

Essentials of RA

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Devices in the EU: The Essential Requirements Checklist

The European Union directives regarding medical devices—the Active Implantable Medical Device Directive,¹ the In Vitro Device Directive² and the Medical Device Directive³—establish the minimum requirements for medical device safety and performance within their annexes. The manufacturer of the device must show compliance with the applicable requirements in order to affix a CE mark to the device and subsequently distribute it in the European Union.

The purpose of this article is to provide a detailed instruction for how to format and present a document that demonstrates fulfillment of the essential requirements. As an example of the steps to develop a checklist, the requirements applicable to a sterile, disposable medical device will be used throughout the article.

The accepted method of demonstrating fulfillment is the use of an Essential Requirement Checklist. The format of the checklist has been proposed by the Global Harmonization Task Force Study Group 1,⁴ as shown in **Table 1**.

Device manufacturers should maintain a copy of this checklist as part of the technical documentation, and a checklist should be established for each product family.

The manufacturer must evaluate each requirement to determine its applicability. For sterile medical devices, Medical Device Directive (MDD) requirements 1 through 9, 13 and 14 are typically applicable. However, requirements 10 through 12 must also be considered, and a determination of relevance should be made on the checklist.

The first step is to read each requirement carefully and determine whether the requirement will apply to your device. If the requirement does not apply, a short explanation of why is use-

ful to document your reasoning. This will prevent second-guessing when the checklist is used by others. If the requirement applies, provide information that addresses each aspect of the requirement. Look for key words and phrases such as “risk evaluation”, “design and manufacturing controls” or “characteristics and performance”.

It is often helpful to highlight the key words and phrases to facilitate addressing the requirement thoroughly. There are some key words and phrases that appear throughout the essential requirements and should be addressed consistently throughout the checklist. Another tip is to reword the requirement to capture its meaning. However, the original text should be used in the final checklist.

Step 1—Determine Applicable Requirements

Requirement 1. How does the manufacturer ensure that the device is designed and manufactured so that the risk of use of the device is minimized?

Requirement 2. How does the manufacturer ensure that the design and construction of the device conforms to state of the art and that risks are minimized or protection measures are taken or the user is informed?

Requirement 3. How does the manufacturer ensure that the device performs as intended and is designed, manufactured and packaged so that the device functions as intended?

Requirement 4. How does the manufacturer ensure that characteristics and performances of the device do not deteriorate over the lifetime of the device?

Requirement 5. How does the manufacturer ensure that the device is designed, manufactured and packaged so that the characteristics and performances of the device do not deteriorate during storage and transport to the customer?

Requirement 6. How does the manufacturer assure that the

Table 1. The Format of the Checklist Proposed by the GHTF Study Group¹

Requirement	Applicable?	Standard or Procedure	Record
1. The devices must be designed and manufactured so that when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.	Yes	EN ISO13485:2003 ISO14971 SOP0401—Risk Analysis	Certificate Nr. ## RA ##

risks associated with the use of the device are acceptable when compared with the benefits?

Requirement 7. How does the manufacturer ensure that the materials and substances associated with the device are safe?

Requirement 8. How does the manufacturer ensure that the device is designed, manufactured and packaged in such a way to maintain its cleanliness and/or sterility?

Requirement 9. How does the manufacturer ensure that the device operates safely in its intended environment?

Requirement 13. How does the manufacturer ensure that the labeling provides all the required information?

Requirement 14. How does the manufacturer ensure that the device performs as intended?

Step 2—Determine Applicable Standards

The second step is to determine how the applicable requirements will be fulfilled. The manufacturer can use standards, internal test methods or both to demonstrate compliance. The International Organisation for Standardization (ISO) ISO/

through the use of a quality system standard such as EN ISO13485:2000 or EN ISO13485:2003. Risk is evaluated through the use of ISO14971.

Requirement 2. Design and construction (manufacture) are assured through the use of a quality system standard such as EN ISO13485:2000 or EN ISO13485:2003. Risk is evaluated through the use of ISO14971. The risk analysis will show how the risk was brought to an acceptable level and what protection measures are taken and what precautions or warnings are added to the labeling.

Requirement 3. Design and manufacture are assured through the use of a quality system standard such as EN ISO13485:2000 or EN ISO13485:2003. Packaging suitability is assured through the use of a standard for the packaging of terminally sterilized devices such as EN 868-1 or ISO11607. Device performance can be assured through a vertical standard such as ISO10555 (intravascular catheters) or through internal test methods.

