The European Association of Medical devices Notified Bodies

Team-NB Position Paper

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Best Practice Guidance for the Submission of Technical Documentation under Annex II and III of Medical Device Regulation (EU) 2017/745

Information to be supplied by the manufacturer –

a collaborative notified body approach.

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Scope of Document

This best practice guidance document has been developed by members of Team NB who have reviewed the best practice guidance documents (exceeding twenty in number) submitted by individual Team NB notified body members, with the purpose to develop a unified approach on the expectations of technical documentation submissions from manufacturers.

This technical documentation submission guidance is aligned to the requirements of Medical Devices Regulation [MDR] (EU) 2017/745, described in detail in Annexes II and III of Regulation (EU) 2017/745.

Disclaimer:
The content of the best practice guidance is based on the interpretation of the Medical Device Regulation EU 2017/745 by Team NB and affiliated notified bodies. During a technical documentation assessment, it may be required that additional documentation/information may be needed to be submitted as part of the technical assessment that goes beyond what is listed in this guidance document, and each notified body reserves the right to request additional information.

This guidance is intended to be comprehensive, but not exhaustive in its request. Reference to MDCG guidance documents should be considered as suggested guidance for the purposes of this document.

Where specific standards (including harmonised standards) are referenced in this document by number, such references are indicative only. In accordance with Article 8 of Regulation (EU) 2017/745, the use of harmonised standards remains voluntary. Conformity with the relevant General Safety and Performance Requirements of Annex I may be demonstrated by other means, provided that an equivalent level of safety and performance is achieved. This position is consistent with the principles set out in MDCG 2021-5 guidance on harmonised standards and the European Commission's Blue Guide on the implementation of EU product rules. Guidance provided in this document should not be construed as imposing a mandatory requirement to apply any particular standard.

Unless otherwise stated, all standards, IMDRF documents, MDCG guidance, and other referenced documents reflect the version of the document current at the time of publication.

General Considerations

The most common reasons for delays in Technical Documentation assessments by notified bodies are:

- **Incomplete Submissions** – Insufficient or missing information not provided that is required for the conformity assessment activities. This includes an incomplete or inconsistent description of devices covered by the application and the related Technical Documentation (variants, accessories, combined devices covered by the Basic UDI-DI to be assessed).

- **Lack of Cohesive Structure of Technical Documentation** - The information is presented within the Technical Documentation but is difficult to locate.

- **Inconsistent language within the Technical Documentation** - The information is presented in multiple languages, requiring additional translations. In some cases, the intended purpose or other key information is presented in multiple locations with different information.

- **File format and file naming complicates retrieval** – Most notified bodies' employees work within MS Windows environment. This means that all files should be preferably in PDF format, where possible. Microsoft Office document formats can be acceptable. Scanned documents are to be avoided.
  - Because Windows environment limit the acceptable length of the path and file name, do not use file names that combined with the path are longer than 160 characters. Please be aware of white spaces within names: they are encoded as "%20" and consume three characters. Tip: Use "_" instead.
  - No individual PDF file in the submission shall exceed 100 MB.
  - Please bookmark the PDF files for easier use. Documents of ten pages or more should have their own internal table of contents.
  - Please see IMDRF/RPS WG (PD1)/N27R2 for further guidance.

To avoid delays and to further improve your submission, please consider the following practical points:

Communication with the notified body before an application is lodged

- Manufacturers should contact their notified body to clarify the language requirements for the technical documentation submission of the individual notified body as mentioned in MDR Article 52 (12).
- Manufacturers should also contact their notified body to clarify the requirements related to documentation labelling and methods for submission to the notified body.
- Additional guidance on topics suitable for discussion with the notified body prior to submission are provided in MDCG 2019-6 Section: I.6.3. What is considered "structured dialogue"?
- While IMDRF/RPS WG/N9 FINAL:2024 (Edition 4) Non-In Vitro Diagnostic Device Regulatory Submission Table of Contents (nIVD ToC) is not directly applicable to the MDR application submission, the general principles described in the document are recommended.

Technical documentation submission

- The technical documentation must be provided in a clear, organised, readily searchable and unambiguous manner per Annex II. The submission should be accompanied by an index or table of contents with appropriate hyperlinks, as necessary, to aid navigation. The number of folders should be kept to a minimum and if possible, follow a logical flow per Annex II of MDR. Manufacturers are advised to contact the notified body prior to submission and agree the preferred folder structure.
- It is important for manufacturers to provide good quality translations of technical documentation; poor quality translations may, at a minimum, lead to additional questions and time spent on the assessment and, at worst, could lead to a negative recommendation for certification.
- The most recently updated comprehensive reports and data should be included. Abbreviated or partial test reports are not considered acceptable.
- Verification reports provided should be complete, i.e. not a report with subsequent amendments or revisions as the device was changed.
- The technical documentation should document how the manufacturer ensures compliance to every applicable MDR Annex I GSPR. Note that, per section, a simple collection of test/verification reports does not fulfil this requirement. For example, verification and validation protocols and reports should be linked to the risk IDs indicated in the risk assessment; therefore, it will be clear which IDs are mitigated by the indicated documents.
- There are many areas of the technical documentation that will require the duplication of information for multiple documents such as device description. Please ensure that the information is correct throughout all areas where this information is duplicated and consider the risk of potential errors/inconsistencies when updating (e.g. Basic UDI-DI, UDI-DI, intended use, indications for use, contraindications, warnings, etc.).
- Ensure the data in the technical documentation is consistent with the data provided in the respective application forms.
- Valid justifications should always be provided or accompanied where there are deficiencies in the requested data.
- Where ISO standards are mentioned in this guidance, please consider conformance to the state-of-the-art (SOTA). Where appropriate, please provide a rationale and/or gap analysis to justify the use of a standard version that is not aligned with the SOTA.

As part of the technical documentation assessment, please be aware that there are multiple individuals from the notified body involved in the assessment and therefore you may be requested to provide duplication of documents. During the final technical documentation assessment, additional evidence/documents may also be required.

Leveraging of evidence from previous conformity assessments

For certain classifications of medical devices, the MDR requires that manufacturers submit an initial application for certification under MDR to notified bodies (NBs). NBs are required to undertake the applicable conformity assessment activities, typically a combination of quality management system audits and technical documentation assessments to verify compliance to the MDR requirements before certification can be granted. For certain cases, it may be possible to leverage evidence from previous conformity assessments to support initial MDR certification.

In the case of conformity assessments previously performed by the notified body under the Directives (or the MDR) and where the requirements have not changed significantly, and the evidence provided by the manufacturer to meet such requirements has not changed, the notified body may be able to leverage/utilise sections from the previous assessments (e.g. sterilisation or packaging) to establish compliance to the MDR requirements without having to re-evaluate the evidence. In this case, the review ID / project number or other identifier should be provided. Such an approach could help avoid duplication and reduce the durations of the NB MDR conformity assessment activities and hence contribute to faster transition of medical devices from the Directives to the MDR.

It is important to note that the manufacturer should continue to provide full technical documentation in line with Annex II and Annex III of the MDR. However, it would aid the NB technical documentation assessment process if manufacturers clearly indicate whether the evidence/data they have submitted as part of an MDR application (or technical documentation) has changed or not; the extent of changes compared to what may have been previously assessed by their notified body (this may be provided separately or included in the GSPR checklist) under the Directives; and references to NB reports where such evidence was previously assessed.

Please tell the NB where and when the subject device was previously assessed (e.g. reference the previous assessment number).

