Review your Technical Documentation like a Regulatory Authority ✅

Introduction

Technical Documentation, also known as technical files, dossiers, submissions and a few other things but you get the jist. These terms change around the world, but they’re ultimately doing the same thing.

All regulatory jurisdictions require technical documentation to be submitted as evidence to demonstrate that the medical device conforms to the regulations that

apply in a particular jurisdiction. Technical Documentation provides a detailed overview of how the medical device was developed, designed and manufactured.

Developing and maintaining technical files can be an extremely laborious process, especially when it comes to regulatory submissions.

This little guide has been put together to provide an overview of what a reviewer will look for when evaluating your Technical Documentation.

Technical Documentation Checklist

Now, depending on where you are located, or what regulatory classifications apply to your device, there will be different requirements that have to be considered.

This guide we have is going to be generic to all devices, so we won't be looking at for example, how to structure technical documentation around a Class I sterile device under the Medical Device Regulation - 2017/745 which only requires aspects related to obtaining sterility to be reviewed by the notified body.

The layout for our technical documentation is going to be in line with Medical Device Regulation - 2017/745 Annex II for ease as it's becoming the most widely used.

Appendix 1 details a checklist that can be completed or used as an aide memoire for preparing technical documentation.

Review your Technical Documentation like a Regulatory Authority

Whilst the entirety of Technical Documentation is important, Notified Bodies (NBs) and Competency Authorities (CAs) only have so much availability and time to review, like any of us.

So, sampling becomes very important.

Typically, a notified body will allocate around 3 days for Technical Documentation - this depends on a few things such as the risk class, number of staff, how novel the device is amongst a few other things.

With this sampling, there are a number of key areas the NB / CA will review to ensure they are satisfied:

- Intended Purpose
- Regulatory Classification

- What's on the Label (claims)
- General Safety and Performance Requirements (GSPRs) including List of Applied Standards (LOAS)
- Risk Management
- Equivalence - is this device leveraging equivalence of another device that is already placed on the market?
- Usability
- Stability / Shelf life including journey hazard simulation

> 💡 Notified Bodies and Competent Authorities are now commonly rejecting Technical Documentations submitted that are not searchable. Scanned copies of documents are now commonly not accepted (apart from certain examples).
>
> If you are a reviewer, think of the size of the documentation and time allocated to it. Depending what Notified Body you are with, they may make it a mandatory requirement to have Technical Documentation in a searchable format.

Intended Purpose

The intended purpose is the single most important statement in Technical Documentation.

It is however, one of the most commonly overlooked elements of Technical Documentations.

The concept of intended purpose is covered in the Blue Guide, section 2.7: manufactures have to match a level of protection corresponding to the use they prescribe to the product under the conditions of use which can be reasonably foreseen.

The phrase "Intended Purpose" is found 87 times in Regulation 2017/745 - Medical Device Regulation and scattered throughout the document.

This forms a part of the device description in the Technical Documentation. It also defines the starting point for the claims of the device that form the starting point for clinical evaluation.

Furthermore, in line with Article 7 of the MDR, claims, intended purpose, indications, contra-indications and risk-benefit ratio are all related and follow from or determine each other.

Here are a few things the review will be looking at for your intended purpose:

- is it the same throughout the technical file?
- Are they confusing intended purpose with indications for use?
    - The intended purpose should specify the disorder, condition or risk factor of interest that it is intended to detect, define or differentiate

Intended purpose is different from indications for use.

These are commonly confused areas. The intended purpose is essentially the effect of the medical device, whereas indication for use are the areas, diseases etc., that would be treated.

Indication for use is all about the patient.

Regulatory Classification

This is a fundamental aspect of regulatory management and technical documentation submissions.

Regulation 2017/745 Article 51 defines devices to be divided into the following classes (I being the lowest, III being the highest):

- Class I
- Class Ir/Is/Im (reusable surgical, sterile and measuring).
- Class IIa
- Class IIb
- Class III

Technical documentation drawn up by the manufacturer shall include the risk class of the device and the justification for the classification rule(s), as well as to dedicated guidance where available.

Let’s go through an example of classifying a device.

Let’s choose a heart stent as our device with the following intended purpose.

This device is intended to widen arteries.

