

EUROPEAN SOCIETY OF CARDIOLOGY

POSITION ON THE

RECAST OF THE EUROPEAN UNION MEDICAL DEVICE DIRECTIVES

Introduction

The European Commission announced its proposals for a new Regulation to govern the evaluation and approval of medical devices in Europe, in September 2012¹; draft legislation will be debated by the European Parliament and the Council of Ministers during 2013.

The European Society of Cardiology (ESC) welcomes many provisions in the draft Regulation and recognises the progress that has been made to improve the regulatory system in the interests of safety for patients in Europe. The medical profession including cardiologists are the major users of permanently implanted medical devices for their patients. Physicians act as an important link between regulators, device manufacturers, and patients. Physicians should play an important role in the clinical evaluation of medical devices and they should offer independent scientific expertise in any approval process.

Against this background, the ESC proposes amendments to the draft Regulation of the European Parliament and of the Council on medical devices, in several key fields:

- » strengthening safety by establishing the clinical efficacy of new devices when required
- » ensuring transparency to health professionals and patients of evidence about medical devices
- » formalising a European system for obtaining expert scientific and medical advice
- » quality control of individual Notified Bodies evaluating high-risk medical devices
- » ensuring that post-market surveillance is assessed independently of manufacturers

1. Patient safety and clinical evaluation

The priority must be to ensure the safety of patients, when new class III (implantable) devices are introduced that have the potential to cause serious risks. This means that when such risks can be anticipated there should be a requirement for the manufacturer to establish the clinical efficacy of its device before it is approved for general market release.

The ESC supports risk-based classification of devices. The draft Regulation retains the requirement for a conformity assessment whereby the manufacturer should establish the performance and safety of a device according to its claims for the functions of the device. Annex XIII of the Regulation indicates how the manufacturer should undertake clinical evaluation, and it confirms that with lower-risk devices, trials of efficacy may not be required. With high-risk devices, and when advised by independent medical experts, the ESC recommends that the approval process should require randomised trials to assess efficacy.

It will be difficult to establish the efficacy of new devices in short-term studies although it may be possible to establish their initial safety. If the requirements for evaluation are reduced for a new device that is the “first in class” to satisfy a previously unmet clinical need, then additional surveillance after marketing will be required. Longterm studies of any class III device should involve sufficient follow-up to establish both safety and efficacy. When a new class III high-risk cardiovascular device is proposed as an alternative to existing, safe and effective devices, it should not be approved on the basis of equivalence; new clinical evaluation should be required. For example, cardiovascular devices in direct contact with flowing blood carry high risk and so any new device that differs in blood-contacting surfaces or in the flow conditions that it imposes would require new clinical studies.

2. Transparency

In order to use medical devices rationally, physicians and surgeons need to base their choices of which devices to use, on an appraisal of their efficacy and safety. The ESC recommended in 2011 that the evidence prepared by manufacturers when submitting

their devices for approval should be made publicly available – including details of technical performance and pre-market clinical studies². Granting physicians access to this information complements peer-reviewed scientific literature, and may be essential for comparing alternative devices within any class.

Patients should also be allowed to obtain the evaluation of any medical device that has been recommended for them, if desired.

The ESC recommends that the Regulation should specify open access to:

- » all data submitted by the manufacturer in its dossier prepared for the Notified Body, including the results of clinical investigations,
- » the subsequent evaluation by the Notified Body, and
- » the conclusions of the relevant national competent authority concerning any clinical trials.

The only exception to this policy would relate to any manufacturing details that are protected intellectual property, in which case the reasons for non-disclosure should be given. A summary prepared by the manufacturer (as proposed in the current draft Regulation) is insufficient. In short, any evidence submitted and considered when an informed decision has been made about approval of a new device, should be disclosed, including any expert advice given to the regulatory authorities.