Abbreviations

ADMET	Absorption, Distribution, Metabolism and Excretion Tests
AI	Artificial Intelligence
BPG	Best Practice Guide
BOM	Bill of Materials
B/R	Benefit/Risk
BtX	Breakthrough
CDP	Clinical Development Plan
CECP	Clinical Evaluation Consultation Procedure
CEP	Clinical Evaluation Plan
CER	Clinical Evaluation Report
CJD	Creutzfeldt-Jacobi Disease
CLP	Classification, Labelling and Packaging Regulation
CMR	Carcinogenic, Mutagenic, Reprotoxic
COA	Certificate of Analysis
CS	Common Specification
CTD	Common Technical Document format (ICH)
CV	Curriculum Vitae
DOC	Declaration of Conformity
ECHA	European Chemicals Agency
EMA	European Medicines Agency
EMC	Electromagnetic Compatibility
EMDN	European Medical Device Nomenclature
ETO	Ethylene Oxide
EU	European Union
GMDN	Global Medical Device Nomenclature
GSPR	General Safety and Performance Requirement
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IFU	Instructions for Use
IMDRF	International Medical Device Regulators Forum
IQ	Installation Qualification
MDCG	Medical Device Coordination Group
MDD	Medical Device Directive
MDR	Medical Device Regulation
MDSAP	Medical Device Single Audit Program
MDSW	Medical Device Software
ML	Machine Learning
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
MVP	Master Validation Plan
NB	Notified Body
OOS	Out of Specification
OQ	Operational Qualification
PMCF	Post Market Clinical Follow Up
PMS	Post Market Surveillance

PQ	Performance Qualification
PROM	Patient Reported Outcome Measure
PSUR	Periodic Safety Update Report
QMS	Quality Management System
RCD	Randomised Controlled Trial
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RM	Risk Management
RMF	Risk Management File
SAL	Sterility Assurance Level
SaMD	Software as a Medical Device
SAP	Statistical Analysis Plan
SDS	Software Design Specification
SIMD	Software in a Medical Device
SOP	Standard Operating Procedure
SOTA	State of the Art
SOUP	Software of Unknown Provenance
SRS	Software Requirements Specification
SSCP	Summary of Safety and Clinical Performance
SUD	Single Use Device
SVCH	Substances of Very High Concern
TD	Technical Documentation
TSE	Transmissible Spongiform Encephalopathy
UDI	Unique Device Identification
UDI-DI	Device Identifier
UDI-PI	Production Identifier

ANNEX II TECHNICAL DOCUMENTATION

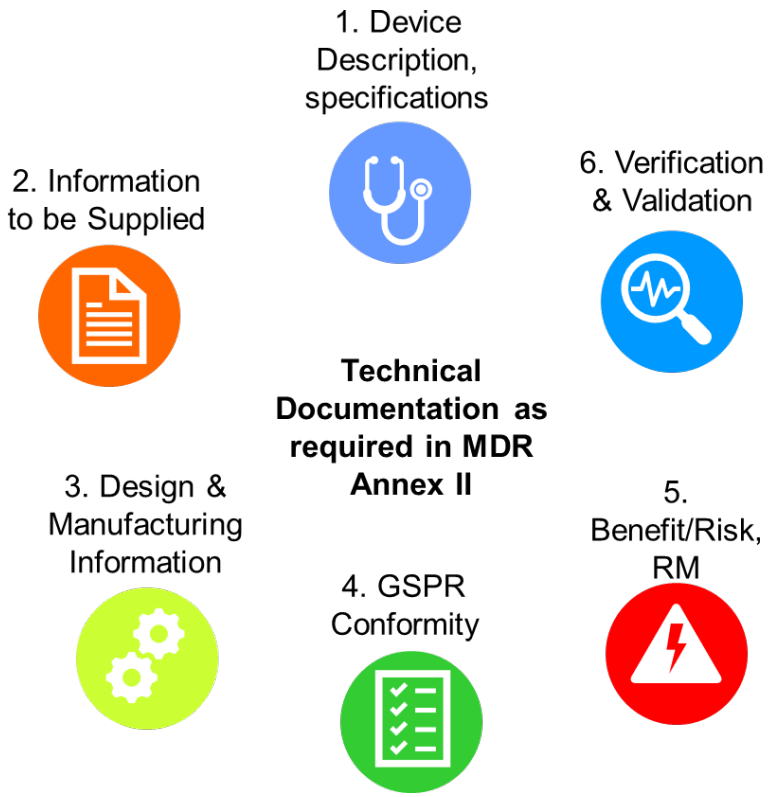

Figure 1. Medical Device Technical Documentation, overall picture.

1. Device Description and Specification, Including Variants, and Accessories, Classification & Materials

Please ensure that the product name, intended purpose/intended use is consistent throughout the different evidentiary documents. If not, please provide an explanation within the main technical document describing the differences and how they would still be applicable to the name/intended use being assessed under the MDR.

1.1 Device description and specification

(a) product or trade name and a general description of the device including its intended purpose and intended users.

- Applicable EMDN codes (as per MDCG 2021-12) as well as information on whether the device is for single use only, multiple use, reprocessing and its number of cycles should be included. Additionally, the applicable MDA/MDN/MDS/MDT code per (EU) 2017/2185 should be reported.
- The general device description should enable understanding of the design, packaging, sterilisation, or other characteristics of the device.
- Sufficient information should be provided to understand the intended purpose and the different design features.
- The intended purpose or intended use should include enough details to enable ready understanding of the medical device per article 2 (12). See more information in the Clinical Evaluation section of this BPG.
- See EN 62366-1 clause 5.1 or ISO/IEC Guide 63 clause 3.4 for minimum contents of use specification:
    - Intended medical indication (can include conditions(s) or disease(s) to be screened, monitored, treated, diagnosed, or prevented).
    - Intended patient population (e.g. age group(s), weight range, health or condition) with clear indications and contraindications.
    - Intended part of the body or type of tissue applied to or interacted with.
    - Intended user profile (summary of the characteristics of the user group, as well as any required occupational skills, physical capabilities, job requirements and working conditions).
    - Use environment (can include attributes for hygienic requirements, frequency of use, location, lighting, noise, temperature, mobility, and degree of internationalization) and;
    - Operating principle.
- Document intended use only where it is compulsory (E.g. in specifications, CEP/CER and IFU). Typical problem is different versions of intended use in multiple documents.
- Please note that all indications, patient populations, user profiles and use environments that are not limited or excluded must be supported by pre-clinical or clinical data. Can the device be used on a mountain top or in heavy rain? Can blind users apply the device safely?
- Provide enough detail to explain the disease conditions the device is intended to treat or monitor.
- The intended users of the device (e.g. Physicians, surgeons in a specialty, clinical nurses, lay-persons, etc.) should be identified.
- In the case where the device is software (SaMD) or software constitutes a major part of the device, the software versioning policy should be described and the software version should be specified throughout of the technical documentation, where relevant.

(b) the Basic UDI-DI as referred to in Part C of Annex VI assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability.

- Clear identification of device by unambiguous reference, allowing traceability (Basic UDI-DI), together with other traceable reference number (e.g. product code, catalogue number, etc.).
- Information to be consistent also with the information on the labelling and Declaration of Conformity.

(c) the intended patient population and medical conditions to be diagnosed, treated and/or monitored and other considerations such as patient selection criteria, indications, contra-indications, warnings.

- The Technical Documentation should include intended patient population (including intended parts of the body or type of tissue applied to or interacted with) and medical conditions to be diagnosed, treated and/or monitored and other considerations such as patient selection criteria, indications, contra-indications and warnings, intended conditions of use (environment, frequency, location, mobility). See more information in the Clinical Evaluation section of this BPG.

(d) principles of operation of the device and its mode of action, scientifically demonstrated if necessary.

- Please include a detailed explanation of how the device is intended to function. Include the principles of physics, chemistry, mechanics, biodegradation etc. that enable the device to function as intended. The amount of information to be included shall be commensurate with the complexity of the device. The scientific demonstration may include the design verification and validation, including pre-clinical or clinical studies, and other relevant information.

(e) the rationale for the qualification of the product as a device.

- Per MDR, Article 2, please explain how the product qualifies as a medical device. Or explain if it is a product without an intended medical purpose (Annex XVI). Please note this is different from the classification of the device per MDR Annex VIII.
- Consider the use of the various guidance documents and manuals in help determining the classification of borderline device

(f) the risk class of the device and the justification for the classification rule(s) applied in accordance with Annex VIII.

- Please indicate the device classification and rationale per MDR Annex VIII. Each potentially applicable rule shall be listed and justification why they are applicable or not applicable shall be documented. Upon selection of the applicable classification rule, each point of the rule shall be justified. If multiple classification rules apply, all should be identified and the strictest rules resulting in the higher classification should apply.
- If the device contains multiple components that on their own might be classed differently, this shall be documented. Please note the higher classification should apply.
- For guidance on classification, see MDCG 2021-24.
- If a medical device is standalone software, guidance for the qualification and classification of the software can be found in MDCG 2019-11. There should be a rationale for why the software is a medical device and for its classification. If applicable, the software should be broken down into modules, some that have a medical purpose and some that do not. The modules with a medical purpose must comply with the requirements of the MDR and must carry the CE marking. The non-medical device modules may not be subject to classification on their own, but when they are used in combination with the medical modules to deliver the intended use, the safety and performance of the combination (integration per EN 62304) shall be provided.
- For “borderline products”, see MDCG 2022-5 and Manual on borderline and classification for medical devices under Regulation (EU) 2017/745 on medical devices.
- If the device is a Well-Established Technology (WET) as per MDR Article 52 (4) and (5), a rationale supporting the determination of the device as a WET should be included considering the definition in MDCG 2020-6.

(g) an explanation of any novel features.

