

Directive 2007/47/EC Modifications to the Medical Devices Directive



Member States Shall.....

- “Adopt and publish by 21 December 2008 the laws, regulations, and administrative provisions to comply with this Directive.”
- Apply measures from 21 March 2010.



1. Software is an active medical device
2. Clarification on single use of medical devices.
Delay in decision regarding reprocessing of medical devices
3. Appointment of single European Authorized Representative explicitly noted
4. Member states may now require information on Class II a devices
5. Closer inspection of design documentation
6. European Databank will be operational



7. Class I (sterile and measuring) devices may now select Annex II
8. Outsourced design and manufacturing must be more closely monitored
9. Records must be retained for 5+ year
10. Modifications to Classification Criteria (Annex IX)
11. Additional requirements added to Essential Requirements (Annex I)
12. Borderline products are clarified



13. Devices with phthalates must be labeled accordingly
14. Clinical data now required for ALL devices, including Class I
15. Provision to allow e- labeling?
16. Custom devices now subject to post market surveillance
17. Requirements for devices to be used in a clinical investigation have changed



1. Software is an active medical device

Software, included into the definition of Medical Device (Article 1)

“Medical device means any instrument, apparatus, appliance, **software**, material or other article, whether used alone or in combination, 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 for the purpose of...”



Annex IX, Classification Criteria, Software added as an “Active medical device”*

“Stand alone software is considered to be an active medical device.”

* This has always been the position of the Notified Body Guidance NB-MED 2.2 Rec 4 Software and Medical Devices.



Annex I, Essential Requirement, 12.1a, software validation

“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.”



Note, one caveat to software...

“Software for general purposes when used in a healthcare setting is not a medical device.”

Recital (6)



2. Clarification on single use of medical devices

Article 1, Definition of single use device

“device intended to be used once only for a single patient”



Annex I, Essential Requirements, Section 13, as it relates to single use devices

- Indication of single use is consistent across the Community.
- IFU must document risk if the device were to be reused based on known characteristics and technological factors.
- If no IFU (Class I or Class IIa (13.1)), information made available to the user upon request.



Delay in decision regarding reprocessing of medical devices

Article 12, Reprocessing of medical devices

- Report to the Parliament before 5 September 2010 on the issue



3. Appointment of single European Authorized Representative (AR) explicitly noted

The AR gets a mandate to act, and be contacted, in lieu of the manufacturer in terms of meeting the obligations by the Directives for all classes of devices.



Designate Single Authorized Representative

Article 14, paragraph 2

“...designate a single authorised representative in the European Union”

Recital (14)

“...designation should be effective at least for all devices of the same model.”



4. Member states may now require information on Class II a devices, Article 14

Member states were given the latitude in transposing Article 14 of the directive, to require “to be informed of all data allowing for identification” of Class IIa, IIb, and III “when such devices are put into service within their territory.”



5. Closer inspection of design documentation

Notified Bodies will be required to perform an inspection of design documentation for a representative sample of devices using industry standard statistical techniques and commensurate with the risk of the device.



Definitions added to Article 1, device subcategory and generic device group

“set of devices having common areas of intended use or common technology”

“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”



Annex II, Section 7.2, Annex V, Section 6.2, and Annex VI, Section 6.2

“For devices in Class IIa the notified body shall assess, as part of the assessment in Section 3.3, the technical documentation as described in Section XXXX for at least one representative sample for each device subcategory for compliance with the provisions of this Directive.”



Annex II, Section 7.3

“For devices in Class IIb the notified body shall assess, as part of the assessment in Section 3.3, the technical documentation as described in Section 3.2(c) for at least one representative sample for each generic device group for compliance with the provisions of this Directive.”



Annex II, Section 7.4, and Annexes V and VI, Sections 6.3

“In choosing representative sample(s) the notified body shall take into account the novelty of the technology, similarities in design, technology, manufacturing and sterilization methods, the intended use and the results of any previous relevant assessments (e.g. with regard to physical, chemical or biological properties) that have been carried out in accordance with this Directive. The notified body shall document and keep available to the competent authority its rationale for the sample(s) taken.”



6. European Databank will be operational

Article 14a, European Databank

- Registration of Authorized Representative and data on clinical investigation added.
- Implemented no later than 5 September 2012.
- Operational functioning evaluated 11 October 2012.



7. Class I (Sterile and Measuring) devices may now select Annex II

Annex VII, Section 5

Class I devices in sterile condition or with a measuring function must observe provisions in Annex VII and “one of the procedures referred to in Annex **II**, IV, V or VI.”