Requirement 4. The suitability of the device over its lifetime is demonstrated through shelf-life testing. Shelf-life test-

It is the **manufacturer's responsibility** to identify the applicable standards during the design control process. Compliance with standards provides a presumption of fulfillment of the requirement.

TR16142⁵ provides a starting point for the selection of standards. In vertical standards associated with particular devices, (e.g. ISO14630 for surgical implants), there may be additional guidance on what is required to fulfill the essential requirements.

It is the manufacturer's responsibility to identify the applicable standards during the design control process. Compliance with standards provides a presumption of fulfillment of the requirement. The hierarchy of standards for acceptance in Europe is as follows:

- Harmonized standards (e.g., Comité Européen de Normalisation and European Standards [EN] documents).
- International standards (e.g., ISO documents).
- National standards (e.g., American Association for Medical Instrumentation documents).
- Guidance (e.g., Notified Body Medical Devices Group and Food and Drug Administration [FDA] documents).
- Internal test methods.

The manufacturer should use the highest level of standard available. For example, a European harmonized standard is more acceptable than an American standard. If the manufacturer chooses not to use the highest level standard available, equivalence to the higher level standard must be shown. For example, if a manufacturer chooses to use ISO 11137 for sterilization validation, equivalence to EN 552 must be demonstrated, and any deviations or omissions must be justified. The manufacturer must have controlled access to the standards referenced as part of its quality system.

Requirement 1. Design and manufacture are assured

ing must be performed on devices that are stored throughout the expiration-dating period, often called "real time aging". However, an expiration date may be assigned based on the results of testing on product that is aged using an accelerated aging procedure. There are some references to the process for accelerated aging, American Society for Testing and Materials F1980 and FDA guidance. Product functionality and package suitability are demonstrated, as in requirement 3, at the end of the aging period.

Requirement 5. Design and manufacture are assured through the use of a quality system standard such as EN ISO13485:2000 or EN ISO13485:2003. The suitability of the packaging to protect the product during storage and transport can be demonstrated through testing according to International Safe Transit Association standards and includes an evaluation of product functionality during the transport testing.

Requirement 6. Risk is evaluated through the use of ISO14971. The conclusion of the risk analysis will indicate that the benefits outweigh the risks.

Requirement 7. Design and manufacture are assured through the use of a quality system standard such as EN ISO13485:2000 or EN ISO13485:2003. The biocompatibility (7.1) of the device is evaluated using ISO10993-1. Contaminants and residues (7.2) may include the evaluation of EtO residuals using ISO10993-7 or viral load using EN 12442. Other contaminants or residues may be applicable to a particular device. Interaction of the device with substances with which it may come into contact (7.3) is typically evaluated as

part of design validation. Evaluation of any portion of the device that may be considered a medicinal product (7.4) must be in accordance with the drug directive. Evaluation of the risk associated with any substances that may leak out of (7.5) or into (7.6) the device during use is accomplished through risk analysis, ISO14971.

Requirement 8. Design and manufacture are assured through the use of a quality system standard such as EN ISO13485:2000 or EN ISO13485:2003. The risk of infection (8.1) is evaluated through risk analysis, ISO14971. Control of tissues of animal origin (8.2) is accomplished through the use of EN 12442. Packaging microbial integrity (8.3) is assured through the use of a standard for the packaging of terminally sterilized devices such as EN 868-1 or ISO11607. Sterility (8.4) is assured through validation of the sterilization process using EN 552, EN 554 or EN 550. Controlled environmental conditions (8.5) can be accomplished following ISO14644. Packaging suitability for nonsterile devices (8.6) is typically not applicable for sterile devices. Labeling of devices provided by the manufacturer in both a sterile and nonsterile state (8.7) can be accomplished through the use of symbols according to EN 980.

Requirement 9. Design and manufacture are assured through the use of a quality system standard such as EN ISO13485:2000 or EN ISO13485:2003. Functionality of the device with other devices (9.1) is typically an internal test methodology. The risks associated with ergonomic concerns, environmental interactions and calibration (9.2) are evaluated through risk analysis, ISO14971. The risk associated with fire or explosion is evaluated through risk analysis, ISO14971.