- A description of novel features of the device needs to be provided as part of the device description/specification section.
- Please explain whether novel features are novel in comparison to other devices in the market and/or novel in comparison to other devices of the manufacturer.
- Novel features must be accompanied by scientific evidence, e.g. from clinical investigations. Novel features might require a clinical investigation also in the case of Class IIa or IIb devices. This may be briefly described here with reference to the detailed information elsewhere in the technical documentation.
- The degree to which the device is novel may be defined based on the criteria given in the EU Commission Guidance 2020/C 259/02. The impact of this novel feature on the technical or clinical safety and performance of the device should be briefly described here with reference to the detailed verification/validation studies.

- If no novel features are claimed, this also shall be explicitly stated.

(h) a description of the accessories for a device, other devices and other products that are not devices, which are intended to be used in combination with it.

- The following information should be provided for any accessories (including Class I) associated with the device:
    - Brief description of the accessory/accessories and how they are used with the device(s).
    - Classification of the accessories and rationale for classification.
    - Technical Documentation references (file name, issue status, date). Indicate clearly if the accessories are packaged with the device or provided separately or both. Also clarify if the accessories are already certified and if yes, provide the certificate references.
    - Please note evidence should also be provided within the Technical Documentation to demonstrate compatibility of the devices with any applicable accessories.
    - The Technical Documentation should identify any accessories which are not included with the device, but which are necessary for its use.
- For other devices and other products that are not devices but are intended to be used in combination with the device under review, please include
    - Sufficient detail to identify the other device or product
    - Whether it is supplied by the manufacturer along with the medical device
    - Compatibility information
    - Reference to chemical and biological compatibility information, where relevant.

(i) a description or complete list of the various configurations/variants of the device that are intended to be made available on the market.

- All configurations/variants of the product covered by the Technical Documentation need to be clearly identified.
- Please provide sufficient information to distinguish different variants of the device.

(j) a general description of the key functional elements, e.g. its parts/components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition. Where appropriate, this should include labelled pictorial representations (e.g. diagrams, photographs, and drawings), clearly indicating key parts/ components, including sufficient explanation to understand the drawings and diagrams. For software, decomposition into software systems, items, units and related integration shall be provided in accordance with EN 62304, considering the assigned software safety class.

- For software, decomposition into software items and units—including their integration—should follow the structure defined in EN 62304, considering the assigned software safety class. A high-level architecture, including system modules and their integration, shall always be provided. More detailed architectural descriptions and specifications (unit specifications and description) shall be included in accordance with the software safety class as defined by EN 62304.

- Detailed drawings of components, sub-assemblies, final assemblies which form the key functional elements to be provided.
- The material composition used for the key functional elements shall be identified with qualitative and quantitative information.
- Critical aspects of the specifications including tolerances should be included. This may consist of Critical to Quality aspects, critical dimensions, and a list of critical components/ingredients should be provided.
- For active medical devices, electrical circuit diagrams should be a part of the Technical Documentation and should enable the reviewer to understand the electrical safety concept and identification of all relevant electrical components. The level of detail, whether a high-level diagram or detailed schematics, should be commensurate with the level of understanding required, considering the associated risk. High-level diagrams should always be provided to ensure a clear understanding of the overall system architecture and operation, while detailed schematics and PCBA layouts may be necessary for novel electronics solutions or high-risk electronics modules.

Note: This is important for pre-clinical aspects, such as safety concepts, risk management aspects, testing of e.g. physical/mechanical/electrical properties etc., compatibility with other products/accessories, etc. as well as clinical aspects.

(k) a description of the raw materials incorporated into key functional elements and those making either direct contact with the human body or indirect contact with the body, e.g., during extracorporeal circulation of body fluids.

- Submission should include the device Bill of Materials. Substances incorporated and potentially released from the device (in substance-based devices) must be unequivocally identified in the Bill of Materials, e.g. by the specification of the CAS numbers.
- The Technical Documentation should identify the raw materials incorporated into key functional elements of the device including information on any coatings that are critical for device safety and performance. The nature of contact with the human body (e.g. direct or indirect contact, contact with circulating body fluids, etc.) should be clearly identified.
- The submission should clearly indicate whether the device utilises or is used in conjunction with any human or animal- based products or other non-viable biological substances. Materials which are or include derivatives of human or animal origin or other non-viable biological substances should be clearly identified. The inclusion of nanomaterials shall also be identified.
- The technical documentation should also identify the raw materials used in the packaging of the device, including primary and secondary packaging.

(l) technical specifications, such as 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.

- Complete technical specifications for the device and any variants/configurations, including indication of which of these are presented in the product specification made available to the user.

1.2 Reference to previous and similar generations of the device

(a) an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist.

- All submissions should be accompanied by a market history to enable an understanding of the context of device development.
- If the device is new and has never been marketed by the manufacturer anywhere in the world, please state this explicitly.

For existing devices:

- Ensure that a market history is provided indicating the nature and timing of any changes and that any associated documents (i.e. risk analyses, labelling, clinical evaluation reports, verification / validation data, etc.) account for these changes.
- Provide evidence (e.g., NB Reference numbers of previous assessments) to demonstrate that NB has been notified of all significant changes (if applicable).
- For initial applications under MDR, please confirm whether the device has been previously marketed under MDD and whether any changes have been made in comparison to the MDD-certified device.
- Market history should include EU and approvals in other geographies, including sales volumes per country.
- If the device is a system, ensure that the number of units sold is broken down by device component and per year.

(b) an overview of identified similar devices available on the Union or international markets, where such devices exist.

- Refer to MDR article 2 (7) and MDCG 2020-5, section 5 for the definition of similar device and its relevance.
- Provide an overview of identified similar devices available on the EU or international markets if such devices exist. This should include a comparison of these devices with the device under assessment to show the similarities and differences.

Note: The similar devices identified in this section should align with those identified in the clinical evaluation, including the PMCF plan.

1.3 Common Pitfalls in Device Description & Specifications

- Inconsistencies are observed within the various documentation: For example, abbreviations are used in DoC, while the labelling uses the full device name, or the variants and configurations (including packaging configurations) are not very clear or are inconsistent throughout the TD.
- Rationales for various definitions and classifications are not detailed enough: For example, for devices including a drug substance, justification is not included as to why the drug substance is considered ancillary to the mechanical action of the device.
- Contraindications do not include specific anatomy or special population when no evidence for the safe use in such anatomy/special population is provided.

2. Information to be Supplied by the Manufacturer (Includes Declaration of Conformity, Labelling, IFU, Implant Card, Surgical Technique brochure etc.)

Note applicable to all the labelling materials, except the DoC:

- Within the technical file, please provide a list of EU countries in which the medical device is intended to be marketed and evidence that the national requirements of the languages used are adhered to.

- In the case where the marketed countries are not fully defined yet, a master template in the language required by the notified body may be acceptable for initial MDR certification. After initial MDR certification, all languages should be included in the latest technical file.

2.1 Declaration of Conformity (DoC)

For devices being assessed for initial MDR certification, please provide a draft EU Declaration of Conformity according to MDR Annex IV. For devices already MDR certified, please provide a signed EU Declaration of Conformity.

2.2 Labelling

- Please provide the label or labels on the medical device, in the languages accepted in the Member States where the device is envisaged to be sold. This includes Device or Product labelling, Sterile packaging labelling, Single unit packaging labelling, Sales packaging labelling, Transport packaging labelling and labels displayed in software.
- Please also include information on markings or labelling applied on the device itself (if any), including a specification of the method by which it is applied (e.g. laser marking of titanium implants).
- Medical devices generally use multiple levels of labelling, and it is recognised that not all devices may have the different levels of packaging specified in this section or different terms may be used than those specified here. Legible versions of all applicable levels of labels should be provided (e.g. secondary pack, primary pack) and should be representative of the finished form, showing all included symbols.
- Provide drawings with the packaging configuration (showing placement of all labels) and label specifications (layout, size).
- The position of labels on the finished product should be clear. If the device is contained within a sterile barrier system, clearly identify the label for the sterile package. If any of the packaging is printed with information for the user (including pictures / schematics of the device) this should also be provided.
- Verification of label contents must be carried out in accordance with MDR Annex I GSPR 23. There is a commitment by the Manufacturer to apply UDI carriers on the device label as per MDR Article 27(4) and depending on the classification of the medical devices as per MDR Article 123 part 3(f).
- Please ensure that any specific requirements of mandatory harmonised standards or Common Specification (CS) are addressed in the labels and information for use. For example, EN ISO 15223-1 defines symbols to be used in labelling, or the CS for Annex XVI devices include labelling requirements. In addition, the specific requirements for the label and IFU of all other harmonised and non-harmonised standards which are applied must be implemented in the IFU.