8. Outsourced design and manufacturing must be more closely monitored

If the design or manufacturing of a device is done by a third party, you must demonstrate that you have adequate controls in place to ensure the continued efficient operation of the quality system.



Annex II, V, and VI, Indent added to Section 3.2(b)

“where the manufacture and/or final inspection and testing of the products, or elements thereof, are carried out by a third party, the methods of monitoring the efficient operation of the quality system and in particular the type and extent of control applied to the third party.”



9. Records must be retained for 5+ years

Records must now be maintained for inspection by the Competent Authorities for the useful life of the product or 5 years from date of manufacture, whichever is *greater*. For implantable devices, records need to be kept for 15 years from the time the last product was manufactured.



10. Modifications to Classification Criteria (Annex IX)

- Definitions: active medical device (1.4), central circulatory system (1.7), continuous use (2.6)
- Rule 5, connections active device, Class I
- Rule 6, use direct contact with CNS, Class III
- Rule 15, disinfecting invasive devices, Class IIb



Definition of central circulatory system has been expanded (1.7)

Now includes the vessels aortic arch (*arcus aortae*) and descending aorta (*aorta descendens*) to the aortic bifurcation (*bifurcatio aortae*). Any devices that come in contact with these vessels will now be considered Class III.



Definition of continuous use has been expanded (2.6)

...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.”

* This has always been the position of the MEDDEV 2.4.1 Rev 8 July 2001 Guidelines for the Classification of Medical Devices



11. Additional requirements added to Essential Requirements (Annex I)

- Ergonomic design (ER 1)
- Level of training and knowledge of user (ER 1)
- Clinical Evaluation (ER 6a)
- Biophysical modelling (ER 7.1)



Instructions for Use (IFU) must now be revision controlled

Where appropriate, the new Directive states that the date of issue or latest revision of the IFU must be clearly indicated.

Essential Requirement, 13.6 (q)

“Date of issue or the latest revision of the instructions for use.”



12. Borderline products are clarified, as well as the requirements for devices which also meet other directives

- Whether a product is classified as a medicinal product or device will now be determined by the Principal Mode of Action rather than by the Intended Use!
- Device and PPE, must meet MDD and relevant part of PPE Annex II
- Devices which are also machinery, must meet MDD and Machinery Directive Annex I



Medical Device and Medicinal Product

Article 1, paragraph 5 (c)

“In deciding whether a product falls under that Directive or this Directive, particular account shall be taken of the **principal mode of action** of the product;”



Device and PPE, must meet MDD and relevant part of PPE Annex II

Article 1, paragraph 6

“Where a device is intended by the manufacturer to be used in accordance with both the provisions on personal protective equipment in Council Directive 89/686/EEC (*) and this Directive, the relevant basic health and safety requirements of Directive 89/686/EEC shall also be fulfilled.”

* amended by Regulation (EC) No 1882/2003



Devices which are also machinery, must meet MDD and Machinery Directive (Annex I)

Article 3

“Where a relevant hazard exists, devices which are also machinery within the meaning of Article 2(a) of Directive 2006/42/EC ... shall also meet the essential health and safety requirements set out in Annex I to 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 to this Directive.”



13. Devices with phthalates must be labeled accordingly

Annex I, 7.5

- If devices contain phthalates (carcinogenic, mutagenic or toxic to reproduction) labelled on the device or packaging
- If devices for treatment of children or pregnant nursing women, justification for use of phthalates



14. Clinical data now required for ALL devices, including Class I

- Now required for ALL devices, including Class 1
“clinical data is generally required for all devices regardless of classification*”
- Defined in Article 1, (k)
- More stringent requirements as to what constitutes “clinical evaluation”
- Mandates stronger enforcement by authorities
- Annex X significantly changed
- Centralized data on clinical investigations in EU databank appears to be an EU Commission objective

*Directive 2007/47/EC, Recital (8)



Article 1(k), Clinical Data defined

(k) “clinical data” means the **safety** and/or **performance** information that is generated from the **use of a device**.

Clinical data are sourced from:

- clinical investigation(s) of the device concerned; or
- clinical investigation(s) or other studies reported in the scientific literature, of a similar device for which equivalence to the device in question can be demonstrated; or
- published and/or unpublished reports on other clinical experience of either the device in question or a similar device for which equivalence to the device in question can be demonstrated;



Annex I, Essential Requirements, Section 6a

“Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex X.”



Clinical Data - Annex X, Clinical Evaluation

(a) Section 1.1 is replaced by the following:

1.1. As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I, 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. **The evaluation of this data, hereafter referred to as clinical evaluation, where appropriate taking account of any relevant harmonized standards, must follow a defined and methodologically sound procedure based on:**

Red text denotes changes based on Directive 2007/47/EC.



