Guidelines for submission of Technical Documentation for Medical Devices according to MDR

Introduction

Manufacturers need to draw up Technical Documentation for their medical devices and keep it up to date. The Technical Documentation shall allow assessment of the conformity of the device with the relevant requirements of the MDR.

This document aims to provide information on the elements that need to be included in the Technical Documentation and instructions on the submission of the documentation to HTCert.

Submission of Technical Documentation

HTCERT has implemented a Technical Documentation submission procedure aiming to avoid issues such as incomplete submissions and poor structuring of the documentation which are the most common reasons for delays in Technical Documentation reviews.

The manufacturer has to upload the Technical Documentation of the medical device following a predefined folder structure provided by HTCERT and to fill in a specific form that correlates the assessment points (MDR requirements) with the relevant support documents.

After the submission of the Technical Documentation, a completeness check is performed to confirm the reception of all files as stated by the client and that they are within the formatting limitations accepted (e.g., files, are not protected or locked, compressed file(s) can be extracted, hyperlinks or cross-references to other documents or embedded documents are functional, etc.). The completeness check will not be successful unless all relevant documents / reports are provided.

The technical documentation assessment against the MDR requirements (Annexes I, II and III) starts when all the required documentation is made available to HTCert in the structure provided. The review process is limited to three rounds of assessment. If deficiencies remain unaddressed at the end of the three rounds this will lead to refusal of the application for the subject device(s) and notification of the refusal to EUDAMED.

The documentation required for the conformity assessment procedures can only be submitted by the clients via the link provided by HTCert. Documentation submission via email, file sharing host or in any other form is not accepted.

All information about manufacturing and design activities performed by suppliers and/or subcontractors has to be submitted directly by the manufacturer and cannot be provided to HTCert by the supplier or subcontractor directly, bypassing the manufacturer.

All documentation must be in English or Greek language unless there is a specific instruction on a topic.

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Content Requirements

A. General Information

Each Technical Documentation shall contain an introductory section providing general information on the manufacturer and the EU Authorized Representative (if applicable).

B. Device description and specification

In this section a description of the device, its specifications, variants and accessories intended to be used with the device has to be provided. The sub-topics asked in this section are as follows:

General Information

- Product or trade name and EMDN.
- A complete list of product codes and trade names under which the device is placed on the market should be stated.
- Rationale for the MDR Qualification of the product as a device.
- Type of the device (the device may be implantable or custom-made or software etc)
- Classification of the device
- Classification rule and provision of the rationale. If multiple classification rules apply, all should be identified and the strictest rules resulting in the higher classification shall apply. If the device contains multiple components that on their own might be classed differently, the higher classification shall apply.
- If there are any existing approvals of the device, the relevant information should be provided. (e.g., MDD, FDA)

Detailed Description and Intended Use

- Detailed description of the device.
- Intended use / purpose of the device.
- The intended patient population and the medical conditions to be diagnosed, treated and/or monitored and other considerations such as patient selection criteria, indications, contra-indications, warning.
  For Class Ir devices: Description of the surgical techniques used with the products - especially taking into account the expected or possible.
- Principles of operation of the device and mode of action.
- General description of the key functional elements, e.g. device parts/components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition.
- Description of raw materials, components, packaging materials, including the following:
  - Overview of all raw materials, components, packaging materials
  - Specifications of raw materials/ components/ subassemblies
  - Specifications of packaging materials (primary and secondary packaging)
  - Certificates of analysis from the suppliers, material certificates, inspection certificates
  - Identification of substances that come into direct or indirect contact with the human body.
- Statement whether the device is manufactured utilizing tissues or cells of human origin, or their derivatives, whether it is manufactured utilizing tissues or cells of animal origin, or their derivatives or if it incorporates, as an integral part, a substance which, if used separately, may be

considered to be a medicinal product, including a medicinal product derived from human blood or human plasma.

- Description of the accessories for the device, other devices and other products that are not devices, which are intended to be used in combination with it.
- A complete list of the various configurations/variants of the device that are intended to be made available on the market.
- Features, dimensions, and performance attributes, of the device and any variants/configurations and accessories that would typically appear in the product specification made available to the user, for example in brochures, catalogues, and similar publications.
- Explanations of any novel features, if applicable.
- An overview of previous generations of the device, if applicable, including approvals in EU and other geographical areas or, if the device is new and has never been marketed by the manufacturer anywhere in the world, a statement for this.
- An overview of identified similar devices available on the Union or international markets, where such devices exist.

C. Information to be supplied by the Manufacturer

The sub-topics asked in this section are as follows:

- Labels of the device and of its packaging (single unit packaging, sales packaging and transport packaging), in all languages accepted in the Member States where the device is intended to be sold.
- Instructions for use in all languages accepted in the Member States in which the device is intended to be sold.
- In case of implantable medical device, except sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips and connectors, the “Implant card” should be provided.
- Website Address where this information (IFU) is made available and kept up to date.
- Promotional Material if the product is already in the market, or draft documents for new products

Note: Submission of the English version only can be accepted for the initial assessment of the Technical Documentation.

