

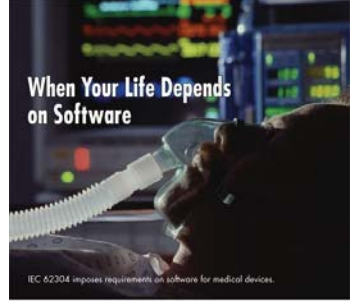
Amendments to the MDD 93/42/EEC

In accordance with Directive 2007/47/EC of the European Parliament and
Council of September 5, 2007

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I. New Definitions / Extended Scope

- Article 1, section 2(a): “Medical Device” - Software included in the scope of the MDD – “Stand Alone” product
 - Article 1, section 2(a): Definition of Medical Device.
 - Annex IX, section 1.4: Considered as an “Active Medical Device”.
 - Classification depends on Intended Use.
 - New Essential Requirement 12.1a: “...validated according to the state of the art taking into account the principles of development lifecycle, risk management and verification & validation.”
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- Article 1, section 2(k): “Clinical Data” – the safety and/or performance information that is generated from the use of a device. Sources of clinical data are mentioned in the clinical section of this document.
 - Article 1, section 2(l): “Device Subcategory” - a set of devices having common areas of intended use or common technology. Eg. Tracheostomy tubes, tracheal tubes
 - For Class IIa (Annex II, Section 7.2; Annex V, Section 6.2; Annex VI, Section 6.2), NB shall assess the technical documentation of at least one representative sample for each ‘device subcategory’
 - Article 1, section 2(m): “Generic Device Group” - a set of devices having the same or similar intended uses or commonality of technology allowing them to be classified in a generic manner not reflecting specific characteristics. Eg. Intraocular lens, implantable contact lens
 - For Class IIb (Annex II, Section 7.3), NB shall assess the technical documentation of at least one representative sample for each ‘generic device group’
 - Article 1, section 2(n): “Single use device”
 - It means a device intended to be used once only for a single patient.
 - Annex I, 13.3(f): Manufacturer’s declaration of single use must be consistent across the EC
 - Relationship with other directives:
 - Article 3: Devices which are based on the principal mode of action of medical devices, but are also covered by the machinery directive need to meet the ER (Annex I) of the Machinery directive to the extent to which they are more specific than the ER of MDD
 - Article 1, section 6: Devices which are covered by the PPE directive and the MDD need to fulfill the basic health and safety requirements of the PPE directive as well
 - Human Tissue: Article 1, section 4(a)
 - Earlier drafts (Dec ’05) included devices with an ancillary human tissue engineered product (with non-viable cells only) within the scope of the MDD
 - Now, only medicinal product constituents or medicinal products derived from human blood or plasma with an ancillary action are included in the scope of the MDD

II. Essential Requirements	
ER No.	Changes made
ER 1	<ul style="list-style-type: none"> ▪ Design for patient safety – risk of use error to be reduced by considering ergonomics and environment of intended use. ▪ Design for intended user – consider technical knowledge, education, skills, experience and mental/physical condition.
ER 6a	<ul style="list-style-type: none"> ▪ Clinical evaluation of all devices required as per Annex X. This is a part of the general requirements and thus is applicable to all devices.
ER 7.1	<ul style="list-style-type: none"> ▪ Valid biophysical or modeling research results can be used to substantiate characteristics and performance as referred in the general requirements
ER 7.4	<ul style="list-style-type: none"> ▪ Medicinal product / Human blood derivative as an ancillary substance <ul style="list-style-type: none"> • NB verifies usefulness; • EMEA/CA determines safety, quality & clinical benefit/risk; • EMEA/CA issues opinion considering substance mfg. process and usefulness determination made by NB. • For Medicinal products either EMEA or CA whereas for Human blood derivatives only the EMEA. ▪ Changes to ancillary substance <ul style="list-style-type: none"> • Particularly mfg. changes; • Inform NB – will consult the CA/EMEA originally involved – determine if change in safety& quality; • EMEA/CA considers usefulness and determines if negative impact on clinical benefit/risk; • EMEA/CA will advise NB if clinical benefit/risk is affected; • NB considers this scientific opinion while reconsidering conformity assessment procedure and make the final decision.
ER 7.5	<ul style="list-style-type: none"> ▪ Devices containing phthalates which are carcinogenic, mutagenic or toxic to reproduction of category 1 or 2. ▪ Labeling on device and/or unit packaging or sales packaging to indicate device contain phthalates. ▪ If intended use involves treatment of children, pregnant or nursing woman, ▪ Mfr. provides justification, residual risk information, precaution information in IFU and technical documentation.
ER 12.1a	<ul style="list-style-type: none"> ▪ Validation of software according to ‘state of the art’ considering development lifecycle, risk management and V&V.
ER 13	<ul style="list-style-type: none"> ▪ 13.3(f) Indication of single use should be consistent. ▪ 13.6(h) If ‘single use device’ re-used, IFU should have technical factors and characteristics that could pose a risk. ▪ 13.6(o) IFU – details of human blood derivatives. ▪ 13.6(q) Date of issue or latest revision of IFU.

