MEDIMARK® EUROPE NEWS **March 2009**

Medical Device Directive 2007/47/EC: Changes to MD 93/42/EEC. Application date: March 21, 2010.

The most important changes are the requirements of clinical data and design documentation for all classes of devices. It will particularly concern the manufacturers of class IIa devices because they are audited by a Notified Body. However, manufacturers of Class I devices are also concerned through their ISO 13485:2003 audit or when a competent authority makes an inspection of the technical files at the European authorized representative premises. Guidance documents and secondary legislation ought to be developed in order to ensure that the new provisions are adequately implemented but in March 2010 we have not seen much of these guidances.
However, besides these main new requirements, the new medical device directive has introduced a lot of other changes which may impact your European business. MediMark Europe has performed an original work in creating a comprehensive glossary of these changes.

Authorized Representative: a single one
Where a manufacturer who places a device on the market under his own name does not have a registered place of business in a Member State, he shall designate a single authorized representative in the European Union. This designation should be effective at least for all devices of the same model. (In the previous version of the MD Directive, it was written “the person(s) who is (are) responsible for marketing them who is (are) established in the Community)

Classifications
- The definition of central circulatory system has been extended to the aorta arcus and aorta descendens to the bifurcatio aortae. It moves any devices contacting these vessels into Class III.
- Devices for use in direct contact with the central nervous system would also be in Class III.
- Devices which are specifically to be used for disinfecting invasive devices are in Class IIb. (instead of class IIa before)
- Invasive devices with respect to body orifice intended for connection to an active Class 1 medical device are in Class I (These devices were not classified).

Class 1 compliance module
Manufacturers of Class I sterile and/or measuring medical devices have the option of using the full quality assurance conformity assessment module (Annex II). It will be not necessary anymore to have a separate EC Certificate - Annex V for the manufacturers having chosen Annex II for their other higher class devices.

Clinical Data Requirements for all Classes
Clinical Data would be required for all devices, even those in Class I, the lowest risk category. The Essential requirements include a new section 6a : Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex X.
The Annex X says that the characteristics and performances under the normal conditions of use of the device, and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 6 of Annex I, must be based on clinical data.

(suppression of the wording “in particular in the case of long term implantable devices and class III)
The evaluation of this data, (clinical evaluation), taking account of any relevant harmonized standards, must follow a defined and methodologically sound procedure based on:

1.1.1. either a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device, where:
   - — - there is demonstration of equivalence of the device to the device to which the data relates, and
   - — - the data adequately demonstrate compliance with the relevant essential requirements;

1.1.2. or a critical evaluation of the results of all clinical investigations made;

1.1.3. or a critical evaluation of the combined clinical data provided in 1.1.1 and 1.1.2.

The clinical evaluation and its documentation *must* be actively updated *with data obtained from the post-market surveillance*. Where post-market clinical follow-up as part of the post-market surveillance plan for the device is not deemed necessary, this must be duly justified and documented.
Where demonstration of conformity with essential requirements based on clinical data is not deemed appropriate, adequate justification for any such exclusion has to be given based on risk management output and under consideration of the specifics of the device-body interaction, the clinical performances intended and the claims of the manufacturer. Adequacy of demonstration of conformity with the essential requirements by performance evaluation, bench testing and preclinical evaluation alone has to be duly substantiated

Confidentiality by the Competent Authorities
The adverse events reported to the competent authorities and information contained in certificates issued, modified, supplemented, suspended or withdrawn are excluded from the scope of their confidentiality.

Continuous use definition
Continuous use means an uninterrupted actual use of the device for the intended purpose. However where usage of a device is discontinued in order for the device to be replaced immediately by the same or an identical device this shall be considered an extension of the continuous use of the device.

Control of Third party quality system
In the light of the increased use of third parties to carry out the design, manufacture and/or final inspection and testing of the devices on behalf of the manufacturer, it is important that the manufacturer demonstrates that he applies adequate controls to the third party to continue to ensure the efficient operating of the quality system.

Declaration of Conformity:
The declaration of conformity must cover one or more medical devices manufactured, clearly identified by means of product name, product code or other unambiguous reference and must be kept by the manufacturer. It shall declare the compliance with the requirements of 93/42/EEC “as amended by 2007/47/EC until March 21, 2010. Declaration of conformities issued after this date can make reference only to 93/42/EEC.

