent development of diabetes in those at risk. Medical simulation devices used for training purposes are not classed as devices as they serve no diagnostic or therapeutic purpose.

It is imperative for the MHRA to take a lead in the regulation of stratified medicine and companion diagnostics if the UK is to be a world-leader in this area and maximally benefit from the substantial government-funded activities in the area, including the planned £50m Stratified Medicines Catapult<sup>18</sup>. £200m is targeted for stratified medicine.

The Agency could work more closely with others in this area, such as the Technology Strategy Board, academia and the Horizon Scanning Centre. A Devices Forum, where a particular topic, such as nano-materials or synthetic hollow organ replacement devices, could be discussed, bringing together the relevant people, would be a valuable tool. This could build on the existing Medical Device Technology Forum programme. Working in partnership in the education of professionals and home users is also required. Increased public visibility of the MHRA to companies developing new devices is needed; this is not easy as a large proportion of the UK medtech industry is made up of SMEs. This will require working through medtech networks and possibly with the recently formed Academic Health Science Networks (AHSNs).

Keeping better abreast of developments in devices will help the Agency to develop and influence regulations at an early stage.

**Recommendation 12 – Support the safe introduction of new and innovative technologies into clinical practice**

The MHRA has a broad role in supporting the safe introduction of new and innovative technologies into clinical practice. To fulfil this role effectively the Agency needs access to networks which are operating at the leading edge of product and clinical innovation in order to ensure that future regulations are fit for purpose and regulation does not act as an unnecessary impediment to the introduction of beneficial new technologies.

## Other emerging challenges

### Cosmetics

There has been a rise in the use of devices for cosmetic purposes. Dermal filler injections are a specific cause for concern. Adverse incidents related to their use range from mild and self-limiting problems to those which cause chronic disability and even death. The incidence rate of adverse events is difficult to know because the number of injections/treatments per year is not known. The general consensus is that temporary fillers such as hyaluronic acid (HA) are safe and permanent fillers less so. Some manufacturers have robust adverse events reporting systems in place with effective audit trails, suggesting favourable safety profiles; however these systems are dependent on information provided to the manufacturer, usually by the injector or the patient.

In the UK, there is no restriction on who is allowed to inject dermal fillers and practitioner background is diverse, ranging from dermatologists and plastic surgeons to beauticians, hairdressers and self-injectors. Under-reporting of adverse incidents is likely to be due in part to lack of familiarity with reporting systems and in part to an inability to recognise complications.

Good practice is evidence-based and more data on adverse events caused by nonsurgical cosmetic procedures may lead to improved patient safety. Boundaries

between frank skin disease and “poor cosmetic outcome” may be unclear, particularly if the practitioner has no clinical qualification or diagnostic ability.

Building up public awareness about the potential dangers involved in the use of cosmetic devices would be a useful step in influencing those considering these treatments and so improving the situation.

### **Shift from use of devices from secondary care setting into community**

There is a shift towards use of devices of increasing complexity into the community and by patients in their homes. The technology of the future will involve increasing numbers of “intelligent” devices which make measurements of physiological parameters or disease markers. Such devices may even “intelligently” deliver treatment in someone’s home, based on these measurements, or provide feedback to patients or those caring for them.

### **Fraudulent activity**

While regulatory systems can aim to deter, and minimise the risk of deliberate subversion and fraud, it would be unrealistic to expect any regulatory system to be completely impervious to deliberate and potentially criminal actions intended to undermine or bypass its operation. It is particularly important that any regulatory response is risk and evidence-based. The vast majority of the industry see the regulations as a significant component of their own risk management programmes and adhere to the rules.

As a point of principle, the best response to subversion of existing regulatory requirements is unlikely to be a fundamental change in those requirements. Better implementation across Europe of post-marketing surveillance arrangements may provide greater deterrent to any future attempts at deliberate fraud, and should offer patients improved reassurance.

The Agency is limited in what it is able to do when a company closes down after problems have been identified with one of its devices, but if the company is still in existence then a variety of regulatory tools that can be and are used. Expectations need to be managed in terms of what the Agency can and cannot do; this should be part of the Agency’s Communications Strategy.

## Conclusions

This Independent Review is intended to provide the Chairman and the Chief Executive of the MHRA with the Review Group's views and recommendations for the Agency's consideration, in the context of proportionality and regulatory cost. Some of the recommendations will be easier and quicker to take forward while others will require further development and prioritisation. The key recommendations that relate to how the MHRA operates could be implemented relatively quickly whilst those which involve influencing and working with others will require a more strategic approach.

The MHRA plays a leading role in the safety of medical devices and it operates in an environment which is changing with increasing challenges. The number, diversity and complexity of devices is increasing. There are changes in public perceptions and expectations in relation to medical devices, as well as the ways in which they are used, and where. The device sector used to be dwarfed by the pharmaceutical industry but this is no longer the case<sup>19,20</sup> and with the new risk profile for devices, MHRA needs to focus on identifying issues earlier and minimising risk. The MHRA needs to increase the priority it affords to devices and establish a new Devices Expert Advisory Committee (DEAC).

The safe use of devices is becoming an increasingly networked activity. The MHRA needs to work with the Royal Colleges and specialist societies and in partnership with these and other bodies, such as NICE and NHS England. The MHRA will need to make continued efforts with its key stakeholders to increase Adverse Incident reporting, which is critical to the early detection and resolution of potential problems with devices. Communications with both healthcare professionals and with the public about the benefits and risks of devices need to be improved, particularly with the challenges of increased use of more complex devices in the home setting and cosmetics.

The MHRA needs to maintain its leading role in Europe. It must support innovation and ensure that any future regulations are fit for purpose and serve the needs of patients.

## Appendices

Appendix A: Membership of the Independent Review Group

Appendix B: Terms of Reference for the Independent Review Group

Appendix C: Organisations providing views

Appendix D: Table of topics and themes – in and out of scope

Appendix E: Size of the Devices Sector and funding

Appendix F: The regulatory framework for medical devices

Appendix G: CE classification

Appendix H: MedTech Industry - Key figures

## Appendix A: Membership of the Independent Review Group

### Chair

Professor	Terence	Stephenson	Chairman of the Academy of Medical Royal Colleges
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### Members

Professor	Norman	Williams	Royal College of Surgeons
Mr	Peter	Kay	Royal College of Surgeons
Professor	Bruce	Campbell	National Institute for Health and Care Excellence
Professor	Chris	Mason	London Regenerative Medicine Network/UCL
Professor	Patricia	Peattie	AoMRC Patient Lay Group
Dr	Archie	Prentice	The Royal College of Pathologists
Mr	Dominic	Meek	Royal College of Physicians and Surgeons of Glasgow
Dr	Iain	Simpson	Royal College of Physicians London/British Cardiovascular Society
Mr	Simon	Emery	Chairman of the Academy of Medical Royal Colleges -Wales
Miss	Kathy	Harley	Faculty of Dental Surgery
Ms	Vivienne	Parry	Broadcaster and science writer
Dr	J-P	van Besouw	The Royal College of Anaesthetists
Professor	Alison	Noble	Royal Academy of Engineering
Ms	Sandra	Lawrence	Association of British Healthcare Industry (ABHI)
Mr	Richard	Milner	British Association of Plastic Reconstructive and Aesthetic Surgeons
Mr	Mark	Henley	
Professor	Alan	Murray	Healthcare Scientist, University of Newcastle