III. Conformity Assessment

- Design Documentation Review
 - For Class III explicit prior authorization required
 - Class IIb: Technical documentation review of at least one rep. sample from generic device group (Annex II, Section 7.3)
 - Class IIa: Technical documentation review of at least one rep. sample from device subcategory (Annex II, Section 7.2; Annex V, Section 6.2; Annex VI Section 6.2)
- Subcontractor Control
 - Annexes II & V, Section 3.2(b)
 - Description of the methods of monitoring of efficient quality system operation
 - Description of type and extent of control applied to subcontractor (third party)
- Post Market Surveillance
 - For all Class of Devices => State of the Art.
 - Annex X, 1.1c: “The clinical evaluation must be actively updated with data obtained from the post market surveillance”
- Changes to EC certificates and obligation to inform
 - Article 16(5): Notified Body must inform the CA for all changes to certificates and other Notified Bodies on suspension, withdrawal, refusal (and issuance, upon request).
- Custom Made Devices (Annex VIII): More Evidence of compliance required.
 - Annex VIII, section 5 added requirement for PMS vigilance system reporting to authorities.
- Document Retention
 - Retention of documents for administration purposes to the lifetime of the product.
 - Technical documentation to be kept at least 5 years after the manufacture of the last product for 15 years, for Implantables.
- Borderline Medicines/Devices
 - Article 1, section 5(c): “.... In deciding particular account shall be taken of the principle mode of action of the product.”
- Medicine/Device Combinations (Annex II, III): Consultation timelines, details made explicit

Annexes	Conformity Assessment Procedures for Classes					
	I	I Sterile	I Measuring	IIa	IIb	III
II (+Sect. 4)						X
II (-Sect. 4)		X	X	X	X	
III					X	X
IV		X	X	X	X	X
V		X	X	X	X	X
VI		X	X	X	X	
VII	X	X	X	X		

X: In Accordance with the Directive 2007/47/EC

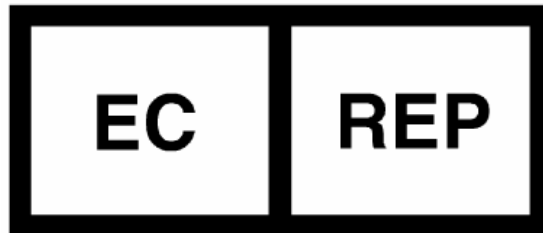
Table 1: Revised Conformity Assessment Table as per 2007/47/EEC

IV. Classification

- Annex IX: Classification Criteria
 - Definitions
 - Active Medical Device: Stand-alone software is considered to be an active medical device.
 - Central Circulatory System: Central circulatory system has been expanded to include arcus aorta, aorta descendens to the bifurcatio aortae (i.e. AAA devices now become class III)
 - Implementing Rules
 - Continuous use means ‘an uninterrupted actual use of the device for the intended purpose’. Duration of invasiveness based on the accumulated use of the same device or even a replacement device.
 - Classification rules:
 - Rule 5: Surgically invasive devices which are connected to an active medical device, which is Class I, are also classified.
 - Rule 6: Surgically invasive devices for transient use:
 - which control the heart or the central circulatory by being in direct contact with them are now Class III.
 - intended for direct contact with the CNS are Class III.
 - Rule 7: Surgically invasive devices for short-term use which control the heart or central circulatory are in Class III.
 - Rule 13: Devices incorporating human blood derivative are Class III.
 - Rule 15: Devices used for disinfecting invasive medical devices are now Class IIb rather than Class IIa.
 - Rule 16: Active/non-active devices specific for recording X-ray diagnostic images are in Class IIa (E.g. PACS)
- Procedures for clarifying the classification of a device have been simplified