Design Documentation Review all classes
For *Class* III devices explicit prior authorization with regard to conformity, including an assessment of the design documentation, is required for them to be placed on the market. In performing its duties under the quality assurance and verification conformity assessment

modules for all other classes of devices it is essential and necessary for a notified body, in order to be assured of the compliance of the manufacturer with Directive 93/42/EEC, to review the design documentation for the medical device. The depth and extent of this review should be commensurate with the classification of the device, the novelty of the intended treatment, the degree of intervention, the novelty of the technology or construction materials, and the complexity of the design and/or technology. This review can be achieved by taking a representative example of design documentation of one or more type(s) of devices from those being manufactured. Further review(s), and in particular the assessment of changes to the design that could affect conformity with the essential requirements, should be part of the surveillance activities of the notified body.

Device incorporating a medicinal product
For these substances, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking account of the intended purpose of the device, seek a scientific opinion from one of the competent authorities designated by the Member States or the European Medicines Agency (EMEA), acting particularly through its committee in accordance with Regulation (EC) No 726/2004, on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the substance into the device . When issuing its opinion, the competent authority or the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body.
The opinion of the competent agency or national authority must be drawn up within 210 days after receipt of a valid documentation

Device incorporating Blood derivatives
Where a device incorporates, as an integral part, a human blood derivative, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking into account the intended purpose of the device, seek a scientific opinion from the EMEA, acting particularly through its committee, on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the human blood derivative into the device.

Ergonomic design in the Essential requirements
It is necessary to consider ergonomic design in the essential requirements in order to reduce, as far as possible, the risk of use error due to the ergonomic features of the device. The technical knowledge, experience, education and training and where applicable the medical and physical conditions of intended users (design for lay, professional, disabled or other users) shall be taken into account.

European databank
The data related to custom-made devices are excluded. The data related to clinical investigation are added in the scope of the European databank.
The Commission shall, no later than 2012 evaluate the operational functioning and the added value of the databank. On the basis of this evaluation, the Commission shall, if appropriate, present proposals to the European Parliament and the Council or present draft measures.

IFU by other means
The new directive does not permit e-labeling but it allows the Commission, where justified, to “adopt measures allowing instructions for use to be provided by other means.”

IFU Date of issue
The date of issue or the latest revision shall appear on the instructions for use

Phtalates

The devices must be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction, in accordance with Annex I to Directive 67/548/EEC.
If parts of a device (or a device itself) intended to administer and/or remove medicines, body liquids or other substances to or from the body, or devices intended for transport and storage of such body fluids or substances, contain phthalates which are classified as carcinogenic, mutagenic or toxic to reproduction, of category 1 or 2, in accordance with Annex I to Directive 67/548/EEC, these devices must be labelled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging as a device containing phthalates.
If the intended use of such devices includes treatment of children or treatment of pregnant or nursing women, the manufacturer must provide a specific justification for the use of these substances with regard to compliance with the essential requirements, in particular of this paragraph, within the technical documentation and, within the instructions for use, information on residual risks for these patient groups and, if applicable, on appropriate precautionary measures."
The Commission should give a mandate to CEN and/or CENELEC to specify technical requirements and a suitable specific label for phthalate-containing devices within 12 months after entry into force of this Directive.

Post market Surveillance
The manufacturer shall institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective action.

Preclinical evaluation
The data concerning preclinical evaluation are now included in the section 3.2 of the Annex II Quality System

Registration of Class IIa
Member States may request to be informed of all data allowing the identification of the devices with the label and the Instructions for Use. For all medical devices of classes IIa, IIb and III. (previously, it was only for Class IIb and III).

Reprocessing
Particular care should be taken to ensure that the reprocessing of medical devices does not endanger patients" safety or health. The Commission shall, at the latest three years after the adoption of this Directive, submit a report to the European Parliament and to the Council on the issue of the reprocessing of medical devices in the Community.

Retention of documentation for implantables
The manufacturer or his authorised representative must, for implantable devices to increase the time period for the retention of documents for administrative purposes to at least 15 years.

Serious Adverse events during Clinical investigation
All serious adverse events must be immediately notified to all competent authorities of the Member States in which the clinical investigation is being performed (instead of the competent authority of the country where the serious adverse event occurred).

Single Use information
If the device bears an indication that the device is for single use, the manufacturer shall add in the Instructions for Use information on known characteristics and technical factors that

could pose a risk if the device were to be re-used. For devices in Class 1 and 2a where no IFU are necessary (section 13.1 :can be used safely without instructions), the information must be made available to the user upon request.

Software
The definition of medical device is broadened to include software, whether stand alone or incorporated into another device. Stand alone software is considered to be an “active medical device.”. 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. Software for general purposes when used in a healthcare setting is not a medical device.

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