2.3 Instructions for use/Device Operating Manual(s)

- Please provide the instructions for use (IFU), in the languages accepted in the Member States where the device is envisaged to be sold. Manufacturers must ensure that the information within the IFUs, especially related to intended purpose, indications, contra-indications, and other safety related information such as side effects, warnings is aligned with similar information from other sections such as risk management, clinical evaluation, usability, pre-clinical performance data etc.
- IFUs must contain all the information required as per applicable requirements specified within MDR Annex I GSPR 23.
- Please ensure that any specific requirements of relevant standards or CS are addressed by the IFU. For example, EN 60601-1, EN 60601-1-X, EN 60601-2-X, EN ISO 17664, EN ISO 14630 have specific requirements for the IFU.
- For devices where cybersecurity is applicable, please follow the requirements of MDCG 2019-16: information for healthcare providers regarding intended use environment.
- Please provide surgical technique, user manual, installation and service manuals if applicable
- For devices provided without an IFU/Leaflet/Instructions, provide the information detailed in MDR Annex I GSPR 23.4(p) and 23.4(v).

2.4 Electronic IFU (e-IFU) information (if applicable, and as per (EU) 2025/1234 amending EU 2021/2226)

- If electronic IFU will be utilised, ensure compliance has been clearly outlined and evidence included to demonstrate compliance with all relevant aspects of Regulation 2025/1234 amending Regulation 2021/2226. To ensure unconditional access to the e-IFU and to facilitate the communication of updates, those instructions should be available on the website of the manufacturer in an official language(s) of the Union determined by the Member State in which the device is made available to the user or patient. Instructions for use in electronic form, which are provided in addition to complete instructions for use in paper form, should be consistent with the content of the instructions for use in paper form.
- Please submit e-labelling information as provided on the device or on a leaflet.
- Provide documented risk assessment covering the elements as required by the e-labelling regulation (this can be in the Risk Management section of the technical file).

2.5 Patient handbook

Some devices incorporate all the information relevant for the patient/user within the IFU itself. Some devices are accompanied by a patient handbook with additional instructions specific to the patient, for example with devices (or parts, components of the devices) that are patient operated. If the device is supplied with a patient handbook, this should be provided in the languages accepted in the Member States where the device is envisaged to be sold. The planned approach for translation of any information not in harmonised symbols should be described, if applicable.

2.6 Physicians'/other users' handbook

If a separate physicians' handbook is relevant for the device, this should be provided in the languages accepted for translation of any information not in harmonised symbols should be described, if applicable.

2.7 Implant card information

Please provide the implant card and information to be supplied to the patient with an implanted device, if applicable. The implant card and other information per Article 18 of MDR, and any additional in the information as specified in the MDCG guidance (MDCG 2019-8) on implant cards should be included. The device type according to MDCG 2021-11 should be included. The location of the implant card within the device or system packaging should be clearly specified. The planned approach for translation of any information not in harmonised symbols should be described, if applicable.

2.8 Copies of promotional materials including any that make specific claims related to the device

- All material provided by the manufacturer shall be submitted for review against MDR Article 7.
- Only marketing literature that mention that the device fulfils the requirements of CE marking shall include the CE mark along with the NB identification number.
- Supporting evidence should be provided in the relevant pre-clinical and clinical sections to substantiate any claims made in the labelling or marketing literature.

2.9 URL of the website where the IFU and/or any other labelling information as relevant will be made available as per MDR Annex I GSPR 23.1

MDR Annex I GSPR 23.1 requires that information related to identification, and safety and performance of the device should be made available and kept up to date on the manufacturer's website if the manufacturer has a website. The URL of the website where such information will be made available should be included.

2.10 Common Pitfalls for Information to be Supplied by the Manufacturer

- Basic UDI-DIs are being assigned incorrectly – this leads to amendments during the technical assessment. Please ensure the correct Basic UDI-DI is assigned when technical documentation is first submitted to the notified body.
- Basic UDI-DI is not consistent across the application, Declaration of Conformity (in the application phase a draft DOC), Technical Documentation, PSUR and vigilance reports.
- IFU – the intended use and the indications are being used interchangeably. Please use MDCG 2020-6 definitions.
- IFU does not include all the requirements per GSPR 23.4. For example: i) Compatible accessories / devices to be used in combination are not listed; ii) links to the SSCP (if SSCP is applicable).
- Lack of 1:1 alignment across all the information provided – do not let the SSCP deviate from the IFU or the patient information leaflet.
- Information in the patient part of the SSCP is a copy of the healthcare professional part (i.e. the level of knowledge of patient/lay user is not considered).

3. Design & Manufacturing Information

(a) Information to allow the design stages applied to the device to be understood;

Please provide information to allow the design stages applied to the device to be understood. Design stages/phases are typically closed by phase reviews with meeting minutes and a report, which can be informative enough. Standard operating procedures (SOPs) for design and development are not required; these typically do not apply to the specific device and will not provide understanding on the design stages of the particular device.

(b) Complete information and specifications, including the manufacturing processes and their validation, their adjuvants, the continuous monitoring and the final product testing. Data shall be fully included in the technical documentation;

Please provide detailed description of manufacturing processes including:

- Manufacturing flowcharts (identifying the processes implemented and specifying whether they are validated or verified, together with the in-process and final controls performed), including where these stages are subcontracted.
- Detailed description of manufacturing procedures and controls including where these stages are subcontracted. The control criteria on the critical characteristics of the device, including where these are subcontracted, must also be provided.
- Critical process verification reports:
    - The manufacturer should include verification protocols/plans/reports for processes that are verified (as opposed to validated) and are considered critical for the safety and performance of the device.
    - Notified body reviewers may request this information for other verified processes (not originally included with the submission) during the assessment process if required.
- Incoming material testing procedures. Acceptance criteria & results of incoming inspections from a sample batch for the critical raw materials and/or sub-assemblies and/or components.
- Continuous monitoring / in-process controls. Specifications / acceptance criteria.
- Specification of final (release) product and testing. Acceptance criteria & results of final inspections from a sample batch for the finished devices.
- Identification of party responsible for inspection of subcontracted processes.
- Information on specifications and their validations (e.g. coating processes, injection moulding, bonding, welding, cleaning, rinsing, sterilisation packaging, software processes, etc.).
- Any intermediate cleaning stage(s) must be specified.
- A description of the validated manufacturing process(es) and Validation report(s) (OQ and PQ), including where these processes are subcontracted. This must at least identify the following information:
- Description of the validated process with the precise identification of the equipment concerned.

- Identification of associated validation reports (IQ/OQ/PQ) with their reference, revision number and revision date.
- Identification of critical process parameters as well as validated tolerance intervals (Minimum / Maximum).
- The manufacturer should include validation protocols/plans/reports for processes (including subcontracted ones) that are validated and are considered critical for the safety and performance of the device. Notified body reviewers may request this information for other validated processes (not originally included with the submission) during the assessment process if required. These validation documents shall include justification for worst case product size, sample size etc. When the same process is performed at multiple sites with same/similar equipment, please provide validation at both sites. In the absence of a full validation at additional sites, a justification is expected to be included.
- Please provide the Master Validation Plan (MVP) and Validation Reports of processes considered critical for the safety and performance of the device. Please consider this requirement also for critical processes being outsourced. Further information might be requested during the Technical Documentation assessment and/or during audits.
- Provide a description of working environment including its classification and its controls.
- Provide a description of any adjuvants used. These may include “additives (antioxidants, UV stabilizers, colour additives, dyes, etc.), and processing aids (solvents, lubricants, antifoaming agents, etc.)” per ISO 10993-1. Provide details of continuous monitoring processes.
- Where a process has been the subject of a previous assessment with the same notified body in the context of Regulation (EU) 2017/745 in a Master-File format (validation of a process covering several devices covered by different Technical Documentations and / or dependent on different categories and/or generic groups), please provide:
    - Identification of the process(es) concerned.
    - Identification of the number and date of previous assessment report, with a satisfactory outcome.
    - A rationale for the proposed inclusion of the device, which is the subject of the assessment, in the validation of the process previously assessed (inclusion of the product within a defined family without challenging the worst-case scenario).
- If the device is required to be installed and/or commission at the user location, please provide information on tests to be carried out as a part of the installation and commissioning of the device.
- As a general principle, if any of the information requested in the Manufacturing section is not available in English, the Manufacturer should either provide translations or provide supplementary summary reports with translations of relevant information/sections. Or in cases where the information/reports are data heavy (or mainly graphical in nature) with very few words, the Manufacturer may annotate English translations of relevant words within the reports.

(c) Identification of all sites, including suppliers and sub-contractors, where design and manufacturing activities are performed.