If we look at Regulation 2017/745 - We can assess from the Rules in Annex VIII that the most applicable rule is rule 8 which specifies the following➖

All implantable devices and long-term surgically invasive devices are classified as class IIb unless they: are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are classified as class III;

NOTE: remember our discussion earlier about intended purpose vs indications.

Now we can see from here, that our device is a Class iii - as high as they go.

What is on the label?

Reviewers will commonly reverse engineer the review.

This means beginning by looking at your device claims, i.e., what do you say this device will do on the labelling that the user will see?

The review of this will cover various things, such as:

- Indications for use
- Patient population
- Contraindications, warnings and/or precautions (depending on how you lay the file out)
- Symbology (sterile, do not damage etc.,) in line with ISO 15223 and/or ISO 20417 - information to be supplied by the manufacturer.

> 💡 A low hanging fruit that catches many organisations out is using a wrong NB number or address on their label. Don’t get caught out by this.

The reason the reviewer is looking at this is because of a key word that we will use throughout this article. Substantiation.

> 💡 The question the review is asking at the beginning, in the middle and at the end of your Technical Documentation review is, can this legal manufacturer substantiate the claims they are making?

General Safety and Performance Requirements (GSPRs) including List of Applied Standards (LOAS)

Previously known as the Essential Requirements (ER) under the Medical Device Directive. The new equivalent is the GSPRs.

Fulfilling the GSPRs listed in Annex I of Regulation 2017/745 is one of the most fundamental preconditions to placing any medical device on the European market.

Within Article 5 (2) of Regulation 2017/745 “Placing on the market and putting into service”, the "requirements" are a set of product characteristics, which are considered by the European authorities as being essential to ensuring that any new device will be safe and perform as intended throughout its life.

Here are some examples of the GSPRs:

- GSPR 3 - Manufacturers shall establish, implement, document and maintain a risk management system.
- GSPR 23.2 - Information on the label (a) - The label shall bear all of the following particulars: the name or trade name of the device;

At the beginning, the manufacturer must go through each GSPR and determine whether they are applicable to their device or not.

I know, every single GSPR, with every single device.

Fortunately, the EU Commission have developed and issued a standard checklist for the GSPRs of MDR, which is available for download here -

https://health.ec.europa.eu/system/files/2021-05/mdcg_2021-8_annex6_0.docx

For our example GSPRs above, most manufacturer will not be able to non-apply those.

Here is an example of a completed GSPR below:

General safety and performance requirement (GSPR)	Does ER apply to the invest. device? Yes/No	Standards and common specifications used in full or in part	Evidence of conformance, documentation	Justification/ comment in case of deviation
CHAPTER I, **GENERAL REQUIREMENTS**				
3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall:	Yes	EN ISO 14971 EN ISO 24971	Risk Management Procedure – RISKSOP01	N/A

Once the manufacturer has identified with GSPRs are applicable and which are not, they can then utilsie the harmonised standards they've referenced, for example ISO 14971, ISO 15223, etc., they can form the List of Applied Standards (LOAS).

A reviewer will want to see these to ensure that where possible the manufacturer has leveraged harmonised standards, and where they haven't.

> 💡 Ensure to document whether you are applying standards or common specifications partially or in full.

Remember and keep your referencing consistent with this (EN ISO, BS ISO etc.,).

Risk Management

Pretty much every part of a technical file is key. However, Risk Management is one of the most fundamental areas that will be reviewed and links out to each element of the technical documentation.

As part of your technical documentation review, the reviewer will want to see the risk management file (RMF).

ISO 24971 Annex G provides guidance of what an RMF should consist of, but this should consist of the following (but not limited to):

- Risk management plan
- Preliminary Hazard Analysis (PHAs)
- Risk Management Report

> 💡 ISO 24971 - Medical Devices - Guidance on the application of ISO 14971 is a great document to accompany risk management activity.

Validations

It is likely that your device has an element of testing required to be conducted to prove that it works as intended without inadvertently causing any adverse effects while carrying out its intended purpose.

This varies widely, but there are a few things that all medical devices will be subject to. We won't go too much into biological or clinical evaluation in this document

otherwise it’d end up the size of the MDR. Here are some of the things you may need to consider with prompts of the questions they’re attempting to answer:

- Shelf life - Are we sure that the device will remain stable etc., while not in use?
- Stability study - Are we sure that the device will remain stable (or sterile) etc., while its in use.
- Biological evaluation (ISO 10993) - Are we sure that the device will not cause any biological harm to the patient?
- Clinical Evaluation (or clinical investigations) - Not the same thing.
- Journey hazard simulation - Are we sure that the device will stand up to normal transportation and handling?
- Usability - Are we sure that the device can be used as intended by the patient population??

