

Revised EU Directives: Many Changes in Store



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The text of a directive revising European medical device regulations is scheduled to take effect in March 2010.

Since the European single market activities of the late 1980s, three main medical device directives have passed into law in the countries that make up the European Union (EU). These New Approach directives regulate how devices may be placed on the market and identify postmarketing vigilance requirements. These three directives are as follows:

- Active Implantable Medical Devices Directive (AIMDD), 90/385/EEC.¹
- Medical Devices Directive (MDD), 93/42/EEC.²
- In Vitro Diagnostic Medical Devices Directive (IVDD), 98/79/EC.³

The two-digit numbers at the beginning of the directives indicate the year in which the text was published in the *Official Journal of the European Communities (OJ)*; it can be concluded that there was a span of eight years between the first and the third. During this period, a number of the generic elements of the directives changed, so it was logical that at some stage in the directives' lives, their requirements should be aligned.

The opportunity for alignment came with the review time scale included in the MDD, article 11, paragraph 4. It required the European Commission to review the operation of specific aspects of the directive five years from the date of its entering into force. These aspects included four areas: adverse incident reporting, clinical investigations for Class I and Class IIa devices, design dossier examination by notified bodies, and combination products.

The MDD took effect June 15, 1998, and the review of its operation began in 2003, with the European Commission

and member national competent authorities (NCAs) taking the opportunity to review all three directives at the same time.

This review resulted in a revising directive, 2007/47/EC, which was published in the *OJ* on September 21, 2007.⁴ This directive makes no changes to the IVDD, but in many respects it brings the other two directives broadly into line with the IVDD.

This article will not cover the details of the four-year revision process, with its many disagreements and eventual compromises between the European Commission, European Parliament, and European Council. Suffice it to say that some areas, such as the reuse of single-use devices, are still not covered by the directives. In addition, to avoid repetition, only changes to the MDD will be covered in any detail. In general, the same changes apply to the AIMDD.

Unfortunately, consolidated versions of the revised directives were not available at the time of writing, although these were promised by the European Commission before the end of 2007. Until they are available, interested parties will have to read the 35 pages and 141 amendments of the revising directive together with the current consolidated versions of the directives to understand all that has changed. The most significant amendment topics for manufacturers are indicated in Table I.

Definitions

The revising directive clarifies what constitutes *software* within the scope of the MDD. Software that is intended to be used specifically for diagnostic or thera-

peutic purposes will be subject to the directive's requirements. Recital (6) of 2007/47/EC amplifies this by stating that software for general purposes when used in a healthcare setting is not a medical device. The classification definitions in Annex IX have also been amended to include software as an active medical device.

Clinical data is defined as "the safety and/or performance information that is generated from the use of a device." Such data may be sourced from clinical investigations of either the device itself or equivalent devices, published scientific data on equivalent devices, or from published or unpublished reports on other clinical experience of either the device or equivalent devices.

Device subcategory and generic device group are defined in the context of the extent of documentation that notified bodies (NBs) must, in the future, examine during quality management system audits. The definitions are virtually indistinguishable from each other (*device subcategory* means "a set of devices having common areas of intended use or common technology;" *generic device group* means "a set of devices having the same or similar intended uses or commonality of technology").

However, *device subcategory* applies specifically to Class IIa devices, whereas *generic device group* applies specifically to Class IIb devices. The quality system annexes have been amended to require NBs to assess the technical documentation for at least one representative sample for each device subcategory or generic device group to determine compliance with the directive.

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Single-use device is defined as a device intended to be used once only for a single patient. The definition has been included because of concerns that regulation of the reuse of single-use devices within Europe is not universal and, in some cases, is contradictory. During development of the revising directive, arguments were presented for both control under the revising directive and for an outright Europe-wide ban.

The European Commission has always presented the view that the directives apply only up to the point of putting a device into service, as defined. The control of reprocessed devices, unless marketed as fully refurbished under the refurbisher's name, is outside of the directives' scope and should, therefore, be left to the NCAs to decide. The European Parliament did not agree, however, and has required the Commission to develop proposals for the regulation of reprocessed single-use devices by September 2010. The Commission has already started this process by posting a public consultation questionnaire regarding reuse on its Web site, which has received approximately 75 replies.

Two additional essential requirements have been included in the revising directive where single-use devices are concerned. However, these state that manufacturers must ensure that the indication of single use is consistent across the community, and that information on factors that could pose a risk if the device were to be reused. The requirements must be included in the instructions for use.

