The CE mark for implantable medical devices

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A vital aspect of device and implant regulation is continual surveillance of performance after approval. Most permanent implants seldom reveal their strengths and weaknesses until they have been in clinical use for a number of years. It is vital that clinicians report problems to the manufacturers and regulatory authorities to enable emerging hazards to be promptly identified.

Surprisingly little is know about the regulation of medical devices, particularly implantable devices, among members of the medical profession, and even less by those most affected by their quality — patients. In many parts of Europe, there was little control of medical device production and use until the mid-1990s, when the European Community (EC) Medical Devices Directives (MDDs) came into force. These directives introduced a unified set of essential requirements (ERs) concerning device performance to ensure a minimum level of safety. Only devices meeting these requirements could bear the 'CE mark' (Conformitée Européene), now mandatory for sale across Europe and also anywhere within the European economic area, since Switzerland and the European Free Trade Association countries (Norway, Sweden and Denmark) have also adopted the EC directives.

The European Standards Organization, Comité Européen De Normalisation (CEN), through its standards committees, is continually writing new medical device and implant standards, which are reviewed on a regular basis. Specialists from medicine, industry and regulatory authorities contribute to the publication of such standards. An equally important aspect of device and implant regulation is the continual surveillance of their performance after approval for widespread use. Most permanent implants seldom reveal their true strengths and weaknesses until they have been in clinical use for a number of years. It is vital, therefore, that clinicians report problems associated with implants, not just to the manufacturers, but particularly to regulatory authorities, to enable European and worldwide experience to be collated, thereby enabling emerging hazards to be identified at the earliest possible stage. The credibility of a CE-marked implant is therefore the joint responsibility of members of the medical profession, implant manufacturers and national regulatory authorities.

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INTRODUCTION

During the 1990s, the EC moved from a position of diverse, largely non-statutory control of medical devices to a single mandatory system enforced by national Competent Authorities (CAs). The Secretary of State for Health is the CA for the UK, acting through the Medical Devices Agency (MDA). Two years after the introduction of the EC directive covering active implantable medical devices (European Community, 1990), the MDD (European Community, 1993) came into effect on 1 January 1995. Member states were required to transpose these directives into their national law. The transition period, during which manufacturers could choose to comply either with the directive or with relevant pre-existing national controls, came to an end on 1 January 1995 for active implants (e.g. cardiac pacemakers) and on 14 June 1998 for non-active implants, including, among others, cardiovascular, orthopaedic and ophthalmic implants.

PRE-MARKET APPROVAL

Since 14 June 1998, manufacturers have had to ensure that their medical devices placed on the market for general use, including those used in vascular and orthopaedic surgery, interventional cardiology and radiology, meet certain minimum safety requirements. The devices must by law carry the CE mark of conformity, indicating that they comply with the so-called ERs of the directives of the EC.

However, the MDD was written to cover all kinds of medical devices (except active implants and in vitro diagnostic devices) where a device is broadly defined as a product (other than a medicine) used for the prevention, diagnosis, monitoring or treatment of illness, disease, injury or handicap. Therefore, the ERs apply to a broad spectrum of equipment. The EC Commission mandated CEN to write a series of harmonized device standards. CEN standards for surgical implants are written on three levels, according to degree of complexity, but follow the same format outlined below:

1. Scope
2. Normative references
3. Definitions
4. Intended performance
5. Design attributes (the characteristics of the device that enable it to work as intended)
6. Materials
7. Design evaluation (the range of bench tests, animal studies and clinical trials that should be undertaken to assess the device design)
8. Manufacturing
9. Sterilization
10. Packaging
11. Information supplied by the manufacturer.

Running parallel with the work of CEN is the activity of the corresponding International Organization for Standardization (ISO), which writes international standards available for worldwide use. Both ISO and CEN standards have enormous influence in underpinning the market approval of devices within Europe and elsewhere. Close cooperation between CEN and ISO committees is maintained in order that standards are harmonized worldwide in the spirit of the Vienna Agreement (International Standardization Organization and Comité Européen De Normalisation, 1991).

In order to comply with the relevant CEN implant standard, it is invariably necessary for the manufacturers to conduct pre-market clinical trials if there are insufficient clinical data already available on their device. Before manufacturers may start a clinical trial, they are required to provide the CA of the countries affected with sufficient information on the device, its preclinical testing and the details of the trial design to enable the CA to make an informed decision about whether they have grounds to object to its taking place. This is in addition to obtaining approval from local or multiple ethics committees.

The MDA takes considerable care in assessing preclinical notifications to check whether the device has received adequate preclinical testing and that the trial design will provide meaningful results. The MDA will object on safety grounds where a manufacturer cannot demonstrate that risks are acceptably low. The MDA's response stems from the view that it is only ethical to test questions relating to device safety/performance in humans where answers cannot be gained by preclinical bench and/or animal studies.