### **Invited Observers and Secretariat**

Mr	John	Williams	Non-Executive Director, ex-Chair of CSD
Mr	John	Wilkinson	Director - Devices Division, MHRA
Mr	Jonathan	Mogford	Director - Policy, MHRA
Ms	Rachel	Bosworth	Director - Communications, MHRA
Ms	Agatha	Ferrao	Department of Health - England
Ms	Anya	Tahir	Department of Health - England
Mr	Martin	Donnelly	DH - Northern Ireland
Dr	Sara	Davies	DG Health and Social Care - Scotland
Mr	Mike	Baxter	DG Health and Social Care - Scotland
Mr	Darren	Ormond	DHSS - Wales
Mr	Carl	Eley	DHSS - Wales
Mr	Graeme	Sandell	BIS
Mrs	Louise	Loughlin	Office of the Chairman & Chief Executive, MHRA
Ms	Asha	Batchelor	Policy Division, MHRA

## **Appendix B: Terms of reference - independent review of expert clinical advice in support of MHRA's medical device regulation**

In the public health interest, the MHRA regulates medical devices to ensure they fulfil their purpose and are acceptably safe. The field of medical devices evolves continuously with the introduction of new science and technologies that introduce new regulatory challenges.

The Independent Review Group will carry out a strategic and comprehensive review of the MHRA's internal technical and clinical resources and access to relevant external expertise in relation to the regulation of medical devices.

In particular the Group will look at the needs of the MHRA in the following areas:

- Linkages to professional bodies and other major stakeholders, especially in the context of outcome audits, and the implications of such audits for the professions, other stakeholders and the Agency.
- The network of accessible clinical experts, including those used to providing advice as well as those who review clinical investigation protocols.
- The role of external experts in supporting the Agency's work. The mechanism for providing for "in-depth" and strategic authoritative advice to the Agency over and above that of the individual, immediately available advisor.
- Linkages to NHS England, Public Health England, the devolved administrations, the NHS, patients and public, developers of devices and private sector providers. Also, interfaces with the National Institute for Health Research, National Institute for Health and Care Excellence and other bodies relevant to the MHRA's role in protecting the public health.
- The development of broader Agency capabilities for informing education and training about medical device safety and what does the Devices Division need in order to manage the network of clinical contacts.
- How the MHRA can work with clinicians through their Colleges and Specialist Societies to facilitate registration and prospective audit of all implanted materials/devices.
- How the MHRA works with scientists, academia and industry to horizon scan.
- The leadership role of the Agency in creating an EU framework for sharing of data and using international links.

### **The Independent Review Group will meet these responsibilities by:**

Seeking qualitative input from major stakeholders including:

- Representatives of patients, carers and the public
- Professional bodies (Royal Colleges and Specialist Societies)

- The Departments of Health and Business, Innovation and Skills (or equivalent across the four nations)
- NHS England and the broader NHS
- Industry
- The Agency Board and Corporate Executive Team
- The existing members of the Committee on the Safety of Devices
- Notified Bodies
- The European Commission
- National Institute for Health and Care Excellence (NICE), National Institute for Health Research (NIHR), Technology Strategy Board (TSB)

### Frequency of meetings

- The Group will meet in September, October and November in 2013

### Independent Review Group reporting

- The Review Group will prepare an independent report by end of December 2013

### Independent Review Group Membership

The membership is made up of:

- The Chair of the Independent Review Group;
- Representatives from the Royal Colleges, relevant national Societies, expertise from key disciplines:
  - Vice Presidents or Chairs of their Safety Committees
  - Presidents of the Royal Colleges or their nominees
  - Relevant national Societies
  - 4 Nations
  - Dentistry
  - Industry background - expertise on materials etc
  - Expertise from Surgery, Anaesthetics, Imaging, Intensive care, Toxicology, Cellular therapies/regenerative medicines, Cardiology
- Secretariat will be provided by the Agency

## Appendix C: Organisations which provided views to the Independent Review Group

Organisation
Association of British Healthcare Industries (ABHI)
British Association of Dermatologists (BAD)
British Cardiovascular Society (BCS) with the Royal College of Physicians (RCP)
British Orthopaedic Association (BOA)
British Society of Interventional Radiology (BSIR)
British Standards Institute (BSI)
Committee on the Safety of Devices (CSD)
Diabetes UK
Faculty of Dental Surgeons
Health Facilities Scotland (HFS), Incident Reporting and Investigation Centre
Health Knowledge Transfer Network
National Joint Registry - HQIP
National Institute for Healthcare and Clinical Excellence (NICE)
NHS England (Sir Bruce Keogh's team)
NHS Supply Chain
Northern Ireland Adverse Incident Centre (NIAIC)
Professor Alan Murray, Healthcare Scientist, Professor of Cardiovascular Physics and author of 'Medical Devices: Use and Safety'.
Public Health Agency, Northern Ireland
Royal College of Anaesthetists
Royal College of Obstetricians and Gynaecologists (RCOG)
Royal College of Surgeons, Edinburgh
Scottish Health Technologies Group (SHGT) on behalf of Healthcare Improvement Scotland
Team NB
Technology Strategy Board
UK Ophthalmic Pharmacy Group

## Appendix D: Table of topics and themes

Terms of Reference	In Scope		Out of Scope, but important
1) Linkages to professions and others	Adverse Incident (AI) Reporting and Analysis Communications Safety Committees Patient Involvement	Communications, patient involvement and resources	Unique Device Identifier (UDI) Duty of candour
2) Expert Network	AI Reporting and Analysis Advice to Notified Bodies (NB) Audit – Internal Expertise 'Free' advice/Indemnity/Reward		UDI Number/quality of NBs Joint Inspections (capability/capacity)
3) Role of Experts - Ad hoc groups - Regular committee (governance/management)	AI Reporting & Analysis Advice to NBs Audit of NBs & MHRA processes Accreditation – Clinical expertise Regulatory Knowledge 'Free' advice/Indemnity		UDI
4) Linkages – NICE, PHE, NHS	AI Reporting & Analysis Safety Committees		UDI
5) Agency Capability, Informing, Education & training	Secondment/Academic Partnership AI Reporting and Analysis Communications Clinical capability/capacity		Science capacity UDI Fraudulent activity/ counterfeits
6) Registries	Data linkage – Science/analysis capability Clinical capacity		UDI Registry compliance Cost-benefit of registries Quality of products Procurement Clinician/Institutional outliers
7) Horizon Scanning	Innovation/Software/Stratified Medicines Capacity/Training		Science capacity
8) EU & International Leadership	Communications Clinical Evidence Innovation/ Software/Stratified Medicines		Fraudulent activity/ Counterfeits Joint audits Legislation development

## Appendix E: Size of the devices sector and funding

### The European medical devices market

Eucomed's 2012 industry figures report estimates the size of the European medical devices market at 100bn Euros. As a percentage of the world medical technology market this is 28% (fig 1). Eucomed also calculate that the medical technologies market in Europe is currently growing at a rate of 4% per annum (fig 2.).