Inclusions and Exclusions

The revising directive confirms which types of devices are included or excluded from the scope of the MDD. Specifically, it addresses devices including or containing pharmaceuticals, human blood derivatives, blood products, tissues or cells of human origin, and tissues or cells of animal origin. It takes into ac-

count the publication of the Advanced Therapy Medicinal Products (ATMP) regulation at the end of 2007.⁵

Two directives that were previously excluded from consideration by medical device manufacturers must now be taken into account.

The MDD made a demarcation between itself and the Personal Protective Equipment (PPE) Directive (89/686/EEC) by requiring the principal intended purpose of the product to be considered; for instance, whether a manufacturer primarily intends a surgical mask to protect the patient or the clinician. Directive 2007/47/EC amends the MDD by requiring manufacturers to fulfill the relevant basic health and safety requirements of the PPE Directive as well as the MDD requirements if the intended use is within the scope of both directives. Only one CE mark will be required, but if more than one NB has been involved in the assessment process, it is believed that both NB numbers will have to appear with the CE mark. This will hopefully be clarified by future guidance.

In addition, the original MDD allowed medical device manufacturers to consider only the essential requirements of that directive, even if the device included aspects that would otherwise fall within the scope of the Machinery Directive (recently revised and published as 2006/42/EC). The MDD revision, however, requires that: "Where the relevant hazard exists, devices which are also machinery within the meaning of Article 2(a) of Directive 2006/42/EC must also meet the essential health and safety requirements set out in Annex I of that Directive to the extent to which those essential health and safety requirements are more specific than the essential requirements set out in Annex I of this Directive."

This is a controversial change, introduced by the Parliament without consultation with the medical device indus-

try or support from the Commission. One industry association commented that this was "another example of intransparent policy making."

It may be helpful to include here an extract from the definition of *machinery* from Article 2(a) of Directive 2006/42/EC, to give an idea of the type of medical device that might now be captured by this new requirement:

- An assembly, fitted with or intended to be fitted with a drive system other than directly applied human or animal effort, consisting of linked parts or components, at least one of which moves, and which are joined together for a specific application.
- An assembly of linked parts or components, at least one of which moves and that are joined together, intended for lifting loads and whose only power source is directly applied human effort.

The interpretation by manufacturers, NBs, and NCAs of "more specific than the essential requirements set out in Annex I" will be interesting as time passes. The Commission will issue new guidance notes before full implementation of the directive. It is hoped that these new guidances will provide clarification.

Custom-Made Devices

There are a number of changes to the requirements for custom-made devices. Those changes include the following seven items:

- The custom-made statement required by Annex VIII for Classes IIa, IIb, and III devices must be made available to the particular patient for whom the device has been made.
- The patient may be identified on the statement by means of name, acronym, or numerical code.
- The statement must now include both the name and address of the manufacturer.
- In the documentation that must be kept available for inspection by NCAs, the manufacturer must now include names and addresses of the manufacturing site(s).

- If the device is implantable, the documentation must be kept for at least 15 years instead of 5 years.
- Custom-made devices will in the future be subject to the vigilance requirements applicable to devices in serial production.
- Registration of custom-made devices in the European databank (EUDAMED) will no longer be required.

Article 7 Committee and the Device Registration

Under the earlier wording of Article 14, NCAs were allowed, for Class IIb and Class III devices, to “request to be informed of all data allowing for identification of such devices together with the label and the instructions for use when such devices are put into service within their territory.” The revision extends this to include Class IIa and active implantable devices.

Device registration is one area of the directives’ implementation in which subsidiarity, or the ability of member states to make their own decisions on what to include in their national regulations transposing the directives, has already played a major role. Some NCAs require little or no information on devices for which there is NB involvement, whereas others have already implemented, or are now planning, comprehensive registration regimes.

Italy, for instance, has a dedicated on-line databank. It requires 55 questions to be answered for each device or device family being marketed in Italy, the upload of some elements of the technical file, and the use of an electronic signature SmartCard for validation of the data entry. Once reviewed and approved by the NCA, the manufacturer must also register to be able to sell devices to medical facilities within the Italian national health service. Payment of a €100 *repertorio* fee per device or device family is required.