D. EU Declaration of Conformity

An EU Declaration of Conformity including all the information listed in MDR Annex IV and translated into an official unit language or languages required by the Member State(s) in which the device is made available has to be provided.

E. Design and manufacturing information

In this section, manufacturer must submit information required to allow the design stages applied to the device to be understood and information on manufacturing processes, their monitoring and validation and the final product testing. The specific elements to be provided in this section are as follows:

Information on the design

- Information regarding the design stages applied to the device, describing the applied design process, the phases within the design of the device and a summary of the results of these phases.
  Regarding previously marketed devices, certified under the MDD, the description of any changes in the design of the device as approved under the directive and information for testing of the current version of the device should be provided.

Information on the manufacturing

- Comprehensible description of manufacturing process, including the procedures / flow charts, sample batch protocols and information on controlled conditions under which certain manufacturing steps take place. Any subcontracted processes should be clearly identified.
- Information on the verification / validation of the manufacturing processes containing a validation masterplan (if available) and the protocols and reports of the verification / validation of the critical processes.
- For Class Ir devices: Evaluation of those production stages whose results may affect reprocessing or whose success can be endangered by a (multiple) reprocessing.

Information on the acceptance criteria and testing

- A description of the testing (incoming, in-process and final tests) including acceptance criteria. If the device is required to be installed and/or commission at the user location, information on tests to be carried out as a part of the installation and commissioning of the device.

Sites Related

- Details for all sites involved in design and manufacturing activities, including the list of all sites, and the suppliers and sub-contractors involved, all existing registrations / certifications held and quality assurance agreements for outsourced processes.

F. General safety and performance requirements (GSPR)

In this section manufacturers have to provide Information on which GSPRs are applicable and which are not, together with an explanation for non-applicability and the methods used to demonstrate conformity with the applicable ones. The following elements are expected in this section:

- A checklist should be submitted presenting conformity with the applicable General Safety & Performance Requirements (GSPRs) of MDR, Annex I.
- Information on how Common Specifications and relevant standards, both harmonized and not, have been considered.
- Information on all applicable regulations or directives if the device is also governed by additional ones.

G. Benefit-risk analysis and risk management

General information on benefit-risk analysis, solutions adopted and the results of risk management shall be provided in this section. Specifically, the following should be presented:

- Benefit-Risk Analysis
- Risk Management Procedure
- Risk Management Plan for the device
- Risk Management File of the device.

H. Pre-clinical data

The documentation in this section shall contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of the device with the requirements of the Regulation and in particular the applicable general safety and performance requirements. A summary of the tests performed shall be provided for each of the following topics (where applicable). Where no testing has been undertaken, the documentation shall incorporate a rationale for that decision.

Biocompatibility

The documentation to be provided should include:

- Biological Evaluation Plan
- Biological Evaluation Report
- Test Reports of performed Biological Tests
- Accreditation Certificates of the laboratories that performed the tests
- Literature review plan, the selection criteria for documents, the list of literature search databases used and the results of the critical evaluation of the literature
- CVs of the expert assessors involved in the biological evaluation

or a rationale for non-applicability.

Physical, chemical and microbiological characterization

The documentation to be provided should include:

- Results of testing from a sample batch for the critical raw materials
- Results of in-process testing from a sample batch
- Results of final testing from a sample batch for the finished device

or a rationale for non-applicability.

Electrical safety and electromagnetic compatibility

The documentation to be provided should include:

- Test Protocols, the reports of tests performed and the conclusions for electrical safety testing
- Test Protocols, the reports of tests performed and the conclusions for EMC testing

or a rationale for non-applicability.

Software Verification and Validation

The documentation to be provided should include:

- A checklist against the requirements of EN 62304, or a description of the alternative standard or procedures followed and a demonstration of their equivalence.
- The software development procedure and plan, the software requirements analysis and the software architectural design and detailed design, as applicable.
- The software unit implementation and verification and software integration and integration testing, if applicable.
- The documentation on software system testing and release.
- The documentation related to the design and maintenance of the cybersecurity features of the device.

or a rationale for non-applicability.

Stability, including shelf life

The documentation to be provided should include:

- Information on planning and overview of performed tests and evidence that the devices meet the defined specifications during the defined shelf life.

- Stability studies should take into consideration storage stability, transport stability as well as in-use stability

or a rationale for non-applicability.

Performance and safety

The documentation to be provided should include:

- The design requirements for the device, the protocols, the test reports and the conclusions for design verification and validation.
- The evidence to support the device lifetime
- The protocols and results for usability studies

I. Devices placed on the market in a sterile or defined microbiological condition

The documentation in this section shall contain a description of the environmental conditions for the relevant manufacturing steps and description of the methods used, including the validation reports, with respect to packaging, sterilisation, and maintenance of sterility. The validation report shall address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues. Specifically,

Devices placed on the market in a sterile condition

- Description of the sterilization method and validation report.
- The documentation on bioburden controls and monitoring
- The protocols and reports for packaging validation.

Devices to be sterilized by the end user

- The description and validation of sterilization method specified in the instructions for use.
- Documentation on bioburden controls and monitoring

Reusable medical devices

- Description and validation for the reprocessing of the device, proving the suitability of the reprocessing specifications described in the instructions for use.