3. Expert advice

Medical devices are increasingly sophisticated. They may incorporate new materials, advanced engineering, and complex information technology. In order to evaluate new devices, expert specialist knowledge is required. While manufacturers, Notified Bodies and Competent Authorities have access to specialist advisers, the system for approving medical devices is European. At this level, however, there are no systematic mechanisms for obtaining detailed expert professional advice on devices, although the principle of using scientific expertise has been adopted by the European Commission in other contexts³.

The Regulation contains general recommendations but no specific proposals to address this requirement. The Joint Research Centre of the EU will be charged with responsibility for advising the European Commission, but in addition the Regulation should specify that an expert advisory structure will be established so that advice can be readily and routinely obtained by regulators for each medical specialty, for example from materials scientists, physicists, engineers, informatics specialists, and clinical scientists. Specialist European advisory panels should be constituted to review medical evidence and give independent expert advice. The recommendations of any specialist advisory group should be published, with the names of all advisers and with their disclosures of any conflicts of interest.

Health care professionals participating in subgroups of the proposed Medical Device Coordination Group (MCDG), including expert specialists nominated by medical professional societies, should participate as active members and not only as observers.

There is a need for specific clinical product standards to be prepared as an international collaboration by independent experts for each category of high-risk medical device⁴, concerning the criteria by which new devices should be evaluated and advising what pre-market clinical evaluation is indicated. Technical standards should be prepared jointly with regulators and device manufacturers. The new European system should specify how such documents will be commissioned. Medical societies such as the ESC can help to identify relevant experts.

4. Notified Bodies

The performance of the Notified Bodies is a crucial element in the European system governing medical devices. The ESC welcomes the proposals in Annex VI of the Regulation to strengthen the supervision of Notified Bodies and to increase quality, transparency and comparability of their processes by enhanced collaboration between competent authorities and the European Commission.

The ESC advises that it is essential that high-risk medical devices are evaluated only by Notified Bodies with proven expertise in evaluating the specific type of device under consideration. The Regulation should give the European Commission the authority to

designate capacity for assessing particular applications to a limited number of Notified Bodies with specific qualifications, in areas where expertise is scarce. The decisions of competent authorities when designating Notified Bodies should be reported.

Notified Bodies should not undertake any evaluation of the pharmacological properties of a borderline medical device, which is the responsibility of the European Medicines Agency or a national regulatory body for pharmaceutical products.

5. Post-market surveillance

The decentralization of the system for approving medical devices in the European Union – by delegation to Notified Bodies approved by national Competent Authorities – is considered to support innovation. It has given patients in Europe early access to new devices from which many have benefited. In the event of unexpected complications, however, the system has also placed some patients in Europe at increased risk². A new device may be associated with unforeseen adverse events, some of which may become apparent only during long-term follow-up or when the device is applied in high-risk clinical settings. Approval for a new class III device before there has been extensive clinical experience of its use, must therefore be balanced by rigorous monitoring after approval, in order to provide an efficient early warning mechanism.

For new and innovative class III devices, the ESC supports the concept of obligatory registries with prospective and complete follow-up of all patients for a pre-specified period after approval, with standardised collection of data. Post-market registries need to adhere to uniform quality standards, and their results including complication rates need to be open to public audits. Upon completion, the findings of registries should be published, regardless of their outcomes. Autopsies and explant analyses provide vital evidence about device failure modes and should be encouraged whenever possible⁵. Appropriate thresholds for device withdrawal from the market should be agreed in advance. The involvement of independent scientific bodies such as academic institutions or medical societies like the ESC, who have considerable experience in the design, conduct and analysis of observational studies, should be promoted to strengthen post-market clinical

follow-up (PMCF). The Regulation proposes that the manufacturer will be responsible for collecting data, whereas the ESC considers that the Regulation should specify that manufacturers are responsible for making data collection possible, but that analysis and reporting of PMCF including registries will be conducted independently.

