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RESEARCH ARTICLE

REGULATORY REQUIREMENTS FOR SUBMISSION OF TECHNICAL FILE FOR MEDICAL DEVICE IN EUROPE

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ABSTRACT

Medical Device market is of greater value and having bigger scope of expansion in terms of money & utilization in upcoming years. No fixed format is prescribed for the technical documentation officially. Many entities have published guidance document on the topic of technical file content but any of the multiple formats is not sufficient. Two format guidance which worth reviewing were issued by Team Notified body NBMED and Global Harmonization Task Force (GHTF). Technical file may be considered as one document which is divided into different sections. Mostly Technical file and Design Dossiers are viewed as controlled documents. This article describes in detail about contents of Technical File Submission in Europe which are required for the marketing approval of medical device in Europe.

INTRODUCTION

- A CE Technical File is a comprehensive documentation and collection of data about medical device. The information given in the CE Technical File (Design Dossier for Class III devices) must comply with the In Vitro Diagnostic Medical Devices Directive (IVDD), Medical Devices Directive (MDD) or Active Implantable Medical Devices Directive (AIMD).[1]
- Technical File documentation is required for all medical devices for sell it in Europe. The information included in a technical file must comply with the essential requirements of the Medical Devices Directive to support the on-going safety and effectiveness of the approved products. Notified body will audit technical files as annual basis to assess compliance with the essential requirements and other standards and applicable regulations. The term **"Technical File"** is used for class I, class IIa and class IIb medical devices, and "**Design Dossier**" is for the class III medical devices.
- Technical Files are retained in the manufacturer premises or the authorized representative for potential review of competent authorities and notified body. For review prior CE-Marking of the Product, Design Dossiers have to be submitted to the notified body. After successful review, the notified body issues a design examination certificate according to with the relevant provisions of the Annex I of the Medical Device Directive (MDD).[2]
- Notified body shall review the technical file, unless you manufacture a Class I device that is not provided sterile and does not have a measuring function. In Class IIa, IIb and III devices (general medical device) and List A, List B or self-testing In-Vitro Diagnostic Device (IVD), a more complex CE technical file or design dossier must be prepared.
- Technical file contains all the relevant information that is essential to demonstrate that the product complies with the safety requirements and essential health requirements of the Directive information on manufacture, product design, testing, risk analysis and clinical evaluations must be included in the documentation. The main purpose of the technical documentation is to enable the manufacturer to prove that his product complies with the essential requirements of the Directive.[1, 2]
- The technical documentation may be maintained in electronic or hardcopy form. The technical documentation should be kept at the disposal of the competent Authorities for inspection and control purposes. The technical documentation should be kept for at least five years from the last date of manufacture of the product. The manufacturer should also consider the product liability issues when determining the time and content of technical documentation maintained for obsolete devices.

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- ***Purpose:*** It is most important to provide guidance to the notified bodies, competent authorities and manufacturers on the technical documentation needed to meet the requirements of the medical devices directives.

A technical file may be divided into following different sections. [1, 2, 3]

Product Description

A general description of the device

It includes the information about the device like intended range of variants, description of the packaging (where this is relevant to the preservation of the intended characteristics) and performances of the devices. It also gives a brief description sufficient to allow an understanding of the design, characteristics, and where appropriate, performances of the devices and to distinguish between variants.

A description about the intended use and operation of the devices

A short description of the application of the device, intended purpose, and method of use of the devices are given. This may include, where appropriate, all the details of the intended patient population and medical conditions for which the device is intended. The information may be given by way of reference to the "instructions for use" or operating manual for the devices. It is not necessary to provide the details about the mechanism by which the device achieves its intended purpose.

Device incorporating a medicinal substance

If any of the devices incorporate a medicinal substance, the technical documentation should gives clear information of purpose of incorporating medicinal substance and its mode of action in this application.

This is only applicable where the substance is liable to act upon the body with action ancillary to that of the device. For this reason this will not be relevant to in-vitro diagnostic device (IVD) which does not act upon the body.

The risk analysis should address the benefits and additional risks associated with incorporation of such a substance. The technical documentation should gives the data on the tests conducted in this connection.