Clinical Data - Annex X, Clinical Evaluation

1.1a In the case of implantable devices and devices in *Class III* clinical investigations shall be performed unless it is duly justified to rely on existing clinical data.

1.1b The clinical evaluation and its outcome shall be documented. This documentation shall be included and/or fully referenced in the technical documentation of the device.



Clinical Data - Annex X, Clinical Evaluation

1.1c 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.



Clinical Data - Annex X, Clinical Evaluation

1.1d 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.



Clinical Data - Annex X, Clinical Evaluation

- 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.**



Clinical Data - Annex X, Clinical Evaluation

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.



Clinical Documents of Interest

- MEDDEV 2.7.1 April 2003 Evaluation of Clinical Data
- GHTF SG5/N2R8 May 2007 Clinical Evaluation
- ISO 14155-1:2003 Clinical Investigation of Medical Devices for human subjects



MEDDEV 2.7.1 Evaluation of Clinical Data



EUROPEAN COMMISSION
ENTERPRISE DIRECTORATE-GENERAL

Single Market : regulatory environment, standardisation and New Approach
Pressure equipment, medical devices, metrology

MEDDEV. 2.7.1

April 2003

GUIDELINES ON MEDICAL DEVICES

EVALUATION OF CLINICAL DATA :

A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES



EN 14155-1: 2003, Annex A

BS EN ISO
14155-1:2003
*Incorporating
Corrigendum No.1*

Clinical investigation of medical devices for human subjects —

Part 1: General requirements

EN ISO 14155-1:2003

Annex A
(informative)

Suggested procedure for literature review



GHTF SG5/N2R8 May 2007 Clinical Evaluation

SG5/N2R8:2007



FINAL DOCUMENT

Title: Clinical Evaluation

Authoring Group: Study Group 5

Endorsed by: The Global Harmonization Task Force

Date: May 2007



Larry Kessler, GHTF Chair



Now that the clinical data requirement is more explicit, at a minimum, a literature review will be expected.

- “For some devices, clinical data generated through ***literature searching*** will represent the ***greater part (if not all)*** of the clinical evidence.”
- GHTF Guidance SG5/N2R8, May 2007



MEDDEV 2.7.1, Methodology Literature Route

- a. General: written protocol for identification, selection, collation, and review of relevant literature review
- b. Objective(s) clearly defined
- c. Identification of data: sources of data, extent of searches of databases, rationale for selection/relevance of data
- d. Relevance of data: manufacturer demonstrate EQUIVALENCE=clinical, technical, biological
- e. Assessment of clinical data



MEDDEV 2.7.1, Critical evaluation of the literature

- Description of medical device, intended functions, description of intended purpose and application of use
- Analyze all available data
- Relationship of literature to specific characteristics and features device assessed
- Analyze hazards and risks
- Risk analysis relevant to device design
- Describes methods weighting different papers
- Analyze market experience
- List of publications
- Conclusion with justification, assessment of probable benefit to health from use of device
- Signed and dated by author



EN 14155-1: 2003, Annex A, Literature Review Methodology

1. General: documented systematic plan identification, selection, collation, and review of literature review
2. Objective(s) clearly defined
3. Selection criteria for documents: criteria for selection or exclusion of data with an appropriate rationale, sources of literature and data, extent of searches of databases
4. Assessment of documents: similarity of devices in selected documents, patient or study populations, medical purpose, indications for use, conditions of use
5. Critical Evaluation of the literature: documents obtained and assessed, selection and exclusion criteria justified, review based on device's intended use



EN 14155-1: 2003, Annex A, Critical Evaluation Structured Report

1. Short description medical device
intended functions, type of device, technology and features, description of the intended use
2. Analysis of the selected literature and data
3. Critical evaluation of hazards, associated risks and appropriate safety measures
4. Description methods weighting different papers and statistical methods analysis
5. List of publications
6. Conclusion with justification
probable benefit to health, probable risks of injury or illness from such use, "state of the art," objectives of literature met and identify gaps in evidence necessary to cover all relevant aspects of safety and performance
7. Signature reviewer and date