The manufacturer should provide the following documentation at a minimum:

- The name and address of any critical subcontractors should be identified, along with the service or material supplied by each.
- Copies of critical subcontractor ISO 13485 certificates or other relevant certificates based on the product / service they provide. If a critical subcontractor does not have an ISO 13485 certificate from a notified body, additional supplier audits may need to be arranged.
- Identification of subject medical device design sites (identification of all sites, including sub-contractors, where design activities are performed, e.g. outsourced design units, research sites, etc.).
- Identification of subject medical device manufacturing process sites (identification of all sites, including information of manufacturing stages and critical sub-contractors, where manufacturing activities are performed).
- Quality assurance agreements with critical subcontractors (in case of sterile medical devices, the contract with the sterilisation company). Agreements are expected to contain processing specifications including actions/responsibilities in case of OOS events.
- Critical subcontractors (name and address of the company, evidence of qualification of such subcontractors, e.g. certificates, accreditation certificate, etc.).
- If multisite companies are present, specify the site(s) involved in the design / manufacturing of the subject medical device.
- Where legal manufacturers have their devices designed or manufactured by another legal or natural person, the name, address and contact details of that other person should be submitted to the database in EUDAMED electronic system (requirement only applicable from 18 months after the date of publication in EU O. J. of EUDAMED's full functionality).

3.1 Common Pitfalls in Design & Manufacturing Information

- For older legacy devices, no information on design stages applied is provided.
- Manufacturing flow chart does not clearly describe the location of the various manufacturing/inspection steps.
- Only re-validation documentation provided (for example due to a change) without initial documentation to support the validation status.
- Worst case and sample sizes are not justified based on risk analysis.
- When same process using similar type of equipment is performed at multiple sites, the validation of the process at only one site is provided.

3.2 Common Pitfalls in Sites & Subcontractor Information

- Addresses of critical subcontractors are incomplete or secondary sites, where production/design/warehouse activities take place, are missing.
- Product or service specifications contained in the agreement are missing or generically reported (e.g. missing MD description, MD ref. code, BOM specifications, regulatory aspects etc.).

4. General Safety & Performance Requirements (GSPRs)

The manufacturer should provide clear, organised, readily searchable and unambiguous documentation. For example, a compliance matrix/checklist/or other document that includes the following:

(1) Each GSPR of MDR Annex I that applies to the device and an explanation as to why other GSPRs do not apply to the device.

EXAMPLE: A decision column "applicable versus not applicable" for each clause/sub-clause of MDR, Annex I. A "rationale" column on each clause/sub-clause of MDR, Annex I, that apply to the device, with an explanation as to why others do not apply.

(2) The method or methods used to demonstrate conformity with each applicable GSPR.

EXAMPLE: A column "methods used to demonstrate conformity", with each clause/sub-clause of MDR Annex I.

(3) Harmonised standards, Common Specification (CS), or other solutions applied (please refer to the specific edition/issue date).

EXAMPLE: A column "applied standards, CS or others", for each clause/sub-clause of MDR, respectively.

NOTE 1 to (3): This is usually accomplished by means of a list of applied standards and CS, as well as by reference to appropriate standards and CS in the appropriate documents (e.g. test reports).

NOTE 2 to (3): Indicate if full or partial compliance is being claimed. Where (i) key standards or CS have not been applied or not been applied in full, (ii) a manufacturer chooses to use a newer version of a currently harmonised standard, (iii) outdated standards are applied: in all these cases, an appropriate justification should be provided in the Technical Documentation, in the form of a summary or gap analysis regarding ability to comply with associated General Safety & Performance Requirements (Annex I), and a risk analysis and a duly justified conclusion of acceptability of any compliance gaps.

NOTE 3 to (3): Refer also to additional applicable standards, and/or Directives – e.g. Machinery, EMC, RoHS, European Pharmacopoeia, scientific opinions, guidance as necessary to show consideration of the state of the art.

NOTE 4 to (3): Where other solutions have been applied, i.e. there are no standards or CS applied, please provide a justification and, where relevant, the qualification/validation of the method showing that the method is at least equal or better than the ones listed in the standard or CS.

(4) The precise identity of the controlled documents offering evidence of conformity with each harmonised standard, CS, or other method applied to demonstrate conformity with the GSPR.

EXAMPLE: A column to add the "precise identity of the controlled documents" offering evidence of conformity. Identification should be as "Document ID, document date, section, point, page, chapter, link etc."

NOTE 1 to (4): This should include a cross- reference to the location of that document (use precise references – avoid general or generic references) within the full Technical Documentation and, where applicable, the summary of the technical documentation. The more specific the references are to documents supporting compliance, the faster the assessment can be conducted.

NOTE 2 to (4): If no new testing is required, a justification needs to be provided.

(5) Version control or document control, as per manufacturer quality management system procedures (Draft documents should not be provided).

4.1 Common Pitfalls in General Safety & Performance Requirements (GSPRs):

- A justification why standards are (partially) applied to demonstrate conformity to the GSPR of the MDR is absent. E.g., a standard for vascular grafts is mentioned for a surgical mesh, with no explanation or justification why this standard is applied, and which part of it.

- A systematic evaluation of relevant documents as relevant published literature applicable to the device, best practice guidelines, and standards is not part of the technical documentation. In consequence, it is unclear why the selected test methods and acceptance criteria are deemed valid to predict the clinical safety and performance of the device.

- The GSPR requirement no. XX is identified as “not applicable”; however, no justification/rationale is provided.

- GSPRs documentation does not include a clear and unambiguous reference to where the evidence used to demonstrate compliance (for applicable GSPRs) can be found inside the Technical Documentation provided.

5. Benefit-Risk Analysis and Risk Management

For risk management please refer to the MDR requirements as stated in Annex I, clauses 1-9 and Annex II, section 5. Please clearly indicate whether the risk management process is based on EN ISO 14971.

The interface between risk management process and data from pre-clinical evaluations (product verification and validation) and clinical evaluation performed by the manufacturer must be clear and noticeable (refer to Annex VII, 4.5.4(c) and 4.5.5); and the results of the risk management should provide information about the appropriateness of the pre-clinical and clinical evaluation.

- Please provide a copy of risk management procedure(s) that include the definition of any rating systems used for risk analysis and risk acceptability. If this is part of a different document such as the risk management plan or maintained as a separate document that is specific for the subject device, then the relevant information must be included.

- Please provide copies of the relevant risk management documentation to confirm that the risk management procedure is followed (including e.g., the usability risk management procedure, if applicable). Evidence of the "life-cycle management" concept must be provided, i.e., the analysis must be performed throughout the life cycle of the device, from design to disposal, considering all the appropriate PMS data. Guidance on the end of the obligation to update the PSUR is found in MDCG 2022-21.

- Please note that risk management documentation should comprise all parts / components of a device.

- Risk management should be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating.

- Please note that special requirements of Common Specifications on Risk Management need to be included for devices covered by MDR, Annex XVI.

The requirements also apply in case of outsourced processes.

5.1 Risk management plan

- Please provide the risk management plan associated with the device, including:
  - The scope of the risk management activities.
  - The complete description and identification of the devices and accessories in question.
  - The description of the life cycle phases of the device.
  - Assignment of responsibilities and authorities for risk management.
  - Identification of requirements for review of risk management activities.
  - The system used for qualitative or quantitative categorisation of – as a minimum - probability of occurrence of harm and severity of harm.
  - Definition of criteria for acceptable risk levels.
  - Evaluation of any residual risk acceptability, including overall residual risk.
  - Criteria for acceptability of the overall residual risk, the method and evaluation of overall residual risk.
  - Verification of the implementation of risk control measures.
  - Verification of the effectiveness of risk control measures.
  - Identification of activities for collection and review of production and post-production information.

- Please provide evidence that the risk management team comprises appropriately qualified persons, including assignment of a clinical expert.

5.2 Risk analysis / risk control measures

The documentation should contain information on:

- The benefit-risk analysis referred to in section 1 and 8 of MDR Annex I.
- The solutions adopted and the results of the risk management referred to in section 3 of MDR Annex I.
- Evidence given that a safety concept in accordance with section 4 of MDR Annex I is applied, including information to users of any residual risk(s).

The documentation should include:

- Design risk assessment: documented risk assessment for the design aspects of the device.
- Production/process risk assessment: documented risk assessment for th e production/manufacturing process aspects of the device.
- Clinical/Application/Product risk assessment: documented risk assessment for the clinical usage/application aspects of the device.

For design risk assessment, an assessment should be provided whether any design changes add new hazards or reduce the likelihood of occurrence of existing hazards, irrespective of whether the risk assessment has changed.

