

Navigating the New EU Rules for Medical Device Software

Mathias Klümper and *Erik Vollebregt* examine how European Directive 2007/47/EC will affect requirements for medical device software.

Directive 2007/47/EC marks the introduction in the European Union of stricter rules for software used with medical devices¹. The directive, which is set to come into force on 21 March 2010, will require for the first time that certain software be classified as medical devices and validated and CE-marked accordingly. The new rules are incorporated in the directive in the form of amendments to the existing directive on medical devices² (the MDD) and the current directive on active implantable medical devices³ (the AIMDD).

This article reviews the amendments to the MDD and the AIMDD with regard to software and examines the types of software that they cover. It also provides practical information on applicable standards and discusses how companies can ensure they comply with the new rules.

A brief history

The EU directives on medical devices, active implantable medical devices and *in vitro* diagnostics were first drafted the early 1990s, a time when software tended not to be a major component of medical technology products or played only a tangential role. Since then, software engineering has advanced considerably and the technology is becoming an increasingly common feature of medical devices.

The amendments made by Directive 2007/47/EC are designed to recognise this sea change on the software front and the fact that the technology can be subject to safety risks. Consequently, the directive states in its preamble that it is "necessary to clarify that software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of a medical device, is a medical device"⁴. These stricter rules also increase requirements for manufacturers. The preamble states⁵: "Validation of software in accordance with the state of the art should be an essential requirement."

Software and the directives

Only certain types of software are covered by the amended rules. Applicable medical devices and accessories thereto are defined in Article 1, paragraph 2(a) of both the MDD and the AIMDD. According to the amendments, medical devices are defined as:

...any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, together with any accessories, 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...

Consequently, only stand-alone software or software that is used in combination with a medical device for purposes set forth in the directives is covered by them. Only such software must fulfil the strict requirements set forth in these directives, in particular the essential requirements (as set out in Article 3 in connection with Annex I of both the MDD and the AIMDD).

Medical software can be divided into the following three categories:

- software that is in itself a medical device or is an accessory to a medical device;
- software that is a component or an integral part of a medical device; or
- software that is none of the above.

When is software a medical device?

Software is considered to be stand-alone or accessory, and, therefore, a medical device and covered by the new rules, if one or more of the following four criteria are met:

- the software's intended purpose satisfies one of the purposes explicitly mentioned in Article 1, paragraph 2(a) of the MDD, AIMDD or IVD directive. For example, software used for diagnosis, monitoring, treatment or alleviation;

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Software is considered a medical device if it meets one or more of four criteria

Mathias Klümper is a lawyer at Lützel Nießen und Partner, in Düsseldorf, Germany, and *Erik Vollebregt* is a lawyer at Greenberg Traurig LLP in Amsterdam, the Netherlands.

- the software's purpose is to control or influence the functioning of a medical device within the meaning of the MDD or the AIMDD. An example here would be software that takes over the dose-planning function of a medical device;
- the software is used for the analysis of patient data generated by a medical device, with a view towards diagnosis and monitoring. Examples here are software used to process image data from X-ray scanners or for analysing data collected from long-term electrocardiogram monitors; or
- the software is designed to be used for, or by, patients in the diagnosis or treatment of a physical disease or mental health condition.

Software that qualifies as a medical device must be CE-marked in its own right

Software that meets one or more of the aforementioned criteria must be CE-marked in its own right and must undergo conformity assessment as such. Classification rules in Annex IX of the MDD can help decide whether stand-alone software qualifies as a medical device.

Component and integral software

Software is often only a simple component among many constituents of a medical device, or an integral part of a product. In such a case, the software is not a medical device in itself, since it neither fulfils the purposes of a medical device on its own, nor is it related to the core functions of a medical device. As such, it does not need to be CE-marked in its own right. However, it is still covered by the amended directives to the extent that it must be covered in the conformity assessment of the device to which it belongs.

Examples of component or integral software are firmware of a ventilator or infusion pump and software that controls the power management or the cooling system of a medical device.

Software not covered by the directives

Types of software not covered by the amended directives are those that do not fall within the definitions of a medical device or that are not components or integral parts of medical devices. Since these types of software are not covered by the directives, they do not need to undergo conformity assessment, nor do they require a CE-mark.