The ESC recommends also that the concept of conditional approval should be included in the Regulation. This would enable competent authorities in special circumstances (such as the use of a new concept of treatment or a new technological design, or when recommended by an expert advisory panel) to specify that continued access to the market for a device is made dependent on the manufacturer collecting further evidence, systematically, for example from a post-marketing clinical trial, and resubmitting the results to the Notified Body and Competent Authority within a specified time.

Doctors need early access to reports of device failures and complications. The Regulation will strengthen the management of the EUDAMED database of medical devices. Access to its full contents including reports of device failures should be extended to health care professionals and patients. Manufacturers should be obliged to publish their own Field Experience Reports of device failures based on their complete worldwide experience.

Conclusions

The ESC supports the planned reform of the European Union system for approving medical devices, including unification of the directives into a single regulation, coordination between the national competent authorities, and quality control of the Notified Bodies. Modern medical devices benefit patients enormously, particularly within the field of cardiovascular medicine and surgery. A partnership is required between medical experts and industry to develop and evaluate new devices and to ensure the safety of patients, while also encouraging innovation. With the amendments recommended by the ESC, the proposed new European law can help to maintain access for patients to new devices while also ensuring a high level of protection of public health.

References and links

1. European Commission. Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on medical devices, and amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009. Brussels, 26.9.2012, COM(2012) 542 final, 2012/0266 (COD).
http://ec.europa.eu/health/medical-devices/files/revision_docs/proposal_2012_542_en.pdf
2. Fraser AG, Daubert JC, Van de Werf F, Estes NA 3rd, Smith SC Jr, Krucoff MW, Vardas PE, Komajda M; participants. Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform. Report of a policy conference of the European Society of Cardiology. *Eur Heart J*. 2011;32:1673-86.
doi: 10.1093/eurheartj/ehr171.
<http://eurheartj.oxfordjournals.org/content/32/13/1673.full.pdf+html>
3. COMMISSION DECISION of 5 August 2008 setting up an advisory structure of Scientific Committees and experts in the field of consumer safety, public health and the environment and repealing Decision 2004/210/EC (2008/721/EC).
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:241:0021:0030:EN:PDF>
4. Fraser AG, Krucoff MW, Brindis RG, Komajda M, Smith SC Jr. Commentary: International collaboration needed on device clinical standards. *BMJ*. 2011;342:d2952.
doi: 10.1136/bmj.d2952.
<http://www.bmj.com/content/342/bmj.d2952?view=long&pmid=21572135>
5. Rao SV, Califf RM, Kramer JM, Peterson ED, Gross TP, Pepine CJ, Williams DO, Donohoe D, Waksman R, Mehran R, Krucoff MW. Postmarket evaluation of breakthrough technologies. *Am Heart J* 2008;156:201-8.
<http://www.sciencedirect.com/science/article/pii/S0002870308003219>



Background – The European Society of Cardiology

The European Society of Cardiology is a professional medical association with >75,000 members including cardiologists, cardiac surgeons, nurses, and medical scientists, based in 55 member countries in the European Union and adjacent regions. It has active links with another 36 affiliated member societies of cardiology around the world. The mission of the ESC is to reduce the burden of cardiovascular disease in Europe.

Cardiologists and cardiac surgeons in the ESC have great clinical experience and expertise in medical devices – particularly Class III or high-risk implantable medical devices, such as stents for coronary artery disease and heart attacks, pacemakers, implantable defibrillators and devices for heart failure, and prosthetic heart valves; and Class IIa or IIb devices which include machines for advanced diagnostic imaging.

In 2011 the ESC convened a policy conference on the regulatory governance of medical devices in Europe, which reviewed evidence of clinical problems affecting patients that could be related to deficiencies in the system of approval. The conference called for major reforms².

The headquarters of the ESC are at the European Heart House, in Sophia Antipolis in the south of France. It also has an office in Brussels in the EU quarter.

For further information please contact the Department of European Affairs, in the Advocacy and Representation Division of the ESC at the European Heart House:

Ms Sophie O’Kelly, Head of European Affairs

sokelly@escardio.org

+33 (0)4 92 94 86 62

February 26th 2013