World medical technology market\* by region, based upon manufacturer prices, 2012<sup>9</sup>

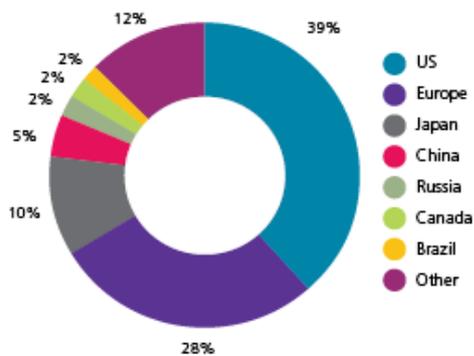


FIGURE 1

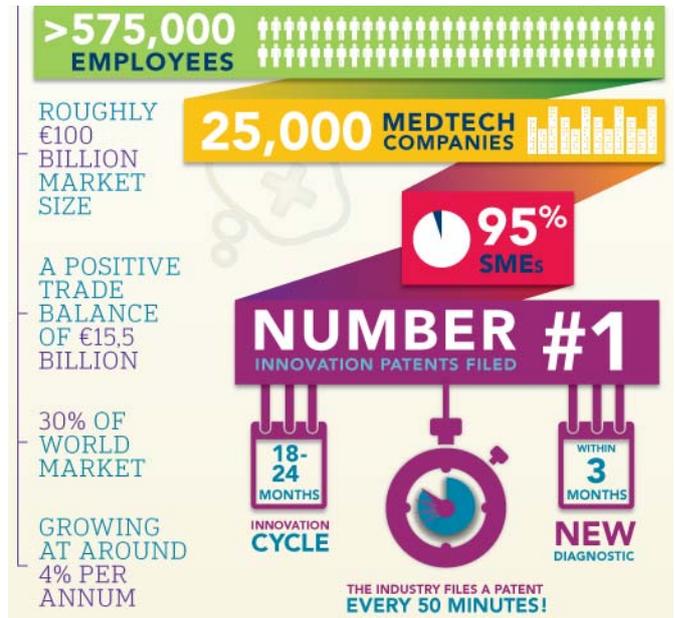


FIGURE 2

Medical Technologies are growing at a faster rate than the pharmaceutical industry. As an example of this, patent requests to the European Patent Office (EPO for medical technologies are almost double that for pharmaceuticals (fig 3). In addition over the last decade medical technologies have seen a steady increase in EPO patent filings whilst pharmaceuticals have remained stagnant.

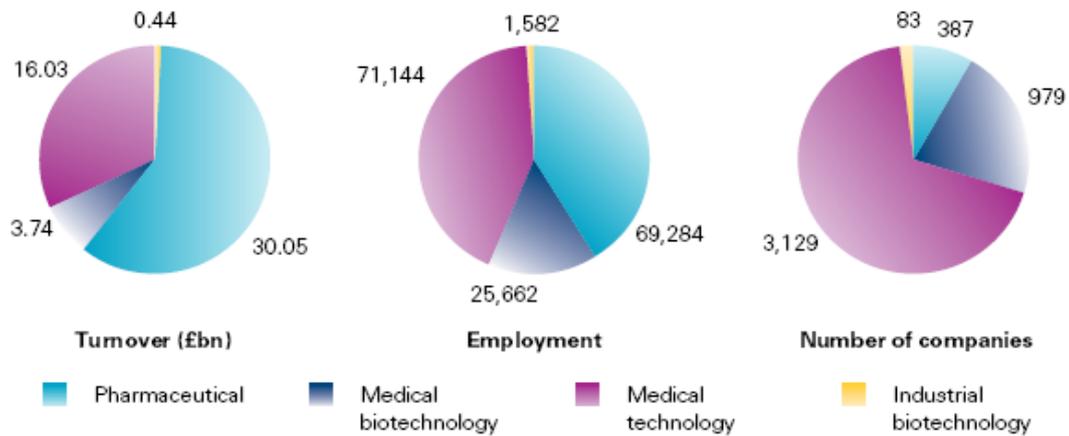
Top technical fields in patent applications. Number of patent applications filed with EPO, 2012<sup>2</sup>



FIGURE 3

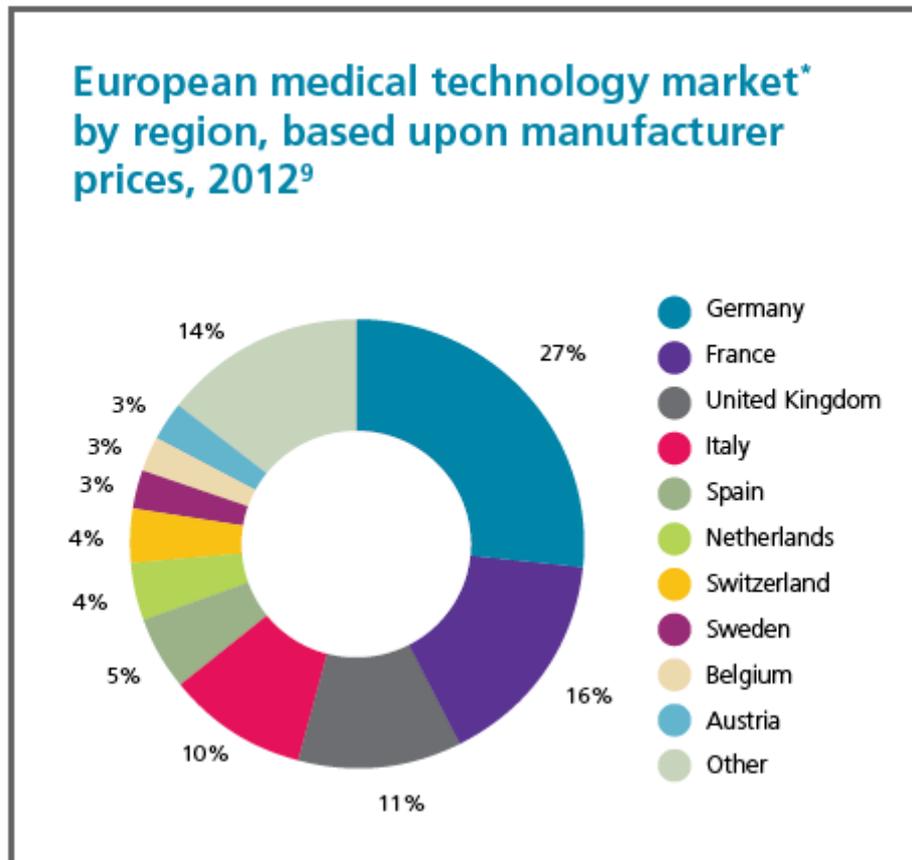
## The UK medical devices market

In 2010 the Department for Business, Innovation and Skill figures showed the medical technology sector in the UK consists of 2,771 companies generating £10.6bn of turnover. The most recent BIS figures show an increase in both figures with 3,129 companies and a turnover for Medical Technologies of £16.03bn (fig 4).



**FIGURE 4**

As a percentage of the EU medical technologies market, Eucomed currently shows the UK as having an 11% share (fig 5).



**FIGURE 5**

## Current funding scheme

Medical device regulation by the MHRA in the UK is funded through general taxation. Increasingly, it is becoming apparent that the current level of funding is insufficient for the system to be able to function effectively and provide the level of protection that is required to adequately safeguard public health.

At a time of increasing pressure on Government budgets, and with a recast of the existing medical devices directives on the horizon, now is a critical time to consider the possibility of alternative funding to resource the MHRA's medical devices activity, putting medical device regulation on a sustainable footing to function and develop going forward.

A lack of resources creates issues both pre- and post-market, through potentially inconsistent oversight of Notified Bodies and insufficient resources available for vigilance and enforcement functions. It also has a knock-on effect on the ability to provide manufacturers and industry with the consistency and predictability that they require to function effectively.

Significant reliance on Government funding may impair the ability of regulatory authorities to fully implement the current regulatory system aside from any future proposed changes. It also may cause difficulties for authorities in appropriately resource their activities, planning and further developing their oversight and building their competencies and expertise. This may not allow for the appropriate level of protection of public health to be afforded to patients.