Software used for administrative purposes, such as in the handling of patient files and data, are not covered by the amendments

Software that falls into this category is that used for administrative purposes such as in the handling of patient files and data, or for educational purposes such as in training physicians in how to use a medical device.

Table 1 summarises the three different categories of software and the degree to which they are affected by the amended directives.

Software	Amended directives	CE-marking
A medical device itself or an accessory to a medical device	Directly applicable to software	CE-marking required for software
A component and integral part of medical device	Not directly applicable to software	CE-marking not required for software. Software must be covered by conformity assessment of the medical device
Neither a medical device, accessory thereto, nor a component	Not applicable	No CE-marking required

While Table 1 and the advice above on software categories can provide a useful first step in classifying the technology, in practice, the demarcation is difficult and requires a deeper look at each individual case. For example, where does software end and electronics begin?

Conformity assessment dilemma

Manufacturers of software falling within the ambit of the directives might select a combination of annexes for the conformity assessment procedure for their software. Unlike conformity assessments for traditional medical devices, in cases where conformity assessment procedures involve "devices which incorporate software or which are medical software in themselves", the "software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification"⁶. However, in such cases, the conformity assessment procedures used will have to be sufficiently sophisticated to deal with the complexity of the software they are assessing. This means that traditional testing and assessment

Conformity assessment procedures will have to be sufficiently sophisticated

procedures might not be sufficiently adequate to gauge all potential risks that might result from the software.

Software and standards

As with all technology products, standards with respect to software help to ensure compatibility, interchangeability and even basic safety. Standards help to provide a framework that captures best practices and “tested and true” solutions to recurring problems. The EU “new approach” directives, in general, also focus on the same principle, ie on a body of rules with an annex containing essential requirements and CE certification procedures, with a reference to (inter)national standards⁷. Notified bodies and national authorities must use these standards as benchmarks for their assessments⁸. Annex I of the MDD provides that “for devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification”⁹. Taking development life cycle into account when assessing software is critical, because a pure product-related evaluation of the software cannot address all risks associated with medical software¹⁰.

What, then, are the standards for medical software? Standards published in the *Official Journal* with respect to the MDD are mandatory, in the sense that, if they are met, compliance with the MDD must be assumed¹¹. The latest publication of the standards applicable to medical devices (and also to software) can be found in the 27 November 2008 issue of the *OJ*¹². Standards that are harmonised in the EU with respect to software in medical devices are:

- EN 60601-1:2005 – general requirements for basic safety and essential performance;
- EN 60601-1-4 – programmable electrical medical systems; and
- EN 60601-1-6 – usability.

An important new standard is EN 62304¹³. This standard defines risk management-driven life cycle requirements for medical device software, both embedded and stand-alone. It covers the development and maintenance of software, but not validation and release. It is intended to represent the current best practice in medical software and is designed to be used with ISO 13485 (comprehensive management system for the design and manufacture of medical devices) and ISO 14971 (application of risk management for medical devices). EN 62304 employs a safety classification system based on possible harm in worst-case scenarios: the higher the risk classification, the higher the burden of controls required from the manufacturer.

A standard that is not EU-harmonised, but is considered important with respect to functional safety of electrical/electronic/programmable safety related systems, is IEC 61508-3.

Answers to queries not addressed by the EU-harmonised standards and other helpful guidance can be found on the website of the US Food and Drug Administration. The agency’s website contains guidance on general principles of software validation, cybersecurity for networked medical devices containing off-the-shelf software, off-the-shelf software use in medical devices, and the content of premarket submissions for software contained in medical devices¹⁴.

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Helpful guidance on software can also be found on the US Food and Drug Administration website

Complying with the new rules

In general, many of the compliance issues that arise do so because manufacturers treat software development as an activity that must conform to the standards applicable to software and the annexes to the MDD. As evidenced above, there is more to compliance than just that. The following paragraphs examine compliance issues that manufacturers typically encounter with respect to software.

Clinical trial requirements

For software that qualifies as a medical device but is not yet CE-marked or is a new version that is not covered by the previous CE mark (for example, because it is an update to remedy a flaw that caused an incident), a manufacturer is prohibited from running that software in human tests outside of an approved clinical trial setting. This rule may appear obvious, but it is, in practice, a frequent source of confusion and mistake on the part of manufacturers.