POST-MARKET SURVEILLANCE

There are also onerous post-approval or post-market surveillance obligations placed upon medical device manufacturers. Post-market surveillance is defined within the MDD as:

> **'an undertaking by the manufacturers to institute and keep up-to-date a systematic procedure to review experience gained from devices in the post-production phase'.**

The seeking and gaining of this experience can involve both proactive and reactive activities. The minimalistic option is simply to wait for complaint reports to be received. Where endovascular implants and other high-risk devices are concerned, however, this is clearly inadequate. Manufacturers are expected to supplement their complaint system with a number of proactive measures to solicit information from their customers. These can take the form of post-market clinical trials, customer feedback surveys, registries, or retrieval studies. Both reactive and proactive measures, however, rely entirely upon contributions and cooperation from the clinicians, surgeons and interventionalists using the devices.

Within the UK, clinicians and other health-care professionals are strongly encouraged to report adverse incidents both to the device manufacturer and directly to the MDA's adverse incident centre (see *Useful address*). The reporting of adverse incidents by users, however, is an entirely voluntary process, not derived from any UK or European law. The MDA has successfully operated this voluntary system for over 10 years, and among many sectors of the medical profession, it is well supported. A standard incident reporting form is available, which requests initial details of the incident and the device involved. Upon receipt of a report, an MDA technical specialist liaises with both the reporter and the relevant manufacturer to try to determine the cause of the incident and whether any steps can justifiably be taken to minimize the chance of the incident reoccurring. MDA clinical staff are fully involved in the investigation, wherever necessary.

The reporting by clinicians of adverse incidents involving implanted devices, either to manufacturers or to the MDA, is not always

prevalent. This may be simply the result of a lack of awareness of the MDA's adverse incident centre or the reporting requirements befalling manufacturers. However, there are three other possible reasons that may play a part.

First, within this particular clinical environment, problems are frequently an inextricable mix of device, patient and clinical technique variables. It is often difficult to identify precisely the cause of a complication. However, it is important that these multifactorial events are reported as they may highlight a health risk that could be reduced.

Second, as it is well known that certain device-related complications cannot yet be 'designed out', one-off or random device failures may not be considered worthy of reporting. The notification, however, of such events can give rise to the detection of a trend if apparently random incidents are occurring in a number of different places.

A third cause for failure to report incidents may be anxiety on the part of users, at least where regulatory authorities are concerned, that the subsequent incident investigation could lead to clinical culpability with possible medicolegal implications. Where incident reporting by clinicians to the MDA is concerned, however, the risk of this happening is minimal. Where so-called 'user errors' are identified, the priority is to pursue improvements to the device design, the information provided or user training to reduce the chance of errors reoccurring. Having a focused responsibility for the safety and safe use of medical devices, rather than for wider clinical audit, enables the MDA to take this pragmatic approach. Incident reporting by clinicians ultimately contributes to the availability of safer, more effective devices for use by the reportees and their colleagues.

Under the terms of the EC directives, the manufacturer carries the statutory responsibility to report adverse incidents to the MDA and to provide subsequent feedback from their investigation. Manufacturers rely heavily upon clinicians to enable them to fulfil this requirement. The MDA, in turn, monitors the manufacturer's action, together with identifying generic device-related problems, which may not come to the attention of any single manufacturer. By asking users to report events both to the MDA and to the manufacturer, the MDA is additionally provided with a valuable means of audit of the manufacturers' reporting compliance. In return for their efforts in keeping the MDA informed of problems, feedback is provided to clinicians by way of hazard and safety notices if a serious threat to safety has been identified. Device bulletins are also issued to the clinical community to address broader issues, typically relating to the safe use of a family of devices, in response to clinical feedback or device testing. In hospitals, these notices are promulgated to departments of clinical risk management and thereon to medical staff and technicians.

KEY POINTS

- The CE mark is now mandatory for all implantable medical devices.
- Little is know about the regulation of medical devices among members of the medical profession, and even less by patients.
- Continual surveillance of performance, after approval for widespread use, is a vital aspect of device and implant regulation.
- Most permanent implants seldom reveal their true strengths and weaknesses until they have been in clinical use for a number of years.
- It is vital that clinicians report problems associated with implants, not just to the manufacturers, but particularly to regulatory authorities, to enable emerging hazards to be identified at the earliest possible stage.

CONCLUSION

This article has reviewed the entire spectrum of pre- and post-market regulation of implantable medical devices. The success of the process relies upon close and continuing communication between the three key players: implanters, manufacturers and regulatory authorities. Each of these diverse groups works within a vastly different and often distant environment, and it is all too easy for the crucial exchanges of information to fall dormant. It is vital that the feedback loop remains complete so that improvements to device safety can continually be introduced at the design stage, thereby preventing patients from being exposed to the same safety-related risks following implantation. HM

Conflict of interest: none.

European Community (1990) *Council Directive 90/385/EEC on the approximation of the laws of the Members States relating to active implantable medical devices.* Office for Official Publications of the European Community, Luxembourg L189: 17–36

European Community (1993) *Council Directive 93/42/EEC concerning Medical Devices.* Office for Official Publications of the European Community, Luxembourg L169: 1–43

International Standardization Organization and Comité Européen De Normalisation (1991) *Agreement of Technical Cooperation Between ISO and CEN (Vienna Agreement).* International Standardization Organization, Geneva. Available at: http://www.iso.ch

Useful address

Reports for adverse incidents involving medical devices within the UK should be sent to:

Adverse Incident Centre
Medical Devices Agency
Hannibal House
London SE1 6TQ
Tel: 020 7972 8080 Fax: 020 7972 8109