Device incorporating nonviable materials of animal origin

If any of the medical devices incorporates non-viable materials of animal origin, the risk analysis within the technical documentation should address the additional risks and benefits associated with incorporation of such materials, and the measures taken (for example, in sourcing of animals, veterinary controls and measures taken to eliminate or inactivate transmissible agents). In vitro diagnostic devices may contain materials of animal or human origin. The technical documentation should include provide relevant details, including sourcing and measures to protect personnel and to preserve the performance of the device.

Device requiring special consideration

Where aspects of the device are the subject of emerging concern (for example, the use of latex potentially leading to allergic reaction), the risk analysis within the 'technical documentation' should address these aspects.

Description about the methods of manufacture envisaged

A short summary is required for the type of manufacturing method (for example, injection or blow moulding, chemical processing and extrusion, assembly, packaging or labeling information) and the method of sterilization, if relevant. This should make clear that the technologies involved and means of assuring the intended characteristics and performances of the devices manufactured.

Description of the adaptors, accessories and other devices or equipments and other interfaces which are intended by the manufacturer to be used in combination with the devices

This type of technical documentation should include the description of other devices or equipment etc. which the device is intended to be used with; for example, where the manufacturer makes specific claims concerning compatibility.
It also includes data on the verification and validation of the safety and performance of such combinations.

Classification of the device under the relevant Directive

The technical documentation should include the rule numbers applied under the Directive, together with a brief rationale for this classification, and reasons why particular rules do not apply, if this is not obvious. In the case of IVDs, the classification of a particular device is obvious.

Technical Requirements

Identification of technical requirements

The manufacturer should make clear the Directive which applies to the particular device concerned. The manufacturer should provide information about the rationale for classifying the product as a medical device.

In this case essential requirements of the Directive (e.g. MDD Annexure I, AIMD Annexure 1, IVDD Annexure I) and other requirements of the Directives which apply should be identified.

Solutions adopted to fulfill the essential requirements

The manufacturers are essential to demonstrate how each of the applicable essential requirements and any derived technical requirements or specifications for the particular device concerned has been met. Essential Requirements Checklist may facilitate demonstration of how the solutions adopted meet the relevant requirements.

Checklist should include

a. List of the essential requirement, which identifies applicability,
b. List the standards applied,
c. Give the basis for claiming compliance for each essential requirement. This will make clear that the solutions adopted to fulfill each requirement or refer to stand-alone specifications, reports and the like.

Standards applied

The manufacturer confirm with particular essential requirements by claiming compliance with available published standards, the Directives require identified standards. The manufacturer should make clear that the standards applied are harmonized standards.

Compliance with such harmonized standards carries the presumption of conformity with relevant essential requirement of the Directive. If any device does not comply with key relevant published standards, a rationale behind it should be given.

Design

The results of the risk analysis

The manufacturer should present the documented results of the risk analysis. The risk analysis should provide information about all hazards known or reasonably foreseeable for the particular product types and technologies involved, together with the likelihood and consequences of occurrence and measures taken to reduce the resulting risks to acceptable levels. This should address all relevant risks. The risk analysis may also include the additional benefits and risks associated with incorporation of such substances. In the case of devices intended and labeled for single use, the risk analysis should address the hazards associated with reuse as an example of foreseeable misuse. The results of the risk analysis should be reviewed and approved by the manufacturer.

Specification of materials, manufacturing or special processing

The technical documentation should specify the materials used in the construction of the device, together with the biocompatibility and biological safety of materials intended to come into contact with the body. This may provide all the information about special processes (e.g. sterilization, moulding) and environmental conditions which are used for production (e.g. electrostatic discharge or prevention of particulate contamination). If any medical devices covered by the in-vitro diagnostic medical devices (IVDD), this should cover characterization of starting materials. In this type of technical documentation, it should specify any special processes, for example sterilization and the results of its which may affect the safety and performance of the finished device.

Specifications, circuit diagrams and drawings for components, sub-assemblies and the complete product including packaging, where appropriate The manufacturer should decide what type of specifications, drawings and diagrams are appropriate and sufficient to enable proper manufacture, installation, maintenance and servicing of the product involved in order giving surety of the intended characteristics and performances are achieved and maintained.

The specifications about the checks, tests and trials that are intended to be carried out as part of routine production

The procedures, work instructions etc. concerning to the conduct of such checks, tests and trials form part of the manufacturer's quality system.