Software that is a medical device but is not yet CE-marked cannot be run in human tests outside of an approved clinical trial setting

Changes to software

Manufacturers often make changes to their software. The altered software is then uploaded onto the medical devices during service or maintenance or even remotely via the internet. If the software is a medical device or the software is certified as embedded in the device, such changes count as changes to the device for the purpose of compliance with the MDD. Therefore, if a manufacturer makes changes to CE-marked software (eg it releases a new version, new intended use, change of platform on which software runs or solving of compatibility issues) it must ensure that:

Changes made to CE-marked software must be validated and approved

- the software still complies with essential requirements in the MDD;
- the changes are documented (see EN 60601-1-4);
- the changes are validated and approved;
- significant changes are reported to the notified body and authorities (if applicable, for example, changes after an incident);
- the changes made do not change the risk classification of the device – if so, the manufacturer must perform a new conformity assessment; and
- the manufacturer contacts the notified body if the CE certificate refers to previous versions of the software.

Where does a medical device end and the network or other software begin?

As medical devices become more and more networked and installed with software that interfaces with other software, it is important for the manufacturer to determine where the medical device “ends”, and, consequently, to determine the corresponding regulatory obligations.

Recital 6 of Directive 2007/47/EC provides that software is a medical device if it is specifically intended by the manufacturer to be used for one or more of the medical purposes articulated in the definition of a medical device. It also provides that software for general purposes, when used in a healthcare setting, is not a medical device.

In addition, the MEDDEV 2.1/1 guidelines with respect to software state that¹⁵: “In the case of software intended for use with multipurpose informatic equipment, a distinction has to be made between software providing for a proper diagnostic or therapeutic tool and software for handling general patient-related data. Only in the first case may a medical purpose be determined.”

However, this distinction is difficult to make with diagnostic software that allows the doctor, while at the patient’s bedside, to view diagnostic images that are enriched with other data from the patient’s electronic records. There is no doubt that the modules of the software that generate the diagnostic images based on the scanner input are a medical device as such or embedded in the scanner. The question would be whether the module that provides the enriched bedside image is also a medical device.

One could well argue that the module providing the enriched bedside image is intended by the manufacturer for diagnosis or monitoring. A problem arises, however, when one considers the latter part of the definition of medical device in Directive 2007/47/EC: “...and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means”. There is a question mark over how to interpret this part of the definition.

On the one hand, it could be argued that “principal intended action in or on the human body” means that only software that actually works in or on the human body falls within the definition of medical device. On the other hand, it could be argued that this part of the definition serves only to define the border between medical devices and medicinal products and, accordingly, is an element of fine-tuning rather than a core element of definition of what constitutes a medical device. We feel that the interpretation that software must actually work in or on the body in order to qualify as a medical device does not do justice to the fact that stand-alone software with an intended medical purpose is supposed to be covered by the MDD according to EU guidance document MEDDEV 2.1/1 and Recital 6 of Directive 2007/47/EC. The extra diagnostic module in this example would, in our view, be covered by the MDD.

Subcontractors and outsourcing parties

Currently, few companies develop all elements of all their software in-house. Parts of the software can be bought off the shelf or, alternatively, can be developed by subcontractors or through outsourcing of development. These software parts are then integrated into the software of the medical device manufacturer. Ultimately, the software, as placed on the market by the medical device manufacturer, must meet all the requirements of the MDD. Consequently, the manufacturer must take certain precautions to ensure its control over the whole chain of development of the software concerned.

Firstly, the medical device manufacturer must ensure that the development process of the software fits the requirements imposed by the annexes to the MDD and the applicable standards, such as EN 62304. To achieve this, it must ensure that it knows from where all the elements of its software originates – the software should not contain any software of unknown provenance (SOUP). Typical examples of SOUP are open source components.

Secondly, the manufacturer must ensure that all of the elements of the software have been developed according to the requirements in the annexes to the MDD and the applicable standards. This means that it is also mandatory for third parties to conform to these requirements and

Determining whether or not software constitutes a medical device can be difficult

A medical device company must know from where all the elements of its software originates

standards. In practice, it is not sufficient to insert a boilerplate clause in an agreement that the developer “must meet all applicable standards and conform to all applicable rules”. Instead, it would be preferable if the standards were explicitly stated in the agreement, thus obligating the developer to share responsibility for the software. Ultimately, however, it is the manufacturer that issues the declaration of conformity and, therefore, faces regulatory liability for the software.