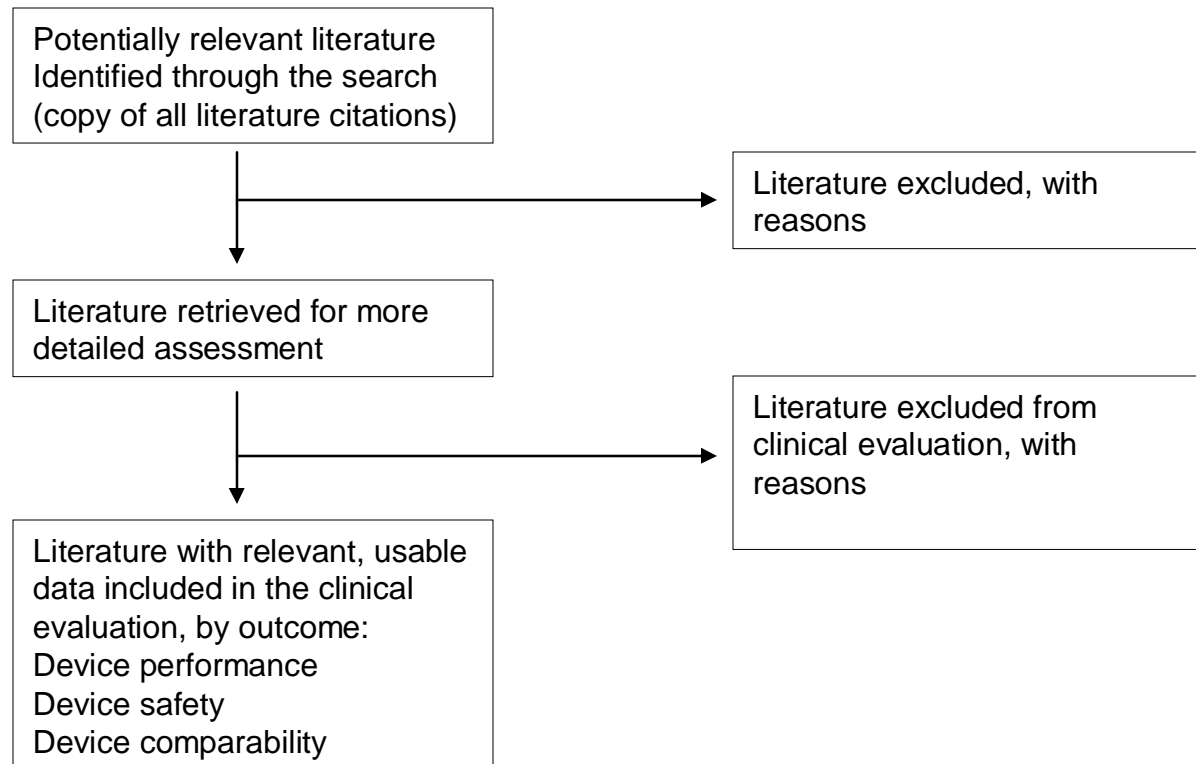


GHTF SG5/N2R8, Appendix A, Format Literature Search Report

1. Device name/model
2. Scope of literature search
3. Methods
 - (i) Date of search
 - (ii) Name of person(s) undertaking the literature search
 - (iii) Period covered by search
 - (iv) Literature sources used to identify data
 - (v) Database search details
 - (vi) Selection criteria used to choose articles
4. Outputs
 - (i) Attach copy of lit citations retrieved from ea database search
 - (ii) Data selection process



GHTF SG5/N2R8, Appendix B, Method Screening and Selection of Literature



GHTF SG5/N2R8, Appendix E, Format Clinical Evaluation Report

1. General details
2. Description of the device and its intended application
3. Intended therapeutic and/or diagnostic indications and claims
4. Context of the evaluation and choice of clinical data types
5. Summary of the clinical data and approval
6. Data analysis
 - 6.1 Performance
 - 6.2 Safety
 - 6.3 Product literature and Instructions for Use
- 7. Conclusions



- CLINICAL DATA and a CLINICAL EVALUATION will now be mandatory. At a minimum, a literature review appears to be necessary.

15. Provision to allow e- labeling?

Recital (10)

“In the light of technical progress in information technology and medical devices, a process should be provided to allow information supplied by the manufacturer to be ***available by other means.***”



16. Custom devices now subject to post market surveillance

Custom devices will now require a post-market surveillance system that is reportable to Competent Authorities (Annex VIII, Statement Concerning Devices for Special Purposes, Section 5)



17. Requirements for devices to be used in a clinical investigation have changed

Annex VIII, Section 2.2 and 3.2, added: investigator's brochure, confirmation insurance of patients, document used to obtain informed consent, intended use statement for device.

Annex X, Section 2.3.5:” All **serious** adverse **events** must be fully recorded and **immediately** notified to **all** competent authorities **of the member states in which the clinical investigation is being performed.**”