## Appendix F: The regulatory framework for medical devices

Medical devices are defined as all healthcare products, other than medicines, used for the diagnosis, prevention, monitoring and treatment of disease, injury or disability. Medical devices bring widespread benefits for patients and the public but no product is free of risk. Regulatory decisions therefore involve weighing risks of harm against the likelihood of benefits and determining whether the risks that exist are outweighed by the benefits that the device brings. If a product is available for use, its risks must be acceptable in relation to the potential benefits to patients and users.

### The legal framework for medical device regulation

Medical devices are regulated under the provisions of a number of EU Directives, covering different categories of medical device. The overarching legislative framework for medical devices is part of the EU's 'New Legislative Framework', which is concerned with facilitating operation of the single market in various areas of product legislation. The principles of this Framework are common across a number of sectors; they are used, for example, in relation to the safety of toys and personal protective equipment. The relevant EU Directives are translated into Medical Device Regulations in UK law.

Broadly, these regulations bring into UK law EU Directives that set out:

- how device manufacturers must ensure that the devices they manufacture are safe and fit for purpose;
- how this is certified prior to marketing;
- who is able to undertake certification;
- how marketed devices should be registered;
- how incidents involving death or serious deterioration of health related to devices must be reported by manufacturers to the competent authority (in the UK, the Medicines and Healthcare products Regulatory Agency – MHRA);
- what the competent authority must do with that information; and
- how the competent authority can inspect, monitor, investigate and enforce compliance with the regulations.

### **(i) Pre-marketing**

Higher risk medical devices such as breast implants are certified by third-party private sector organisations called 'Notified Bodies'. There are over 80 of these independent organisations across Europe, including six in the UK. The role of notified bodies in relation to medical device regulation is to determine whether a particular medical device meets the relevant regulatory requirements and, whether, when used as intended, it works properly and is acceptably safe. This process is known as a conformity assessment.

If a device is assessed by the notified body as meeting the accepted standards of safety, the notified body issues a certificate of conformity which authorises use of a CE mark of conformity. This allows the device to be marketed in all EU countries without further controls.

A manufacturer can select any notified body across Europe, irrespective of location, to assess their product for a CE mark, provided that their field of expertise covers the device being considered. Once assessed and approved for market, the device can be sold in all other EU countries without further assessment by the regulatory bodies in that country (ie the marketing of a device must be allowed in the UK if a notified body in another EU country has approved the device for a CE mark).

For very low-risk devices, such as non-medicated bandages, the CE mark can be applied without independent assessment by a notified body on the basis of a declaration of conformity by the manufacturer.

The manufacturer must develop a quality system to ensure that the production and the product continue to conform to regulatory requirements. The system must include arrangements to obtain, record and review experience of the device from the marketing phase, including reviews of risk analysis and plans for any corrective action that may be required. EU guidance stipulates that this should include reviewing data on long-term effects, in particular in relation to chronic toxicity. This system must also enable the manufacturer to fulfil their obligation to notify the competent authorities of incidents related to their devices immediately on learning of them.

The Notified Body must audit the quality system to determine that it meets the necessary requirements.

### **The role of the competent authority**

Central to EU medical device regulation is the concept of the 'competent authority'. In the UK, the MHRA is the competent authority and has a number of responsibilities for the regulation of devices and promotion of medical device safety.

Competent authorities are responsible for authorising and regularly auditing the performance of notified bodies. Each competent authority is responsible for the designation and authorisation of Notified Bodies operating in that country.

In addition, if a manufacturer decides to conduct a clinical trial on his product to obtain data to support the CE marking process he must seek the approval of the relevant competent authorities before the trial can commence.

## **(ii) Post-marketing**

Post-marketing surveillance by the notified body.

The aim of post-market surveillance by the notified body is to ensure that the manufacturer carries out the approved quality system and is providing the notified body with the agreed information. The notified body must periodically carry out appropriate inspections and assessments to make sure that the manufacturer applies the approved quality system and produces an assessment report. It may also pay unannounced visits to the manufacturer and carry out or ask for tests in order to check the quality system is working properly.

The notified body's periodic surveillance of the manufacturer should include checking the manufacturer's systems for reviewing experience of the device in use.

A notified body may suspend or withdraw a certificate, place restrictions on it or trigger an intervention from the competent authority. In such circumstances the notified body must inform the competent authority in its own country, and the competent authority must inform other competent authorities and the European Commission of such action.

## **Vigilance and incident reporting**

The device manufacturer is central to the vigilance and incident reporting system. Manufacturers must report certain adverse incidents to the relevant national competent authority (the competent authority where the incident has occurred, unless otherwise specified) for recording and evaluation.

One of the roles of the competent authority is to establish a 'vigilance' programme in relation to post-market surveillance of the performance and safety of medical devices.

In the UK, manufacturers must make an adverse event report to the MHRA under the Medical Devices Regulations if they become aware of 'any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or instructions for use which, directly or indirectly might lead to or have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health.'

Manufacturers report any technical or medical reason connected with the characteristics or performance of a device which might lead to death or serious deterioration in health and that would lead to a systematic recall of devices of the same type by the manufacturer. Manufacturers are also encouraged to make reports if in doubt as to whether they fit the relevant reporting criteria and maintain systems and records for post-market surveillance.

Healthcare professionals and members of the public are also encouraged to report adverse events voluntarily, and the MHRA must in turn inform the manufacturer of these.

Where incidents are common, well documented (and identified as such in device risk assessments) and/or have been previously reported, the relevant national competent authority may agree to accept periodic summary reporting instead of individual incident reports.

All adverse incident reports are risk assessed by the MHRA and categorised to determine the nature of the response required. Generally the investigation into the incident is carried out by the manufacturer while the MHRA monitors progress, although the most serious investigations are led by MRHA device specialists.

Following these investigations, the MHRA will monitor the manufacturer response or lead on the response if appropriate. Actions can include recalling faulty products and offering warnings and advice to the health service primarily through Medical Device Alerts, but also through safety pamphlets, posters, and bulletins, and requiring the manufacturer to change designs or information. The MHRA also sends information on all reports received to the relevant manufacturer and all reports are stored in the MHRA's database to assist in spotting trends that require action.

The MHRA has the power to prosecute when regulations have been breached. The courts can impose fines or prison sentences when the law has been broken. The MHRA can withdraw unauthorised/illegal products from the market.

## **Investigations**

The manufacturer is normally responsible for the investigation of an incident, while the relevant national competent authority (normally the one in which the incident occurred) monitors progress. The national competent authority may then intervene, or initiate independent investigation if appropriate.

The manufacturer must inform the relevant competent authority of the results of its investigation, and consult the competent authority on any necessary action. This may include the manufacturer withdrawing a product if concerns warrant it. The competent authority may take further action it deems appropriate, consulting the manufacturer where possible.

## **Co-ordination and information dissemination**

The national competent authorities are responsible for considering the dissemination and drafting of information, and communicating any corrective action needed, in their country. Where incidents of similar types occur in more than one country there may be a need for a coordinating competent authority. This should be the competent authority responsible for the manufacturer, unless otherwise agreed. The coordinating competent authority should take the lead role in discharging the competent authority functions and ensuring information is distributed to all other competent authorities involved and the European Commission.