Reduction of the risks related to use error should cover the requirements set out in section 5 of MDR Annex I. For usability evaluation please refer to the MDR requirements stated in Annex I, clauses 14.6, 21.3, 22.1, 22.2, 23.1a, as well as to EN 62366-1.

For ease of assessment, it is recommended to provide a use flow-chart for the device in question.
Risk analysis should demonstrate:

- All known and foreseeable hazards associated with each device are identified and analysed (i.e., estimation and evaluation of risks for each hazardous situation).
- All known and foreseeable risks, and any undesirable side-effects, are minimised and acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use.
- Estimation and evaluation of risks associated with and occurring during intended use and during reasonably foreseeable misuse are estimated and evaluated, including eliminating or controlling these risks.
- Appropriate controls (i.e., process validations, biocompatibility, sterilisation, clinical, shelf-life or other key verification/validation tests) have reduced all risks as low as possible to acceptable levels considering state-of-the-art for the product(s) under assessment.
- Risk control measures are implemented for each hazard (with references to the documentation where these measures are implemented).
- The effectiveness of risk control measures is verified (with references to the documentation where effectiveness of risk control measures is demonstrated).
- Residual risks and their processing operations are identified, and the acceptability of any residual risk(s) is assessed.
- A statement is given that the clinical benefits outweigh all the residual risks.

- Production and post-production information are evaluated regarding hazards and their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and the control measures are amended if necessary.

5.3 The risk analysis should cover (not limited to):

- Hazards related to all device components.
- Hazards related to clinical use.
- Hazards related to ergonomic features of the device and the environment in which the device is intended to be used.
- Hazards related to technical knowledge, experience, education, training and use environment of users.
- Hazards related to the medical and physical conditions of intended users (lay, professional, disabled, etc.).
- Hazards related to reuse (please note for single-use devices, GSPR 23.4(p) requires the risks of re-use to be addressed, this should be identifiable).
- Hazards related to the manufacturing process.
- Hazards related to cybersecurity.
- Hazards related to updates of device software or to updates of the device platform's operating system.
- If applicable, any required risk evaluation per commission implementing regulation (EU) 2022/2346 for Common Specification for the Annex XVI devices.

Note: additional hazards are also given in EN ISO 14971 and ISO/TR 24971.

5.4 Risk management report

- Please provide the risk management report associated with the device, including:
  - The evaluation of any residual risk(s) acceptability.
  - The evaluation of the overall residual risk acceptability.
  - The evaluation of the benefit-risk ratio.

- A statement should be provided that the device, when used within the intended purpose, constitutes acceptable risks when weighed against the benefits to the patient and is compatible with a high level of protection of health and safety, considering the generally acknowledged state of the art (MDR Annex I, 1).

- For MDR Annex XVI devices: a statement should be provided that the device does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the device use, which is consistent with a high level of protection for the safety and health of persons (MDR Annex I, 9).

5.5 Common Pitfalls in Risk Management

- The description of risk controls is not clear enough to understand what has been done to reduce the risks. E.g., for risks related to deliberate misuse, “IFU” is indicated as risk control, however it did not describe which information has been added to this document to control the risk.
- When a warning or caution in the IFU is used as a risk control measure, it is not supported by Usability Engineering to verify that the information was evaluated for understanding and effectiveness.
- Risk control measures described in the risk management file are not in line with the risk control options under MDR Annex I GSPR 4. E.g., sterilisation validation is mentioned as risk control for biological contamination due to reuse, however the validation itself is not a risk control for this item (i.e. safe design and manufacture, protection measures, information for safety, training to users).
- It is not traceable in the risk management file which referred records relate to verification of implementation and which to verification of effectiveness of each risk.
- The levels for semi-quantitative determination of occurrence rates do not reflect clinical reality. E.g., “occasional” is related to “in every 10-100 cases”. Risks occurring in every tenth patient would typically not be considered occasional, but frequent.
- The risk management plan does not include clear criteria to decide on risk acceptability. The MDR does not allow that the acceptance of risks is alone decided based on risk prioritisation number (RPN), “green” area or similar, but requires that the acceptability of each risk is decided individually based on predefined criteria.

6. Product Verification and Validation

The following sections detail specific technical documentation areas. While each section focuses on its dedicated topic, some general technical documentation requirements may be repeated for clarity.

- In general, the documentation should contain the results and critical evaluation of all verifications and validation tests and/or studies undertaken. For each test performed, the resulting data should be critically analysed and linked towards addressing specific GSPRs and/or related risk control measures.
- Annex II 6.1(b) states the following "Where no new testing has been undertaken, the documentation shall incorporate a rationale for that decision". This section is vitally important for previously marketed devices under the directive applying for MDR certification. MDR applications are considered an entirely new standalone applications from the original MDD designation, however there is potential to use existing data where justifiable and if the state of the art is met.
    - As an example, for devices previously marketed under the MDD there may be slight differences from the MDD version of the device than the MDR version that may have only required a partial retest rather than a complete reverification and revalidation for MDR.
    - In these instances, it is critical that the manufacturer clearly and logically presents this data to the notified body and that they clearly identify and outline what testing is relevant to the current version of the device (this requirement should also be taken in conjunction with MDR Annex II 1.2b).
- If historic testing is referenced, but a subsequent change was made and only some specifications were re-tested, please explain which test reports are superseded and should be reviewed for each relevant specification.
- If multiple design verification / validation studies were conducted, please provide a flow chart or table that shows how the studies were conducted and highlight which study ultimately demonstrates that the design meets the product performance specifications (this requirement should also be taken in conjunction with MDR Annex II 1.2b).
- An overarching design/ development validation/verification plan(s) should be provided along with associated report(s).
- The following points are also relevant to real time and or accelerated aging studies; adequate justification for not performing these studies on a design element should be provided.
- All design requirements and specification documents should be provided.
- A design control input/output matrix should be provided; these traceability matrices shall contain traceable sources to requirements (risk, regulatory performance etc.) and in turn the identification of the protocols reports and test data documents in the technical file relating to their verification and validation including the test evidence. Accelerated aging and real time aging requirements are often useful to add to their T=0 design element as a line item in a matrix.

- The design matrix should clearly identify the user needs the associated design input and essential design outputs and link to the verification evidence and associated validation evidence.
- The design matrix should be clearly presented and organised logically. It may be beneficial, depending on the device, to have headings such as Sterilisation, Biocompatibility, Packaging Requirements, Real-time, Accelerated Aging requirements etc. individually organised and labelled with sources of the requirements. If the device has multiple notified body reviewers, then a logical organisation of this matrix can be of great benefit to the reviewer(s) navigating the requirements.
- A specific case is medical devices that utilise Artificial Intelligence / Machine Learning (AI/ML). For those:
  - Training and testing datasets must be clearly described in the technical documentation.
  - Testing dataset must be representative and independent of the training dataset.
  - All the processes, tools and environments that are used for training, testing and deployment are to be supplied.
  - Verification and validation protocols and reports.
  - There must be evidence for compliance to EU Ethics guidelines for trustworthy AI:
    - Human agency and oversight
    - Technical robustness and safety
    - Privacy and data governance
    - Transparency
    - Diversity, non-discrimination and fairness
    - Societal and environmental well-being
    - Accountability
- Protocols or equivalent should contain a justification based on specific standards, or risk-based, for the sampling size selection. Protocols should contain any product specific data or justifications for sample selection including acceptance criteria, confidence intervals, tolerances, objectives, references to test methods etc.
- Use of clear justification should be provided in the protocols and their conclusions addressed for adequacy in the reports to situations where test results are considered representative for a group of devices, e.g. during comparative testing or worst-case conditions for testing.
- Any pre-conditioning prior to testing should be documented in advance and pre-condition test data should be included with the test reports.
- If compliance is demonstrated without test evidence, it should be clearly justified and detailed scientific/ engineering-based evidence for the justification should be provided.
- Any discrepancies/ deviations and their investigations should clearly be documented in the reports along with the rational for acceptance and, if relevant, a CAPA overview.
- Reports should clearly demonstrate the statistical inferences being made and a link to the raw data provided in the test report or the technical file. It can be beneficial to remember the statistical/test requirements in the following way. **Disclaimer**: **this may not be the preferred approach of your notified body and is not considered guidance, but more a general overview of good documentation practices; it is always beneficial to check with your notified body first for their preferred structure.**

- **Practical**: The raw test data used to generate the data via a validated test method or equivalent.
- **Graphical**: the graphical summary of the data and any statistical inferences being made, e.g. histograms capability 6 packs normality plots etc.
- **Analytical**: The analytical data of the analysis e.g. statistical software output demonstrating p values etc. This is also a requirement for the conclusion in the associated report used to demonstrate compliance to the applicable GSPR.

