

FEATURE

Commentary: International collaboration needed on device clinical standards

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No implantable medical device is perfectly safe. It is the duty of manufacturers and regulators to minimise risks—and the purpose of evaluating and regulating devices is to ensure safety and effectiveness.

The product life cycle of many medical devices is short—often quoted as an average of two years or less—because of the rapid rate of technological change and because of frequent modifications (called iterative changes) to their design, manufacture, or programming. It would be desirable for all implantable devices to undergo long term clinical studies—but there is pressure from interventional specialists as well as from industry to base approval on shorter term studies with surrogate rather than clinical end points. This facilitates innovation but transfers responsibility for proof of safety and clinical efficacy to follow-up studies.

Regulatory approval in Europe hinges on the principle that as long as a device has been shown to perform its stated task, it can be approved if its potential benefits outweigh any expected risks. Approval on this basis can mean estimating benefit before clinical effectiveness has been confirmed, and it means accepting some risk as the trade-off for more rapid availability of devices. The system of approval by 74 notified bodies in the European Union (EU) requires manufacturers to evaluate the risks and propose how these should be addressed.¹ Official guidance published by the European Commission is vague. It relates to general principles, such as which details of a literature search should be included by the manufacturer in its clinical evaluation of a device, rather than to specific requirements for particular devices, such as upper limits for complication rates. It does not mandate when clinical trials are essential. This system means important questions about safety may be left unanswered.

In the United States, however, implantable devices are generally expected to undergo bench testing, animal studies, and clinical investigations before premarket authorisation. The burden of evidence varies with the category of risk and the degree of

novelty, but the emphasis is on clinical effectiveness rather than the European principle of device performance.¹

Despite official protestations to the contrary,² standards for approving medical devices are less rigorous in Europe than in the United States. One consequence is that devices are approved later in the US because of the time, work, and expense of providing data on human safety and outcomes for the Food and Drug Administration (FDA). Manufacturers often seek initial approval for their devices in Europe, where they can recoup some of their costs while gathering information about clinical effectiveness that they will submit later to the FDA.

As this example shows, different countries have responded to the common challenges of evaluating medical devices in different ways.³ But it is not clear whether one system serves patients better than another. Although some populations may benefit earlier from new devices, they may also be exposed to greater risks. This is incompatible with the ethical principle that the risks associated with developing new devices should be equally shared worldwide. Patients everywhere should be protected by similar requirements for medical devices to be safe and effective.

Common standards

To try to overcome these problems, the Global Harmonization Task Force (GHTF)—an informal collaboration between regulatory authorities in Europe, North America, Japan, and Australia—has promoted common principles for evaluating devices, such as when clinical follow-up studies are indicated. Not all task force members have implemented its recommendations, however, and one third of countries still have no regulatory authority for medical devices.⁴

The European Union is reviewing its system for approving medical devices. Since the EU is a member of the GHTF, it would be illogical if the planned recast of the medical device directives were to retain important differences from the

regulations of other GHTF members. Equally, it would be inappropriate for higher levels of evidence to be required in Europe and North America than in parts of Africa and Asia. There should be no “region of least resistance” where devices could be approved more rapidly and on the basis of less evidence. Rather, efforts should be concentrated on developing a global approach. For each type of high risk device this should include a specific determination of how safe is “safe enough” relative to its therapeutic benefits.

The best way to use the limited pool of professional expertise concerning medical devices would be to develop global clinical standards for each class of medical device with moderate or high risks (classes II and III), specifying “objective performance criteria” and requirements for clinical evaluation and postmarketing surveillance. This is a task for all professional medical associations, the World Health Organization,⁵ and others. The medical profession should accept some responsibility for the dearth of detailed clinical standards that regulators can apply. Too few physicians have taken an interest in the regulatory processes governing medical devices.

If international collaborations can lead to common standards, it might be possible to negotiate mutual recognition of approval processes between regulatory authorities without undermining essential aspects of individual national jurisdictions. A device that is evaluated and approved in Europe might then also be considered for approval in the US or Japan, or vice versa. The prospect of a single application leading to worldwide marketing authorisation would compensate for increased investment in

premarket clinical studies. This could make the regulatory system less cumbersome and more efficient, as well as safer for patients. Where once this vision could have been characterised as a remote and idealistic dream, current global device clinical trials, developing international regulatory collaborations,⁶ and advances in information technology now make it feasible.

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