## Adverse incident reporting

Under the EC Medical Devices Directive, the MHRA as the UK competent authority is responsible for the operation of a vigilance system to record centrally and evaluate reports of incidents involving medical devices used in the UK. Manufacturers are obliged to inform the relevant competent authority of any incidents that have occurred in that competent authority's territory. Users (patients, providers and healthcare professionals) can also report incidents involving devices to the MHRA, who will pass that information on to the manufacturer. Health professionals in particular are expected to report adverse incidents under their relevant professional guidance.

To fulfil these obligations, the MHRA runs an Adverse Incident Tracking System, which is used to record and manage all adverse incidents reported to the MHRA. Incident reports, from users or manufacturers, are recorded and a process initiated for ensuring the manufacturer investigates the causes of an incident. The outcomes of this investigation are recorded on the system and (where appropriate) the user who reported the incident is informed of the findings.

Depending on the findings of the investigation, a number of actions can result, including:

- the manufacturer modifying the device or the instructions for use;
- addition of the incident information to 'trending' data which tracks the number of adverse incidents reported;
- publicly issuing a Medical Device Alert (MDA) and using the Central Alerting System (CAS) to distribute the MDA to bring a problem with a device to the attention of relevant healthcare professionals, providers, and organisations and set out actions to avoid further incidents;
- notification of other competent authorities;
- recall of the device from the market;
- further investigation or dissemination of relevant information through other means (device bulletins, education and information tools).

## Individual incident reports

Receipt of an incident report, whether via the manufacturer or a user, triggers the MHRA to request an investigation of the incident by the manufacturer (unless the manufacturer has already begun the investigation). This investigation must result in the manufacturer providing a final report of their investigation to the MHRA, comprising a written statement of the manufacturer's investigation and a record of any action taken as a result of the investigation.

The report should include details of any relevant information obtained during the investigation, including the manufacturer's analysis of the nature of the problem reported based on their inspection of relevant manufacturing records, the returned product itself (if available) and any other relevant information. There must be a conclusion as to the root cause(s) of the incident. The report should also include, where applicable, consideration of whether there is a risk to patients or other users associated with the type of failure identified, whether the incident is isolated or indicative of a more systematic issue (and if so what the scale of the problem is and

whether corrective action is needed), whether the report is relevant to any other products that the manufacturer produces and a review of the risk assessment of the device and the likelihood of recurrence.

This report is then reviewed by an MHRA Medical Device Specialist, who determines if the information and conclusions provided by the manufacturer are appropriate and reasonable. They can seek more information from a variety of other sources as necessary and escalate any concerns that they have, or go back to the manufacturer for more information. The Medical Device Specialist should also record the information from the incident report for wider trending and surveillance activities and then close the investigation if that is justified.

## **The European system for medical device regulation**

The various regulatory systems in respect of medical devices then existing in the member states of the European Union began to be replaced in January 1993 when the first European Directives regulating the marketing of medical devices started to come into effect. The underlying objective of these Directives was to remove technical barriers to trade by providing manufacturers with a single set of regulatory requirements that, once met, would provide free and unhindered access to the EU market. At the same time the Directives aimed at providing users and patients of medical devices a high level of confidence that devices, when used in accordance with the manufacturer's instructions, were safe and would perform as claimed.

The manufacturer affixes medical devices meeting the requirements laid out in the relevant Directive(s) with the CE mark.

The medical device Directives that have been agreed and put into national law so far are:

- the Active Implantable Medical Devices Directive (AIMDD) which came fully into force in January 1995 and covers powered implants (such as pacemakers) or partial implants which are left in the body.
- the Medical Devices Directive (MDD) which came fully into force in June 1998 and covers a broad range of products from sticking plasters to X-ray machines including breast implants.
- the In Vitro Diagnostic (IVD) Medical Devices Directive which covers test kits and instruments used in vitro for examining specimens taken from the human body (eg blood grouping reagents, pregnancy and Hepatitis B test kits). This Directive came into force in June 2000.
- the medical devices incorporating stable derivatives of human blood or human plasma Directives. These came into effect in June 2002 and cover the inclusion of materials such as albumin, thrombin, fibrinogen and immunoglobulins in devices such as stents, leads, heart valves, vascular grafts, catheters, filters and haemostats.
- the Directive re-classifying breast implants as class III medical devices.
- the Directive as regards medical devices manufactured utilising tissues of animal origin;

- the Directive revising the AIMDD and the MDD which came into force in March 2010, and which among other issues clarified the requirements for clinical data and re-classification of a number of products; and
- the Directive re-classifying total joint replacements as class III medical devices.

### Key features of the Directives

The Directives require the competent authority (CA) in each member state to ensure effective implementation. In the UK, the competent authority is the Secretary of State for Health acting through the MHRA. The main responsibilities of the CA, which for devices, have not been devolved in any way to the Devolved Administrations, involve:

- enforcing compliance with the implementing regulations;
- registration of manufacturers of primarily low risk devices;
- assessing notifications for clinical investigations;
- monitoring and designating the notified bodies who assess the conformity of certain classes of devices with the regulatory requirements set out in the various Directives; and
- authorising the use of non-CE marked medical devices on humanitarian grounds.
- All the Directives establish a list of essential requirements which 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 or instructions for use.
- The Directives set out various options which the manufacturer may choose to demonstrate compliance. These will involve, broadly, either 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. In the MDD, this is achieved by a classification system whereby devices are grouped into one of three classes according to a series of rules. Class I covers products generally regarded as low risk such as spectacles, bandages and non-invasive products. Manufacturers of these devices are required to check for themselves that they comply with the Directive, make a declaration to this effect and register their details with the Competent Authority. For medium risk products (Class II a and b), eg contraceptive devices, contact lens care products and for higher risk products (Class III), eg intra-uterine contraceptive devices, devices combined with a medicinal product and breast implants, compliance with the Directive must be independently assessed by a Notified Body. These are independent third party certification organisations designated by the Competent Authority to carry out the conformity assessment procedures stipulated in the annexes to the Directives. Only when the Notified Body certifies that the manufacturing

processes or the products meet the requirements may the manufacturer CE mark the device and place it on the market.

- The Directives establish a vigilance system whereby the manufacturer must report to the CA all serious adverse incidents for evaluation. If appropriate details are also reported to other member states and the Commission in order to prevent similar incidents occurring elsewhere in the Community.

The MHRA has a statutory responsibility to ensure manufacturers comply with the Regulations. It does this by investigating all allegations of non-compliance received as well as operating its own pro-active programme. Where investigation proves the device does not conform to the regulatory requirements, action can be taken to remove the offending device from the market. However in practice unless the problem represents a serious safety matter, the CA and the manufacturer usually will work together to correct the fault amicably in adherence to the Hampton principles.

Member states also have the power to withdraw from the market any product that it considers is a danger to public health. This is termed the "safeguard clause" and is common to other single market measures.

## European regulatory activity

The regulatory system for medical devices operates under a common European framework and the scope for improvement and reform is peripheral to this Review.

All of the current legislation regulating medical devices is in the process of being revised at European level, following an initial consultation by the European Commission in 2008. The revised regulations are likely to include provisions for stronger supervision of notified bodies, improved vigilance systems, clinical investigations and traceability of implanted devices. The new Regulations will not be implemented before 2017-18.

In the meantime, the Commission has been working with member states to develop and introduce a joint plan for short-term actions, focused on improving the implementation of existing regulatory requirements. The first outcome of these collaborations was the Implementing Regulation and Recommendation published by the Commission in September 2013. This included joint audits of notified bodies by representatives of more than one member state, limiting the designation of notified bodies to five years and introducing unannounced audits of manufacturers. Further collaborations going forward are likely to include measures to:

- improve information-exchange and co-ordination of incident analysis among competent authorities;
- reinforce market surveillance activities by competent authorities; and
- improve the traceability of devices to support long-term monitoring of their safety and performance.