J. Additional Information required in specific cases

Devices incorporating medicinal substances

- A statement indicating this fact.
- General information for the Medicinal Substance, including the purpose of its incorporation
- Quality documentation for the ancillary medicinal substance itself, containing:
  - relevant parts of CTD-Module 3,
  - Reference to the European Pharmacopoeia (PhEur) monograph,
  - Quality Overall Summary (CTD-Module 2.3)
- Quality documentation for the ancillary medicinal substance as incorporated in the medical device, containing:
  - qualitative and quantitative particulars of the constituents,
  - description of method of manufacture,
  - controls of starting materials,
  - control tests carried out at intermediate stages of the manufacturing process of the medical device,
  - final control tests of the ancillary medicinal substance in the medical device, stability

- Non-clinical documentation should be provided, containing:
  - non-clinical pharmacology (pharmacodynamics / pharmacokinetics),
  - toxicity (including single-dose toxicity, repeat-dose toxicity, genotoxicity, carcinogenicity and reproductive and developmental toxicity, as applicable),
  - local tolerance.

Devices composed of substances that are absorbed by or locally dispersed in the human body

- A statement indicating this fact.
- Detailed information in relation to:
  - absorption, distribution, metabolism, excretion of those substances.
  - possible interactions of those substances, or of their products of metabolism in the human body, with other devices, medicinal products or other substances, considering the target population, and its associated medical conditions
  - local tolerance of those substances
  - toxicity of those substances, including single-dose toxicity, repeat-dose toxicity, genotoxicity, carcinogenicity and reproductive and developmental toxicity, as applicable depending on the level and nature of exposure to the device

or a justification in case of absence of the above studies.

Devices containing CMR or endocrine-disrupting substances

- A statement indicating this fact.
- Planning and overview of performed tests, reports of tests performed and evaluation of test results.
- If evidence is based on published literature, justification for the applicability of this data to the device, considering the nature and the intended purpose of the device, the contact with various body tissues and other substances etc.

Devices with a measuring function

- Test protocols and reports that determine / verify the accuracy and precision of the device.

Devices to be connected to other device(s) in order to operate as intended

- Test protocols and reports that determine the safety and performance of the device combination, including addressing their interoperability and usability.

K. Clinical Evaluation

The documentation to be provided in this section should include:

- Clinical Evaluation Plan
- Clinical Evaluation Report
- Specification of the frequency of CER updates and provision of this rationale
- CVs of all individual(s) conducting / approving the clinical evaluation
- The literature search protocol, the literature search report, the list of databases used and a copy of all literature articles selected and analysed within the clinical evaluation report
- If clinical investigations have been performed: the clinical investigation plan, the clinical investigation report, communication with the ethics committee and regulatory approval of the clinical investigation, the investigator's brochure(s), a sample of the informed consent for the investigation and statistical analysis plans.
- The rationale if clinical investigation has not been performed for class III and implantable devices.

- If the clinical evaluation of the device relies on a justification of equivalence of comparative devices: detailed demonstration of equivalence regarding technical, biological and clinical characteristics and information on all differences between it and the comparable devices relative to intended use, technical, or biological factors

  For class III and implantable devices: if the proposed equivalent device is produced by a different manufacturer, a copy of the signed contract between the two manufacturers that explicitly allows full access to the equivalent marketed device's technical documentation on an ongoing basis shall be provided.
- For devices incorporating medicinal substances, a conclusion on the risk/ benefit of adding the ancillary substance to the device should be included. If the device covers multiple strengths or indications, this should cover all variants.
- For class III and implantable devices, other than custom-made or investigational devices, a summary of safety and clinical performance (SSCP), including at least:
  - the identification of the device and the manufacturer, including the Basic UDI-DI and the SRN
  - the intended purpose of the device and any indications, contraindications and target populations
  - a description of the device, including a reference to previous generation(s) or variants if such exist, and a description of the differences, as well as, where relevant, a description of any accessories, other devices and products, which are intended to be used in combination with the device
  - information on any residual risks and any undesirable effects, warnings and precautions
  - the summary of clinical evaluation as referred to in Annex XIV, and relevant information on post-market clinical follow-up
  - possible diagnostic or therapeutic alternatives
  - suggested profile and training for users
  - reference to any harmonised standards and CS applied
  - Revision history

  The SSCP should be translated into the languages accepted in the Member States where the device is envisaged to be sold. Submission of the English version only can be accepted for the initial assessment of the Technical Documentation.
- Post market clinical follow-up (PMCF) plan & report or a justification why a PMCF is not applicable should be provided.
- The rationale if demonstration of conformity based on clinical data is not deemed appropriate (Article 61.10 of MDR)
- Potential novel features

L. Post Market Surveillance

The documentation to be provided in this section should include

- Post Market Surveillance procedure
- Post Market Surveillance data including market history, overview of sales and complaints data, trend analyses, vigilance data and data from other PMS sources.
- Post Market Surveillance plan
- Periodic Safety Update Report (PSUR) if applicable
- Post Market Surveillance Report if applicable