The compatibilities and performances intended by the manufacturer

The manufacturer is required to identify the performances, characteristics and compatibilities required to assure the safe and correct operation of the device. A relevant characteristic might be, for example, sterility assurance of a catheter. A relevant performance for example, the ability of the protective packaging to uphold sterility of that catheter when subject to the stresses associated with transport and storage. In the case of In Vitro Diagnostic medical devices, the suggestion of performances should include those required in connection with analytical performance, for example, to do with specificity, sensitivity, limit of detection, and ratio of false to true results, where applicable.

Labeling include any instructions for use

The manufacturer is required by the Directives to comprise in the technical documentation of the label, and where appropriate, the instructions for use, collectively with any changes to these during the lifetime of the product. This should embrace the information to be given, the use of symbols if used and included in the final version of the labeling. The labeling documentation should provide particular information about the device itself or its component parts, on the packaging for each unit, on the sales packaging, or on the leaflet or user manual supplied with one or more devices. Information may be provided by means of electronic display screens or synthesized voice messages.

Identification of shelf-life reflected by any 'use by' date, or other 'lifetime' of the device

In some cases, such restrictions on use will imitate a time-related deterioration in characteristics which are important to product performance and safety. The 'lifetime' of an active medical devices, may be resolute by the period for which the manufacturer will support the device by way of availability of spare parts, manuals, training, service or repairs.

Results of Bench Testing

Bench testing includes in-vitro or animal studies, validation and simulated use testing of software and the results of special processes (e.g. sterilization validation report).Testing should pursue a pre-defined protocol, which should comprise the parameters to be measured, measuring and test equipment to be used including calibration arrangements, acceptance criteria

and statistical treatment of results, together with needed formal approval of the report.

Clinical data

Clinical data includes data from the market experience of the same or similar devices (particularly significant to well established devices), prospective clinical information and investigations from the scientific literature. The manufacturer should make clear that the clinical data is being used to express conformity with each of the applicable essential requirements for the particular device concerned.

Reporting and Documentation of Design Changes

The technical documentation should provide information about the records of each design change and give the reasons for these, in concert with any associated validation or verification data. The documentation should include confirmation for believing that the change and achieves the desired effect, and that the device continues to comply with the requirements of the Directive. It has been submitted to the notified body with conformity assessment involving design or type of device and the manufacturer is requisite to inform the notified body of substantial changes and obtain further approval.

Administrative Details

Declaration of Conformity

Upon completion of all other steps essential for conformity assessment, the manufacturer shall provide a written declaration of the device concerned to meet the provisions of the Directives which apply to them, in any case of whether or not a notified body is involved in the conformity assessment. The declaration must be the final step in the relevant conformity assessment procedure. It may be helpful for the manufacturer to prepare a draft declaration of conformity for notified body review. The declaration should make clear under what the directive and annexure it is made, and the product to which it relates. It should also provide the name and address of the manufacturer, and in the case of devices for which the manufacturer is not resident in the Community, the name and address of the authorized representative of the manufacturer established within the Community.

Application for Conformity Assessment

The manufacturer may lodges an application for approval of the device type and it should include the information like name and address of the manufacturer, facilities, brief description of the device, declaration of conformity, etc. together with the appropriate parts of the technical documentation. Particular notified bodies may have developed for standard forms to be used for application for conformity assessment.

Declaration that no other notified body is used in Conformity Assessment

Conformity assessment involves a notified body within the application for conformity assessment procedure; the manufacturer is predictable to provide a written declaration that no application has been lodged with any other notified body for the same product type and conformity assessment route.

Notified body decisions and reports

The manufacturer must keep the notified body reports and decisions at the disposal of the national authorities for a period of at least five years after the last product to which they relate has been manufactured. These reports and decisions include the notified body certificates of approval of the quality system and the device design or type.

Manufacturer undertaking on procedure to review post-production experience

The manufacturer is requisite by the Directives to institute and keep up to date systematic procedure to review the experience gained from the devices in the post-production phase and to implement appropriate means to apply any necessary corrective action and to notify the competent authorities of relevant incidents.

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CONCLUSION

All the above mentioned aspects have to be taken into consideration for the submission of Technical File. It describes the information about product description, technical information related to the product, administrative details and detail about design of medical device. It has been concluded that the documents and information required for the submission of Technical file for medical device in Europe is quite strict as compared to other countries. So, the regulatory requirements for submission of technical file may be implemented from Europe to other countries for quality and safety of medical device.

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