These proposals are generally consistent with views the MHRA had been advancing at European level about priorities for improving the operation of the regulatory system for medical devices.

With regard to the Commission's plans for regulatory reform the Government should continue to support moves to improve oversight and co-ordination of the regulatory system. Current constraints on information sharing can hamper both international co-operation and work with health professionals to assess and investigate potential problems. Therefore moves to facilitate easier information sharing, among competent authorities and more widely, should be supported. Relevant issues for the ongoing review of the Devices Directives are likely to include mechanisms for improving the performance of notified bodies, strengthening requirements on manufacturers to carry out post-market surveillance of devices (in particular for higher-risk devices), improving the consistency of implementation of the directives by member states and improving information-sharing among European competent authorities. The detail of implementation will be important in ensuring that improvements are deliverable and have the maximum traction.

## Appendix G: CE marking of medical devices – provided by ABHI

### The regulatory system for products on the European market

#### What is CE Marking?

The CE Mark(ing) denotes compliance of a product with a European New Approach Directive. For such products sold in the European Economic Area (EEA) the CE marking must appear either on the product or, where this is not practical eg for reasons of size, on the packaging. Nowadays it can be seen on many consumer products, most commonly toys or electrical and electronic items. Sometimes it is accompanied by a Notified Body number (see below).



Originally, CE was understood to mean *Conformité Européenne*.

#### The New Approach Directives

The New Approach Directives originated in the 1980s and were designed to provide a more flexible approach to regulating products on the European market.

The approach with older directives had been much closer to product specifications and consequently lagged behind technological change. The idea of the New Approach was to set out a number of Essential Requirements that should be met but allowing the manufacturer a degree of latitude in how he chose to do this.

There are a number of New Approach Directives covering several very different areas. These include:

- Machinery
- Construction Products
- Electromagnetic Compatibility
- Toy Safety
- Recreational Craft
- Medical Devices

An important element of the New Approach is the use by manufacturers of so-called 'harmonised standards' to help them meet the directives' essential requirements. For example, in the medical devices area there is a series of harmonised standards covering the various methods of sterilisation and a manufacturer may choose to use one or more of these standards to demonstrate that he has met the essential requirements that relate to sterile medical devices.

## The Medical Device Directives

The medical device directives were developed from the late 1980s onwards. There are three principal directives and a number of others covering more specialised areas. The three main directives are:

- Active Implantable Medical Devices Directive (90/385/EEC)
- Medical Devices Directive (93/42/EEC)
- In Vitro Diagnostics Medical Devices Directive (98/79/EEC)

The first part of the number in brackets gives the year the directive became European law.

The following directives have amended the Medical Devices Directive (MDD).

- Directives 2000/70/EC and 2001/104/EC brought medical devices incorporating stable blood derivatives within the scope of the general directive.
- Directive 2003/12/EC reclassified breast implants into Class III.
- Directive 2003/32/EC lays down detailed specifications in relation to risks of transmitting transmissible spongiform encephalopathies (TSE) under normal conditions of use to patients or others, via medical devices manufactured utilising animal tissue which is rendered non-variable or non-viable products derived from animal tissue.
- Directive 2007/47/EC better specified the obligations of manufacturers, notified bodies and authorities with particular respect to the key issues of conformity assessment, clinical evaluation and post market surveillance.

Examples of products covered by the Active Implantable Medical Devices Directive (AIMDD):

- implantable cardiac pacemakers
- implantable defibrillators
- implantable nerve stimulators
- bladder stimulators
- sphincter stimulators
- diaphragm stimulators
- cochlear implants
- implantable active drug administration devices
- implantable active monitoring devices

The MDD covers an extremely wide range of products, including:

- first aid bandages
- tongue depressors

- hip prostheses
- X-ray equipment
- ECG
- heart valves
- spectacles
- dental materials

The In Vitro Diagnostics (IVD) Directive covers devices used in vitro for the examination of a specimen derived from the human body, including reagents, instruments and specimen receptacles.

There is a related regulation, on Advanced Therapy Medicinal Products (Regulation No. 1394/2007). This covers gene therapy and somatic cell therapy but also human tissue engineered products falling within the definition of medicinal products; some of these have a mode of action akin to that of medical devices. ATMPs are innovative, regenerative therapies which combine aspects of medicine, cell biology, science and engineering for the purpose of regenerating, repairing or replacing damaged tissue/cells. The use of this technology has already led to the development of products that are used clinically for the treatment of burns or ulcers and cartilage repair systems used in the treatment of early arthritis. More complex products are currently being developed for the treatment of heart disease and other degenerative conditions. However, given that the regulatory approach for these products follows more closely that for pharmaceutical products than that for medical devices detailed discussion is outside the scope of this paper.

Each of these pieces of legislation is implemented into UK law by the UK Competent Authority, the Medicines & Healthcare products Regulatory Agency (MHRA). MHRA acts as both the legislative and the regulatory authority.

### How does the system work?

Products covered by the Medical Devices Directive are divided into four risk categories, ranging from Class I, low risk, to Class III, high risk. For historical reasons the two intermediate categories are Class IIa and Class IIb. At a very simplistic level one can say that the higher the classification, the greater the level of control of the product. However, the goal for all products is to ensure that they are safe, regardless of their classification. Manufacturers do this by meeting the Essential Requirements set out in the directive. In the MDD the essential requirements cover:

- chemical, physical and biological properties, eg that the materials used are compatible with biological tissues, cells and body fluids;
- infection and microbial contamination, eg that devices delivered in a sterile state have been manufactured and sterilized by an appropriate, validated method;
- construction and environmental properties; eg that the risk of fire or explosion during normal use is minimised;

- devices with a measuring function, eg that the measurement, monitoring and display scale is designed in line with ergonomic principles;
- protection against radiation, eg that exposure of patients, users and other persons to radiation is reduced as far as possible;
- requirements for medical devices connected to or equipped with an energy source; eg that the risk of accidental electric shocks is avoided;
- information supplied by the manufacturer; eg covering the information needed to use the device safely and to identify the manufacturer.

Products covered by the AIMDD are generally higher risk devices and for the purposes of this summary can be considered as being similar to Class III medical devices.

Manufacturers of Class I medical devices may 'self declare' that they meet the essential requirements of the MDD. They do this by notifying MHRA that they are placing a particular product or group of products on the market and they affix the CE mark to those products thereby indicating compliance. While there is no third party inspection or testing of Class I products, MHRA carries out inspections of a number of Class I device manufacturers each year.

Manufacturers of Class IIa, IIb and Class III medical devices are obliged to subject their products and/or manufacturing processes to scrutiny by a Notified body. Notified Bodies are third party organisations appointed by the national competent authorities, eg MHRA, and who are responsible to certifying that device manufacturers meet the requirements of the MDD or AIMDD.

Products covered by the IVD Directive will not be considered here.

## Conformity Assessment

Conformity assessment for Class IIa, IIb and Class III medical devices is carried out by a Notified Body chosen by the manufacturer. This is also the case for active implantable medical devices.

The level of scrutiny will be greatest for the highest risk devices where the notified body will review a manufacturer's quality system and the relevant documentation, the manufacturer's procedure for monitoring the design of his products, including his clinical data derived from clinical investigations where necessary, and the design dossier. Essentially the notified body will look at all aspects of the medical device, from conception through to monitoring of performance in the marketplace. This is a highly rigorous inspection process and will typically take a number of days to complete.