Requirement 13. Contents of labeling are detailed in EN1041. For those aspects of the requirements that are fulfilled by the use of symbols, EN980 is applicable.

Requirement 14. The requirements for clinical data, either scientific literature or clinical studies, are detailed in NB-MED/2.7/Rec 3. If a clinical study is required to fulfill the requirement, the study must be conducted in accordance with the requirements of ISO14155.

The Essential Requirement Checklist may be used as a tool to keep track of the fulfillment of other regulatory requirements. When referencing standards, the particular requirements of FDA or Health Canada may be added in the standards column.

Step 3—Identify all the Records Demonstrating Fulfillment

The last step is to list all the record(s) that demonstrate compliance with the referenced compliance method. For example, the reference is to an internal validation record, a specific part number or a certificate number. The record is used to audit compliance with the referenced standard; therefore, the record must be easily identifiable and retrievable.

Requirements 1 and 2. The record of quality system compliance is the certificate provided by a registrar or Notified

Body. The record of risk analysis is typically an internal document produced during design control.

Requirement 3. The record of quality system compliance is the certificate provided by a registrar or Notified Body. The record of packaging suitability is typically an internal packaging validation report. The record of product functionality is typically the design verification report.

Requirement 4. The record of shelf-life testing is typically an internal document for the real time aging study and, if applicable, an internal document for the accelerated aging studies.

Requirement 5. The record of quality system compliance is the certificate provided by a registrar or Notified Body. The record of transport testing is typically an internal test report generated during design verification.

Requirement 6. The record of risk analysis is typically an internal document produced during design control.

Requirement 7. The record of quality system compliance is the certificate provided by a registrar or Notified Body. The records of biocompatibility and residue/contaminant analysis are usually test reports from a testing laboratory. The records of design validation are typically internal test reports. The record of risk analysis is typically an internal document produced during design control.

Requirement 8. The record of quality system compliance is the certificate provided by a registrar or Notified Body. The record of risk analysis is typically an internal document produced during design control. The record of packaging suitability is typically an internal packaging validation report. The record of sterilization validation is usually an internal document produced during design validation. The record of labeling is usually a label part number.

Requirement 9. The record of quality system compliance is the certificate provided by a registrar or Notified Body. The record of device compatibility, including a list of expected devices with which the device will interact, is usually a test report produced during design validation. The record of risk analysis is typically an internal document produced during design control.

Requirement 13. The record of labeling compliance is typically the associated part numbers for the labeling, including the instructions for use.

Requirement 14. The record of clinical suitability is typically a scientific literature review or a clinical study produced during design validation.

The Essential Requirement Checklist is a tool for the device manufacturer to demonstrate the fulfillment of the applicable essential requirements identified in the directives. The information gathered throughout this process is recorded in the appropriate section of the checklist. Once the Essential Requirement Checklist is assembled, it is the responsibility of the manufacturer to keep it updated through the product life

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cycle as part of the product technical documentation.

The checklist is an important aspect of auditing compliance of the maintenance of the technical file. Careful preparation of the checklist can facilitate the review of the technical file information by a Notified Body or any other regulatory agency.

NOTES

1. Active Implantable Medical Device Directive, 90/385/EEC. The European Commission Web site on General Index for Medical Devices. Available at: http://europa.eu.int/comm/enterprise/medical_devices/index.htm. Accessed 4 June 2004.

2. In-Vitro Medical Device Directive, 98/79/EC. The European Commission Web site on General Index for Medical Devices. Available at: http://europa.eu.int/comm/enterprise/medical_devices/index.htm. Accessed 4 June 2004.

3. Medical Device Directive, 93/42/EEC. The European Commission Web site on General Index for Medical Devices. Available at: http://europa.eu.int/comm/enterprise/medical_devices/index.htm. Accessed 4 June 2004.

4. Global Harmonization Task Force Study Group 1. Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED). 25 October 2002. GHTF Web site. Available at: www.ghtf.org/sg1/inventorystg1/pd_sg1_n011r17.pdf. Accessed 4 June 2004.

5. International Organisation for Standardization. *ISO/TR16142:1999, Medical Devices – Guidance on the Selection of Standards in Support of Recognized Essential Principles of Safety and Performance of Medical Devices*. Geneva, Switzerland: ISO; 17 January 2003.

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