V. Clinical Evaluation

Reference	Changes made
Article 1, section 2(k)	<ul style="list-style-type: none"> ▪ Sources of clinical data <ul style="list-style-type: none"> • clinical investigations • clinical investigations or studies reported of a similar device to which equivalence can be demonstrated • published and/or unpublished clinical reports of the device in question or the equivalent device.
Annex X	<ul style="list-style-type: none"> ▪ Clinical evaluation required for all medical devices (i.e. all device classes) ▪ Evaluation of side effects and the acceptability of the benefit/risk ratio shall be based on clinical data. ▪ Critical evaluation of: relevant scientific literature OR clinical investigation results OR combined clinical data from both. Literature route to follow MEDDEV 2.7.1 requirements ▪ Implantable and Class III shall have clinical investigations unless duly justified by existing clinical data ▪ Clinical evaluation and outcome shall be documented and actively updated from post-market surveillance; post-market clinical follow-up required unless duly justified and documented ▪ Serious adverse events should be recorded and immediately notified to CA of the Member States where investigation being performed
Article 15	<ul style="list-style-type: none"> ▪ Investigation refused or halted – Member State shall inform all other Member States and the EC ▪ Modification or interruption – concerned Member State shall inform all other Member States ▪ Mfr. or AR shall notify the CA of end of investigation. ▪ Early termination on account of safety – communicated to all Member States and EC



VI. Authorized Representative

- Authorized Representative (AR)
 - Manufacturer must have a single AR (per device) in the EU
 - AR shall inform the CA of the Member State having the registered place of business of the address and description of devices concerned

CONFIDENTIAL

VII. Confidentiality of Data

- Article 20, section 2: Certain data not considered confidential
- One of the key tenets of this amendment to the MDD is increased openness and communication.
- In line with this adjustment to the definition of what documents are not confidential has been made

VIII. 2007/47/EC Implementation Guidelines

- According to second subparagraph of Article 4(1) of Directive 2007/47/EC, the Member States “Shall apply [the transposition measures] from 21 March 2010.”
- Compliance with the new requirements
 - Before 21 March 2010, manufacturers are not obliged to comply with the new requirements by Directive 2007/47/EC. But they may do so on a **voluntary basis**.
 - The directive **does not make a provision for a period of transition**. In the absence of transitional provisions, medical devices placed on the market or put into service after 21 March 2010 must be in conformity with the (new) requirements of the revised directives. In absence of specific provisions regarding products already on the market, medical devices which have been lawfully placed on the market or put into service **prior** to 21 March 2010 can **continue to be marketed** and used after that date and are subject to the general market surveillance provisions (e.g. Safeguard clause).
- Evaluation by NB according to new requirements
 - Any decision that a NB takes **as of 21 March 2010** regarding the delivery or renewal of a certificate **must take account of the new evaluation requirements**.
 - Certificates Issued prior to application of Directive 2007/47/EC
 - Certificates with unlimited validity: Medical Devices to be placed on the market or put into service as of 21 March 2010, existing unlimited certificates need to be reissued with a limited validity of maximum five years before that date, taking account of the other modifications introduced by Directive 2007/47/EC.
 - Certificates with limited validity: Certificates issued in accordance with annexes II and III had to be limited to a maximum validity of 5 years already under existing legislation. In the absence of specific provisions to the contrary, certificates issued **prior** to 21 March 2010, in principle, maintain their validity provided the manufacturer conforms to the new requirements; otherwise it will be suspended.
- Consultation of authorities responsible for pharmaceuticals
 - The situation when a Notified Body must consult a competent pharmaceuticals' agency thus occurs when it is called upon to decide, as of 21 March 2010, about a manufacturer's application for a new certificate, the renewal of an existing one or the approval of modifications concerning the approved quality system or the approved design.
 - The Notified Body must consult a pharmaceutical's agency or the EMEA “before taking a decision” regarding the evaluation of an active implantable medical device (AIMD) which

incorporates medicinal substance with ancillary action to the one of the device.

- Overlap with Machinery Directive

- Directive 2007/47/EC introduced a new paragraph in the Articles 3 of Directive 93/42/EEC, respectively, which states that where a medical device is also machinery, it shall meet the essential health and safety requirements (EHSR) of the Machinery Directive to the extent to which they are more specific than the essential requirements of the Medical Device Directives. The latter ones thus incorporated the relevant essential requirements of the Machinery Directive and it is common ground that in that way the Medical Devices Directives are to be considered more specific and the application of the Machinery Directive excluded.

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