Once the notified body is satisfied that the manufacturer fulfils all his obligations under the relevant directive he will issue a certificate of compliance that allows the manufacturer to make his Declaration of Conformity and affix the CE mark which in this case is accompanied by the notified body number.

Most manufacturers these days will be inspected to some degree against a quality system. The inspections can range from covering the full quality assurance system, through production quality assurance and product quality assurance. Some manufacturers may opt for EC type examination whereby the notified body ascertains and certifies that a representative sample of the production fulfils the relevant provisions. Another route is EC verification where a notified body either examines and tests every product or carries out a statistical verification where a random sample is taken from different batches of products. The last two conformity assessment routes are relatively rare and are unlikely to be used by manufacturers supplying a wide range of products.

Manufacturers are subject to periodic reinspection by notified bodies.

### **Post Market Control**

Manufacturers are obliged to implement a 'medical device vigilance system' in order to monitor the performance of their products once they are being sold on the European market. The degree of market surveillance will vary depending both on the risk classification of the product to the number of products placed on the market.

For low risk devices it may be sufficient for a company merely to monitor customer complaints and react accordingly. For higher risk products the manufacture may be far more proactive and may implement a formal post-market surveillance system where he actively seeks feedback from users and may track individual products. In the case of female urinary incontinence products an industry initiated MREC registry has been set up in the UK by a company to monitor the performance of its product offerings in this disease state. There has also been significant industry support of the British Society of Uro-Gynaecology (BSUG) registry in terms of both development and enrolment.

### **Enforcement activities**

In addition to its role in implementing the EU Directives into UK law and in designating UK notified bodies, the MHRA also has the role of policing the UK market and has a number of sanctions that it can apply.

In the majority of cases MHRA's enforcement actions will be relatively minor, eg in requiring a change to labelling of a product. However, it also has the power to remove products from the market where patient safety is threatened and to bring criminal prosecutions against company personnel; this is rare.

### **Summary**

The European medical device directives are part of the New Approach regulatory system which is designed to provide a flexible approach to meeting the regulatory requirements while providing a high level of consumer/user protection.

The medical device directives are implemented into national law by the relevant competent authority which also designates notified bodies to carry out inspections of manufacturers and their products under the national legislation. Manufacturers of medical devices either self declare, in the case of the lowest risk devices, that they meet the essential requirements or declare once they have a certificate of conformity

from a notified body. Once the essential requirements have been met may the manufacturer affix the CE mark to his product.

CE marking means that a medical device meets the relevant regulatory requirements, performs as intended, complies with the necessary requirements covering safety and performance and is acceptably safe. In general, a medical device cannot be marketed in Europe without carrying a CE mark.

## Appendix H: MedTech Industry - key data

### Medical devices, in vitro diagnostics and imaging

#### Employment:

- The industry employs more than **575,000** people in Europe.<sup>1</sup>
- In comparison, the US MedTech industry employs around 520.000 people<sup>1a</sup>; The European pharmaceutical industry employs 675.000 people<sup>1b</sup>.

#### Companies:

- There are almost **25,000** medical technology companies in Europe.<sup>1</sup>

#### SMEs:

- It is estimated that almost **95%** of MedTech companies are SMEs, the majority of which are small and micro-sized companies.<sup>1</sup>

<sup>1</sup>Source: Eucomed calculations based on the data obtained from National Associations of 15 countries for the latest year available. Countries with (partially) provided data: Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, Netherlands, Poland, Portugal, Spain, Sweden, UK, Switzerland. Europe refers to EU + Norway, Switzerland.

<sup>1a</sup>Source: S. Tripp, M. Grueber, R. Helwig - *The Economic Impact of the U.S. Advanced Medical Technology Industry*, Battelle Technology Partnership Practice, March 2012.

<sup>1b</sup>Source: EFPIA – *The Pharmaceutical Industry in Figures. Key Data 2013*. Europe refers to EU + Norway, Switzerland.

#### Market size:

- The European medical technology market size is estimated at roughly **€ 100 billion**.<sup>2</sup>
- In comparison, expenditure on MedTech per capita in Europe is at around **€195<sup>2</sup>** (weighted average) compared to the US at €380<sup>2a</sup>.
- The spending on medical technology varies significantly across European countries, ranging from around **5% to 10%** of the total healthcare expenditure. It is estimated that around 7.5 % of total European healthcare expenditure is attributed to medical technologies.<sup>2</sup>
- In comparison, expenditure on pharmaceuticals takes up 17% of total healthcare spending in Europe.<sup>2b</sup>

<sup>2</sup>Source: WHO Global Health Expenditure Database, Eurostat, Eucomed calculations based on the data obtained from National Associations of 15 countries for the latest year available. Countries with (partially) provided data: Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, Netherlands, Poland, Portugal, Spain, Sweden, UK, Switzerland. Europe refers to EU + Norway, Switzerland.

<sup>2a</sup>Source: WHO; *Estimates of Medical Device Spending in the United States*, Gerald Donahoe and Guy King, F.S.A., M.A.A.A. AdvaMed, 2012.

<sup>2b</sup>Source: WHO Global Health Expenditure Database, Eurostat, EFPIA, Eucomed calculations.

- The European market is estimated to comprise around **30%** of the world market and is the second largest medical device market after the US (40%).<sup>3</sup>

<sup>3</sup>Source: Espicom, Eucomed calculations. Manufacturer prices. Medical devices and Imaging excluding in-vitro diagnostics. Europe refers to EU (excluding Cyprus, Luxembourg, Malta) + Norway, Switzerland.

- The European medical device market size is growing on average at **4%** per annum.<sup>4</sup>

<sup>4</sup>Source: Espicom, Eucomed calculations. Average growth rate over 2008-2013 years. Manufacturer prices. Medical Devices and Imaging excluding in-vitro diagnostics. Europe refers to EU (excluding Cyprus, Luxembourg, Malta) + Norway, Switzerland.

#### **Trade balance:**

- Europe has a positive medical device trade balance of **€ 15.5 billion** (2012), more than a twofold increase since 2006.<sup>5</sup>
- The EU has a positive medical device trade balance of almost **€ 11 billion** (2012), more than a threefold increase since 2006.<sup>5</sup>
- In comparison, the US medical device trade balance is at € 5.3 billion.<sup>5</sup>

<sup>5</sup>Source: Espicom, Eucomed calculations. Manufacturer prices. Medical devices and Imaging excluding in-vitro diagnostics. Europe refers to EU (excluding Cyprus, Luxembourg, Malta) + Norway, Switzerland.

#### **Medical technologies:**

- There are more than **500,000** medical technologies registered, ranging from syringes and bandages to orthopaedic implants and pacemakers (20,000 generic groups).<sup>6</sup>

<sup>6</sup>Source: Global Medical Devices Nomenclature (GMDN) Agency, 2010.

#### **Innovation (patents):**

- In 2012 more than **10,000** patent applications were filed with the European Patent Office (EPO) in the field of medical technology – equivalent to 7 % of the total number of applications – more than any other technical field. Since 2001, the number of EPO filings in the field has doubled.<sup>7</sup>
- In comparison, around 5,400 applications were filed in the pharmaceutical field.<sup>7</sup>
- **38%** of these patent applications were filed by European countries.<sup>7\*</sup>
- Every **50 minutes** one new European patent application is filed in the medical technology field.<sup>7</sup>

<sup>7</sup>Source: European Patent Office, Eucomed calculations. Medical technology as defined by World Intellectual Property Organization (based on the WIPO IPC-Technology concordance as revised in August 2012). \*European countries refer to EU+ Norway, Switzerland. Patents are attributed by the country of residence of the applicant.