The French NCA, AFSSAPS, has also launched a more detailed registration scheme, although it is voluntary at the moment. The scheme allows the NCA to sort devices on a hierarchical basis according to their degree of innovation. One of the 30 sections within the questionnaire that must be completed requires manufacturers to identify into which of six innovation levels their de-

MAJOR AREAS OF CHANGE	COMMENT
Definitions	Software has to be used specifically for diagnostic and/or therapeutic purposes to be considered as a medical device. Definitions added for <i>clinical data</i> , <i>device subcategory</i> , <i>generic device group</i> , and <i>single-use device</i> .
Authorized Representative (AR)	ARs will be a requirement for non-EU manufacturers of medical devices and active implantable medical devices.
Reuse of Single-Use Devices	The EC must issue a report on the topic of reprocessing of single-use devices by September 5, 2010.
Custom-Made Devices	Now subject to vigilance requirements. A copy of the ‘Statement’ under Annex VIII must be given to the named patient.
European Databank (EUDAMED)	In view of the lack of progress in setting up the databank, the EC must, no later than October 11, 2012, evaluate the operational functioning and the added value of the databank, and present its proposals to the European Parliament and Council.
Instructions for Use	Must now include a revision level or date of issue. No inclusion of acceptability of electronic labeling, but any such future amendments may be authorized in accordance with Article 7, as revised.
Class I Sterile or Measuring Devices	Annex II is added to Annexes IV, V, or VI, thus allowing manufacturers of Class I sterile or measuring devices to use the full quality assurance route to demonstrate compliance of those particular aspects of the device.
Implantable Devices	The information that had previously to be kept for at least 5 years after the last device had been manufactured must in future be kept for 15 years for implantable devices.
Clinical Evaluation	Now clarified that a clinical evaluation is required for all classes of device. The clinical evaluation and its documentation must be actively updated with data obtained from the postmarket surveillance.
Clinical Investigations	Adequacy of demonstration of conformity with the essential requirements by performance evaluation, bench testing, and preclinical evaluation alone must in the future be fully substantiated.
Use of Phthalates	If a device contains phthalates that are CMR (carcinogenic, mutagenic, or toxic to reproduction), category 1 or 2, Annex I, Directive 67/548/EEC (classification, packaging and labeling of dangerous substances), then the device labeling must identify it as such.
Classification	Definition of central circulatory system extended to include additional vessels. Devices intended specifically to be used for disinfecting invasive devices will fall into Class IIb.

Table 1. Major areas of the MDD amended by revising directive 2007/47/EC.

vices fall. Levels range from “no innovation” to “major innovation.” In addition to answering the questions, manufacturers must also supply a photograph of the device, copies of the labeling and instructions for use, the declaration of con-

formity, a description of the technical operation when applicable, and the sales literature.

The revising directive paves the way for such comprehensive registration schemes to become more commonplace.

It allows the nature of such data collection for Class IIb and Class III to be decided by the Article 7 Committee, with oversight from the European Parliament.

Transposition and Future Plans

The revising directive requires member states to publish the national laws implementing the revisions by December 21, 2008, with full application of them by March 21, 2010.

It would be comforting to think that with these amendments, the European device regulatory picture would be stable for a significant period, but this is unlikely for a number of reasons. First, the European Commission is in the final stages of developing a regulation to implement revisions to the underlying structure of the New Approach directives. The device directives, along with around 20 other sectoral directives, are part of this structure. High on the priority list for these amendments are improvements in the consistency and quality of work performed by conformity assessment bodies, as well as improved market surveillance. Finalization of the regulation is expected during the first half of 2008. A review of how the changes affect the device directives will then have to be completed.

In addition, in 2005, the medical device unit within the Commission was charged to begin a review in 2008 of the MDD and AIMDD, together with the directive on human blood and blood derivatives, 2000/70/EC. This review is aimed at simplifying the regulations to make the market more accessible, especially to small companies. The potential

result may be that these directives are combined into a single piece of legislation.

With the soon-to-be-implemented regulation on advanced therapy medicinal products, the Commission must consider whether the full set of medical device directives and regulations should be combined into a single legislative package. But, given the ever-changing technological and political environments, it is probable that further changes to the regulatory requirements would be made at the same time. There is also the question of how to address medical products that currently fall outside of current and planned legislation. These include products that could be considered medical devices except that they contain human stem cells or contain or are made from viable tissues or cells of animal origin. Currently, these types of products are covered only by a variety of national regulations.

Conclusion

Although the exact nature of future legislation for medical devices in Europe is difficult to predict, it is safe to say that further changes are likely. The only wish from industry is that the inclusion of a hint of harmonization in 2007/47/EC will pave the way for greater international cooperation and harmonization, rather than the development of more regional requirements. Tucked away in a new article (Article 20a) in the MDD, it says: "Without prejudice to the provisions of this Directive, cooperation may be part of initiatives developed at an international level." The Commission had

already organized and chaired a workshop on the need for harmonized requirements at the 11th Conference of the Global Harmonization Task Force (GHTF) in Washington, DC, in October 2007. This new article may be a sign that, after 15 years, the importance of GHTF for the future of the global medical device industry is, at long last, being taken seriously.

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