Thirdly, the manufacturer must ensure in the case of a third-party developer that it has access to (or preferably ownership of) the developer’s data that must be submitted in the technical file for CE-marking. Manufacturers without access to, or ownership of, such data might end up having to come to an agreement with the developer involuntarily because the manufacturer may not be able to use the data in the technical file anymore after termination of the agreement with the developer.

Finally, the manufacturer must require that its subcontractors report any design changes in their software, as design changes may necessitate notification to the notified body that audited the software before it was altered and should be included in the manufacturer’s technical file.

Observing the deadline for implementation

By 21 March 2010, all CE certificates and technical files must be compliant with the new rules¹⁶. Since the MDD does not provide a transitional period after the rules enter into force on this date, all software in a medical device or constituting a medical device must conform to the revised MDD and the national implementing legislation¹⁷. This means that all revision of technical files and CE certificates must have been completed before that date. Merely starting a procedure to adapt the technical file or certificate prior to 21 March 2010 is insufficient; the procedure must be completed by that date.

All CE certificates and technical files must be compliant with the new rules by 21 March 2010

Developments in the pipeline

As for future developments in the medical device software arena, national regulators have said that a MEDDEV guideline on software is being developed and that there are other MEDDEVs in the pipeline that might contain provisions on software, for example a MEDDEV on clinical evaluation.

Furthermore, given that software is playing an increasingly important role in the functioning of medical devices, it is likely that the proposed EU recast of the medical devices legislation will put more emphasis on software. It is now clear that formal recast proposals are unlikely to be made public before the beginning of 2010. A new commission is to be installed in September 2009 and it remains to be seen what impact it might have on the draft recast being prepared by the current commission.

The expected EU recast of the medical devices legislation is likely to put more emphasis on software

As medical devices become more networked or network-based, the rules and standards that govern them must also evolve to keep up with these advances. Some medical devices solely comprised of stand-alone software are already provided as a “software as a service” (SAAS) model. Device manufacturers that provide SAAS models would in effect become IT service providers.

Software for remote patient monitoring will become more important and acquire more functionalities. In addition, there is a paradigm shift in healthcare to disease prevention and this will see new software being developed to predict a patient’s likelihood of developing diseases to support lifestyle management and/or prophylaxis. Software-based decision support systems for diagnosis will become more refined and increasingly embedded in hospital processes.

Software developers will increasingly use off-the-shelf software components to build software with an intended use that qualifies it as a medical device.

Software that control medical devices will play an increasingly “active” role as devices such as surgical robots evolve. Thus, the range of situations in which software bugs may directly impact the human body will become ever wider.

Finally, there are a number of e-health initiatives underway at the EU level focusing on software and medical devices, for example, clinical information systems such as medical imaging devices and remote monitoring devices^{18,19}.

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Conclusion

Directive 2007/47/EC clarifies and increases requirements for software relating to medical devices. These clarifications and new requirements were necessary to account for the massive advances in software technology that have taken place since the medical device directives were first drafted at the beginning of the 1990s.

The new requirements amend the MDD and the AIMDD so that the directives cover software that is a medical device in itself or is an accessory to a medical device. The directives are also amended to cover software that is a component or an integral part of a medical device. Only stand-alone or accessory software is directly subject to the directives. For component and integral software, the conformity assessment of the software forms part of the conformity assessment of the overall medical device.

In practice, medical device manufacturers will have to consider which conformity assessment procedure will be adequate to assess their software. Traditional testing and assessment procedures might not be competent for today's complex software.

However, there are a number of harmonised and non-harmonised standards and guidelines that manufacturers will be able to rely on. When considering compliance with the medical device directives, manufacturers should be aware that tests of software relating to medical devices might qualify as a clinical trial and, therefore, must be conducted in compliance with the applicable requirements. With regard to changes to the software during its life cycle, manufacturers might be subject to documentation, approval and reporting obligations. In some cases, a new conformity assessment might also be necessary.

The question of where a medical device ends and where a network or other software begins remains difficult to answer in practice. It will be necessary for harmonisation bodies to provide clarification in this area, possibly through the issuance of MEDDEVs.

Finally, all manufacturers should be reminded of the 21 March 2010 deadline for compliance with the amended requirements, as Directive 2007/47/EC grants no transition period in this respect.

More clarification is needed to determine where a medical device ends and a network or other software begins

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