Final checks to do pre-submission

- [ ] All documents are complete and up-to-date
- [ ] All documents are properly formatted and organized
- [ ] All documents are in the required language(s)
- [ ] All documents are easily accessible and readable
- [ ] All required signatures and approvals are obtained
- [ ] All required translations are available

Conclusion

Technical Documentation is an essential aspect of the medical device development process, and preparing it can be a time-consuming and challenging task. However, it's crucial to ensure that your Technical Documentation is complete, up-to-date, and meets the regulatory requirements of the jurisdictions in which you intend to market your device. By following the checklist provided in this guide, you can be confident that your Technical Documentation will be thorough and comprehensive, making it more likely that your device will gain regulatory approval.

Appendices

Appendix 1 - Technical Documentation Submission Checklist

☐ Technical File Index

1 Device Description and Specification, Including Variants and Accessories

1.1 General

☐ Product or trade name and general description of the device, including intended purpose and users.

☐ Basic UDI-DI or clear identification for traceability.

☐ Intended patient population, medical conditions, patient selection criteria, indications, contraindications, and warnings.

☐ Principles of operation, mode of action, and scientific demonstrations if necessary.

☐ Rationale for qualifying the product as a device.

☐ Risk class and justification for the classification rule(s) applied.

☐ Explanation of novel features.

☐ Description of accessories, other devices, and non-device products intended for use with it.

☐ Description or list of configurations/variants of the device intended for the market.

☐ General description of key functional elements, including parts/components and their composition with visual representations.

☐ Description of raw materials used in functional elements and those in contact with the human body.

☐ Technical specifications, features, dimensions, and performance attributes of the device and its variants/configurations.

1.2 Reference to previous and similar generations of the device

☐ Overview of previous generations produced by the manufacturer.

☐ Overview of identified similar devices available on the market.

2 Informatoon to be supplied by the manufacturer

☐ Label or labels on the device and packaging in accepted languages.

☐ Instructions for use in accepted languages.

3 Design and Manufacturing Information

☐ Information to understand the device's design stages.

☐ Complete information and specifications of manufacturing processes, validation, monitoring, and final product testing.

☐ Identification of all sites, suppliers, and subcontractors involved in design and manufacturing.

4 General Safety and Performance Requirements

☐ Information for demonstrating conformity with general safety and performance requirements.

☐ Justification, validation, and verification of solutions adopted.

☐ Demonstration of conformity, including specific methods and controlled documents.

5 Benefit-Risk Analysis and Risk Management

☐ Benefit-risk analysis as per Annex I.

☐ Solutions adopted and results of risk management as per Annex I.

6 Product Verification and Validation

☐ Results and critical analyses of verification and validation tests/studies for conformity with regulatory requirements.

☐ Sterilisation

☐ Biological Safety

☐ Software verification and validation

☐ Usability studies

6.1 Pre-clinical and clinical data

☐ Results of engineering, laboratory, simulated use, and animal tests.

☐ Detailed information on test design, protocols, data analysis, and conclusions.

☐ Clinical evaluation report, updates, plan, and PMCF evaluation report or justification.

6.2 Additional information required in specific cases

- [ ] Statement for devices incorporating medicinal substances.
- [ ] Statement for devices utilizing tissues or cells of human or animal origin.
- [ ] Detailed information on substances absorbed or dispersed in the human body.
- [ ] Justification for devices containing CMR or endocrine-disrupting substances.
- [ ] Description of environmental conditions for sterile devices and validation reports.
- [ ] Description of methods to ensure measuring accuracy.
- [ ] Description of combination/configuration when connecting to other devices.

Additional areas to consider

- [ ] Post-Market Surveillance
  - [ ] Post-Market Surveillance Plans
  - [ ] User Feedback and Complaints
  - [ ] Post-Market Surveillance Reports
- [ ] Other Supporting Documentation that may support submission
  - [ ] Marketing Materials
  - [ ] Sales Brochures
  - [ ] Other Relevant Documentation