- All outliers in statistical data need to be thoroughly investigated and examined and a root cause provided and assigned before any conclusions can be drawn. Outliers cannot simply be excluded and must be addressed.

- Where necessary it is a requirement to demonstrate that the units used for testing are reflective of the final unit; this may require unit build/production information that is directly traceable to the individual test. These can be provided in summary appendices to a section in the report discussing such build information. If testing has been undertaken on prototypes, previous generations of a device, or devices that otherwise do not represent the finished goods, a justification for the adequacy of this testing should be provided.

- In instances where contract test laboratories have been used the manufacturer must provide a bridge between their protocol and reports and the contractors reports protocols where necessary. Accreditation/ certification credentials should also be referenced in the technical file for these test centres.

- In terms of the lifetime of the device there should be sufficient evidence to support the claims made; it should not be considered that product lifetime is equivalent to shelf life. Depending on the device type, appropriate statistical data should be included to demonstrate the reliability of the device over its lifetime in use.

- Lifetime requirements should also take into consideration other key elements such as risk management, post market surveillance and clinical evaluation.

6.1 Pre-clinical and Clinical Data

6.1.1 Biocompatibility

The following information is to be provided:

1. **<u>Standards and references applied for the medical device related to biological evaluation</u>**

- Standards and references applied in terms of biological evaluation.
    - When specific standards exist for the type of medical devices, it is recommended to use the most specific standard, or the one with the highest level of requirement.
    - If applicable, justification of the equivalence between the used reference and the applicable standard.

- Personnel qualifications:
    - Evidence for qualification of personnel performing the biological evaluation
    - Evidence for qualification of personnel performing toxicological risk assessments / applying ISO 10993-17; if applicable.

2. **<u>Formulation, description, manufacturing and use of the medical device</u>**

- Description of medical device formulation or medical device family under evaluation, if applicable.
- Description of the expected and intended biological effect, if applicable.
- Manufacturing of the medical device: Raw materials, packaging, sterilisation, manufacturing methods, including any additives and processing aids, cleaning agents and device contacting materials.
- Use of the medical device in the target population, including the claimed clinical performance, lifetime, shelf-life and storage conditions, reprocessing (if any), worst-case quantity and typical quantity of simultaneously applied devices per patient and treatment.
- Interactions with other medical devices or medicines which contact the device during clinical use.
- Reasonably foreseeable misuse.

Verify the consistency between the information, contained in the biological evaluation presented and the technical documentation.

3. **<u>Categorisation of the medical device: nature and duration of contact</u>**

- Nature of the contact with the human body.
- Duration of the contact with the human body including consideration of cumulative contact duration, if any.

4. **<u>Identification of potential biological risks of the medical device / possible biological hazards</u>**

- Parameters associated with the nature and duration of contact of the device which are to be evaluated under the assessment of the biological risk.

- Biological hazards identified via the material characterisation (section 5) which are to be evaluated under the assessment of the biological risk including risks associated with the physical configuration of the device.
- Impact of manufacturing processes on materials of construction (e.g. passivation, laser marking, sterilisation).
- Interactions with other medical devices or medicines which contact the device, which can transfer constituents to or impact the physical characteristics of tissue-contacting components of the medical device.
- Changes in the characteristics of the finished medical device over its life cycle.

5. Physical and chemical information for biological risk analysis / medical device characterisation

- Evidence for a thorough and completed chemical characterisation of the device according to ISO 10993-1 and -18, based on existing data (e.g., literature, material data sheets, existing tests) and, where required, newly generated data (e.g., new analytical tests). The characterisation shall address substances that the human body can be exposed to, *inter alia* chemical constituents in the materials as well as manufacturing residues or additives.
- For any analytical testing (e.g., extractable & leachable testing) performed according to ISO 10993-18:
    - Copies of test reports.
    - Justification of the selection of the test article (as being representative of the final device) and relevance of the tests performed (e.g., extraction parameters, selected analytical methods).
    - Information and justification of reporting threshold.
    - Evidence of the ISO/IEC 17025 accreditation or equivalence of the testing laboratory, valid at the time of testing.
    - Results of the tests performed.
- Where relevant, information on physical properties of the device (e.g., surface properties, particles).
- Where relevant, information on changed chemical and/or physical properties of the final device due to impact during the device lifetime (e.g., storage, transport, reprocessing, (re-)use).
- Where the potential of degradation exists, determine the presence and the nature of degradation products according to ISO 10993-9, and then 10993-13, 10993-14 and 10993-15, depending on the material considered, the fate of degradation products in the human body and the degradation time.
- Presence of a report dated and signed by the competent reviewers, along with the articles used and data relating to the substances.

6. Evaluation of available data and decision on biological testing program.

- Gathering and evaluation of all available data (e.g., from literature, chemical/physical characterisation, pre-clinical and clinical data).
- Identify biological hazards, hazardous situations and potential biological harms.
- Where needed, performance of a toxicological risk assessment by competent personnel according to ISO 10993-17 on the results from the chemical characterisation (section 5), with traceable safety conclusions, e.g., margins of safety (MOS) derivations.
- Determine if the available information is sufficient either to demonstrate biological equivalence or if additional data is required for biological risk estimation.
- Justification on the need, or not, to perform biological evaluation tests to respond to the risks previously identified (section 4) which cannot be controlled by the available data. Biological testing is not needed where information from available data is sufficient to conduct biological risk analysis and conclude there are no biological concerns. Testing is needed for those biological effects that could not have been

addressed through this very first step.

- Determination of the testing program, under consideration of animal welfare requirements.
- Reports and relevance of the tests performed.
- For each test defined in the testing program, the following information must be documented in a report:
    - Description of the test method used.
    - Standard applied.
    - Competence of the testing laboratory.
    - Justification of the test article selection as being representative of the medical device.
    - Test conditions.
    - Results obtained.
    - Evidence of the ISO/IEC 17025 accreditation or GLP certificate, including evidence that the tests conducted have been within the accredited scope at the time of testing.
- Perform biological risk estimation, risk evaluation and (if applicable) risk control measures.

7. Overall analysis of the results

- Overall evaluation to demonstrate the control of all potential risks at an acceptable level and the benefit to health from the use of the device as intended by the manufacturer, outweighing probable risks of injury or illness from such use.

- Documented evidence, e.g., Biological Evaluation Report, containing the overall safety conclusion as well as all relevant data from the previous sections (1-6) or at least an unambiguous reference to these data. Note: Applied standards may contain additional documentation requirements (e.g. ISO 7405 or ISO 18652).

- Reference to the risk management file, allowing the tracking of the analysis and the control of the biological hazards.

- Reference to the data collected as part of the Post-Market Surveillance (PMS) allowing the verification of their consideration in the biological risk assessment report

6.1.2 Software & Software Validation (Including Cyber Security)

General Overview

- This section offers a consolidated overview of the complete technical documentation requirements. It summarises key information already discussed in previous sections, aiming for brevity. The technical documentation requirements detailed earlier are relevant for SaMD, MDSW and SIMD.

- A clear statement and documented rationale as to why the product is a Medical Device is required.

  Based on the standard used for compliance, a standards compliance checklist to the

  requirements
- based on the software's risk category is recommended. Direct references to where in the technical file the evidence of meeting the requirements of the chosen standard is located should be present in any compliance checklist presented.

- If a different standard has been used than that of the harmonised version(s), then a detailed document should be provided that explains how the requirements of the harmonised version have been met or exceeded should be provided along with the evidence.

- The Software safety classification (see EN IEC 62304) should be provided and the justification for it should be clearly identified in the technical file. The software version under application should be clearly identified in the application.

- A software traceability matrix that contains traceable sources to requirements (risk, regulatory performance etc.) and in turn the identification of the protocols reports and test data documents relating to their verification and validation test evidence are beneficial to the assessment. As stated previously, these documents should also be submitted in the technical documentation.

- The software standards applied to the device should also be identified in the technical documentation, provide evidence of consideration of all related harmonised and non-harmonised /SOTA software standards / guidance(s).

Note: Some documentation may or may not be required per the standards based on software system/module/item risk classification.

Note: Medical Devices containing artificial intelligence may be placed on the EU market considering that appropriate conformity assessment procedure(s) have been conducted according to MDR/IVDR and horizontal requirements of the AI Regulation as becoming applicable. Team NB and the German Notified Body alliance have produced a questionnaire that manufactures of AI based devices may use as a self-assessment tool and contains specific text in relation to Validation that may be submitted in the technical file. The document, "Artificial Intelligence in Medical Devices Questionnaire" can be found on the Team NB website.

Software V&V

Common required documentation

Across the notified bodies selected, the following common documented evidence is required at a minimum in the technical document. Please note that this list is dependent on the software risk classification of the device under application. All required activities of the chosen standard for compliance should be demonstrated in the file.