## Glossary

**Adverse Incident (AI)** (for reporting purposes) - any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or instructions for use which, directly or indirectly might lead to or have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health.' In this instance a 'serious deterioration' in the state of someone's health can include:

- a life-threatening illness
- permanent impairment of a body function or permanent damage to a body structure
- a condition necessitating medical or surgical intervention to prevent either of the first two criteria (this includes increase duration of surgery and conditions requiring hospitalisation or prolongation of existing hospitalisation)
- indirect harm as a consequence of an incorrect diagnostic result
- foetal distress, foetal death or any congenital abnormality or birth defect.

**BAAPS** – the British Association of Aesthetic Plastic Surgeons. Association "established for the advancement of education in, and the practice of, Aesthetic Plastic Surgery for public benefit".

**BAPRAS** – British Association of Plastic, Reconstructive and Aesthetic Surgeons. Professional association that "exists to promote the best evidence-based practice in plastic, reconstructive and aesthetic surgery in order to achieve the highest standard of patient care through professional support in education, research and the development of knowledge".

**Breast Implant Registry** – a voluntary registry of breast implant usage in the UK which was operated from 1995 to 2005. It was shut down due to a high proportion of women not consenting to their details being recorded, meaning the information the registry contained was of inadequate quality for research purposes.

**Clinical Commissioning Groups (CCGs)** –NHS organisations set up by the Health and Social Care Act 2012 to organise the commissioning of NHS services in England.

**CE mark** – signifies a product meets the accepted standards of safety.

**Central Alerting System (CAS)** – a web-based system for issuing patient safety alerts, medical device alerts, public health notices and other safety critical guidance to the NHS. It enables alerts to be emailed to key contacts across the health care system and allows the onward cascading of this information to relevant health care workers. It also provides a web portal for accessing relevant information.

**Committee on the Safety of Devices (CSD)** – committee of independent experts established to support the MHRA in ensuring that medical devices and equipment meet appropriate standards of safety, quality and performance by giving advice on a range of device related initiatives.

**Competent Authority** – national body responsible for the compliance with and enforcement of the EU Medical Devices Directive as it applies to medical devices,

device manufacturers and Notified Bodies in their Member State. In the UK this is the MHRA. **Device Specialist** (at the MHRA) – Member of MHRA staff, with a scientific or other relevant qualification, responsible for investigating device adverse incidents and developing safety advice.

**FDA** – the United States Food and Drug Administration. The US regulator for medical devices, medicines and a range of other products.

**GHTF** – Global Harmonisation Task Force

**IMDRF** – International Regulators Forum

**KTN** – Knowledge Transfer Networks are one of the Technology Strategy Board's key tools for facilitating the UK's innovation communities to connect, collaborate and find out about new opportunities in key research and technology sectors.

**MCA – Medicines Control Agency** – the predecessor to the MHRA with responsibility for the safety, quality and efficacy of medicines.

**MDA – Medical Devices Agency** – the predecessor to the MHRA with responsibility for medical device safety and regulation.

**MDA – Medical Devices Alert** – notice issued by MHRA with important safety information related to a medical device sent to key contacts across the healthcare system using the Central Alerting System with instructions for further cascading to relevant health care workers, as well as being posted on the MHRA website.

**Medical Device** – defined in European law as “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.”

**MDEG** – Medical Device Expert Group. Established by the EU Commission, MDEG is composed of delegates from member state competent authorities, industry and other stakeholder representatives in the area of medical devices and is the forum in which the implementation of the Medical Devices Directive is discussed. In closed session, MDEG consists of member state competent authorities only and is a forum to discuss all issues relating to the implementation of the medical device directives. MDEG is responsible for publishing guidance documents which reflect the consensus position of its members on interpretation of the Medical Devices Directive.

**Medical Device Liaison Officers (MDLO)** – members of staff designated in all NHS trusts and primary care trusts in England who are responsible for encouraging effective and comprehensive adverse incident reporting through encouragement and training of healthcare and support staff and medical device users.

**Medical Devices Directives** – European Union legislation which, when translated into national law in EU member states, provides the legal framework for regulation of medical devices in Europe.

**MHRA** – the Medicines and Healthcare products Regulatory Agency, the UK competent authority responsible for regulation of medicines and medical devices. MHRA is an Executive Agency of the Department of Health.

**MDSAP** – Medical Devices Single Audit Programme designed to bring greater consistency to the audit of manufacturers in increasingly global supply chains.

**NICE** – the National Institute for Health and Care Excellence, provides independent, authoritative and evidence-based guidance on the most effective ways to prevent, diagnose and treat disease and ill health, reducing inequalities and variation.

**Notified Body** – third-party private sector organisations designated by their national Competent Authority and commissioned by manufacturers to determine whether a particular medical device meets the relevant regulatory requirements and, whether, when used as intended, it works properly and is acceptably safe (the process known as conformity assessment).

**NBOG** – Notified Body Operations Group. A group established by the EC and member states to “improve the overall performance of notified bodies in the medical devices sector by primarily identifying and promulgating examples of best practice to be adopted by both notified bodies and those organisations responsible for their designation and control.” NBOG membership consists of the European Commission and nominees from the member states’ designating/competent authorities. Additionally, membership of the Group is open to EFTA/EEA competent authorities as well as candidate and accession countries. On the whole, members of the Group are nominated by their competent authorities on the basis of their expertise in the area of notified body designation and control.

**National Joint Registry (NJR)** – set up by the Department of Health and Welsh Government in 2002 to collect information on all hip, knee, ankle, elbow and shoulder replacement operations and to monitor the performance of joint replacement implants

**NICOR** – National Institute for Cardiovascular Outcomes Research

**NRLS** – National Reporting and Learning System

**OWAM** – Organisation with a Memory, report of an expert group on learning from adverse events in the NHS chaired by the Chief Medical Officer

**PIP** – Poly Implant Prothèse. Manufacturer of various breast implants, including silicone gel-filled implants, which were found by AFSSAPS to be filled with an unapproved silicone filler.

**Post-market surveillance** – a systematic procedure to review experience gained from their devices after they are placed on the EU market, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of:

- a) any adverse incident which might lead to or might have led to the death of a patient or user or to a serious deterioration in their state of health;
- b) any field safety corrective action (eg systematic recall) undertaken by the manufacturer to reduce the risk of adverse incidents with the device.

**Trending/Trend Analysis** – analysis of data relating to the frequency and characteristics of all adverse device incidents reported involving a particular batch, brand or type of medical device

**Technology Strategy Board (TSB)** – the UK’s innovation agency which offers support and funding to help business develop new products and services.

**Vigilance** – In the context of the EC Medical Devices Directive this refers to:

- a) the part of manufacturers' post-market surveillance system that obliges them to report and investigate adverse incidents involving actual or potential serious deterioration in state of health to the relevant competent authorities, and to inform Competent authorities of any field safety corrective actions being undertaken to reduce the risk of adverse incidents
- b) to the system of post-market surveillance administered by a Member State's competent authority to collate and examine adverse incident reports and other information regarding device safety from manufacturers and users, and take any measures necessary to minimise the recurrence of the adverse incidents.

## End Notes

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