Software development plan

The software development plan should be included and relevant procedures/ description which communicate the software development process and the lifecycle requirements. This should be in conjunction with the system development plan if applicable.

The documentation should provide information describing the development environment used (tools, elements, settings, etc.). As per the requirements of Annex II 3(b), environment settings/configuration parameters that are used for design, manufacturing and final product testing should be included.

Software requirements analysis

The software requirements analysis should be provided - this should include but is not limited to:

- Functional and non-functional (timing, stress language scalability, etc.) requirements.
- Requirements derived from potential software defects and information derived from previous designs.
- Requirements relating to the use of the device e.g. installation.
- Evidence that the requirements analysis considered MDR Annex II 17.4, especially hardware requirements, IT network characteristics (if applicable), and security requirements in relation to access control and unauthorised access.
- Evidence in the documentation information relating to the functionalities, capabilities, input data, output data, system interfaces, alarms, security requirements, cybersecurity requirements, user interface requirements, database requirements, installation requirements, requirements related to methods of operation and maintenance, regulatory requirements, etc.

Software architectural design

The architecture design should be provided, it is acknowledged that it can have graphical representations (UML, class diagrams, blocks etc.) but it should demonstrate how the requirements are allocated to software items that make up the overall software system. The architectural design should consider the internal and external interfaces of the software, the functional and performance requirement of SOUP and its additional hardware and software requirements. Depending on the risk class, it may be required to include segregation measures for risk control purposes, these should also be included here.

A documented SOUP list in tabular form should be submitted, this includes libraries, that clearly indicates Name, Version, Manufacturer of the SOUP and Functional and performance requirements for the SOUP, or reference to said requirements, where applicable.

Software detailed design

For Class B & C risk-based devices, a further refinement of the software architecture is required. A clear identification of the software units that are derived from software items should be provided. This should contain the design data for each software unit and any interfaces between the units and any external components. Details should be provided on the expected inputs and outputs for each software unit.

Verification and Validation

- All plans, protocols, reports and test data relating to verification and validation testing performed in-house and or in simulated use or actual use environment must be submitted.
- Documentation detailing the test environment should also be included in the application.
- Clearly identify where automated testing has been used in verification activities and include the test scripts and test log results in an organised manner in the documentation.
- System level test plans/protocols and repots should be provided.
- Evidence that the different hardware and, where applicable, the different operating systems have been verified/validated should be clearly identified and supplied by the manufacturer.
- If the software is for use with mobile platforms, information demonstrating compliance with GSPR
- 17.3 should be provided.
- The standards used for the validation of standalone software should be clearly presented and the required validation documentation provided.
- Traceability matrices(s) between software testing and specifications (system specifications/system verification, unit specifications/unit verification, etc.) should be provided.
- Evidence of the verification of SOUP items should be included.
- In addition to the individual reports, it can also be beneficial to submit an overall Verification and

Validation summary report that identifies the following:

- The software version.
- A summary of test results.
- Details on any errata or unresolved anomalies, including evidence and a risk rationale as to why these are acceptable.
- Conclusion on acceptability.
- Details on the roles and functions approving the summary.

Software release

- Include the list of known residual anomalies. The following information on each remaining anomaly should be included:
  - Unique Identifier.
  - Brief description of the issue.
  - Severity/Risk Level.

- Justification for why it is acceptable to release the software with the anomaly.

- Evidence in the technical file should also include evidence demonstrating how the released software was created (e.g., procedure and environment used to create the released software). The final released software version number should be clearly identified in this documentation.

- Evidence explaining how the released software is archived and how it can be reliably delivered (e.g. to the manufacturing environment or to the user of the software) should be included. Evidence that all required tasks prior to release were completed should be included in the release notes.

Software risk assessment

The manufacturer should include all software risk assessment documentation (e.g., software hazard analysis, software failure mode and effects analysis, fault tree analysis, traceability etc.).

Note: Some documentation may or may not be required per the standards, based on the software system/module/item risk classification.

Cyber security

- The documentation in relation to the secure design and ongoing maintenance of the medical device in respect to cyber security should be submitted. The manufacturer should clearly state the harmonised or SOTA standard(s) of compliance used for conformance to the relevant GSPRs.

- The manufacturer should provide evidence of a security risk management system that supports a secure development lifecycle, some examples include:

- Security risk management plan, security risk assessment and evidence of the incorporation of security risk controls as identified requirements and evidence of their subsequent verification and validation.

- The identified threats protections incorporated should align with the principles of Confidentiality, Integrity, and Availability (reference MDCG 2019-16 Guidance on Cybersecurity for medical devices).

- The manufacturer should provide the technical documentation that clearly identifies the method for identifying the ongoing monitoring of threats and vulnerabilities as well as the methodologies used e.g., STRIDE, attack surface analysis, data flows etc. Documentation should show how cybersecurity is an active part of ongoing post market surveillance of the device.

- The manufacturer should provide documented evidence for the monitoring of ongoing risks associated with SOUP vulnerabilities and their mitigation.

- Where necessary, evidence of certified/accredited penetration testing should be provided including certification details of the third party and test reports.

- Where cloud-based software providers are utilised, there should be evidence in the technical file of the assigned responsible parties for post market surveillance and the reporting of security issues.

6.1.3 Electrical Safety and Electromagnetic Compatibility (EMC)

This chapter is only relevant for electrical medical device(s). The manufacturer should provide the following documentation:

- Electrical safety test protocols & Electrical safety test reports.
    - Please provide the test protocols and reports for electrical safety testing.

- EMC test protocols & EMC test reports.
    - Please provide the test protocols and reports for EMC testing. Test protocols may be embedded as part of the test report.
- Please include:
    - Overview of tests performed.
    - For tests conducted by a test laboratory include the test reports, certificate and evidence of accreditation of the test laboratory.
    - For safety testing, please provide a description of requirements related to the periodic tests and tests after repairs (e.g. EN 62353). For in-house testing, evidence of the competency of the personnel involved is required as well as evidence of calibration of test equipment/facilities and QMS procedures.
    - MRI safety testing of the device/system (MDR Annex II Section 6.1(b)) should be included if relevant.
    - In cases where an assessment refers to an evaluation report or any company document more than 5 years old, the corresponding data must be provided and a rationale explaining why it remains applicable should be included.

Notes:

- Ensure the provided documentation clearly defines the ESSENTIAL PERFORMANCE of the device and is in line with the risk management documentation (including analysis, plan and reports). Test reports should include evaluation of data and conclusions.
- If a subset of devices has been selected for testing and this subset is intended to represent a larger range of devices, provide supporting documentation that demonstrates how the configurations that have been tested can be considered representative of the wider set of devices/configurations.
- Relevant standards are the EN 60601 series, including EN 60601-1-2 for EMC and EN 60601-1-
- and/or EN 62366 for usability as well as standards in the 80601 series (essential performance).
- When the device is designed to be used sterile, electrical testing should be performed on the sterile device.
- The safety of devices emitting ionising radiation and electrical devices in relation to these characteristics must be considered.

6.1.4 Packaging, Stability and Shelf-Life

The following information should be provided:

- Description of packaging types used - primary, secondary etc.
- Claimed shelf life and evidence, i.e. written evidence and justification with example of the label.
- Assessment of changes within packaging.
- Storage and transportation conditions.
- The standards and revision used for testing. If applicable, a gap analysis to the SOTA standard.
- If packaging/stability/shelf-life is being leveraged from another product, a detailed rationale should be provided on why this is appropriate.
- Evidence for stability after opening of the packaging, as applicable (e.g. single-patient-multiple-use devices).
- Transportation validation.
- Transport and storage validation testing must align with the environmental parameters specified in the device specification.

For sterile packaging:

- QMS ISO certificate of the packaging material supplier and Certificates/COA - for the packaging materials used to ensure the packaging is suitable for the sterilisation method used.
- QMS ISO certificate of the contract packager, if packaging process is outsourced
- Specification of the sterile barrier system (SBS) and example of the label to demonstrate how the SBS is indicated.
- Accreditation certificates for the testing facility.
- Packaging process validation and revalidation
- Protocol and report for the initial packaging process validation
- Protocol and report for the most recent packaging process validation
- If a worst-case representative packaging was used in any of the validations, provide a documented rationale for establishing similarities and identification of the worst-case configuration.
- Real time aging should be performed in parallel to the accelerated aging. If the real time aging test reports are not available, then the plan should be presented covering when the real time test will be completed.
- Protocol for the shelf-life studies covering product functionality as well as packaging integrity and labelling integrity/legibility – accelerated aging and real time aging to be provided.
- Reports for the shelf-life studies covering product functionality as well as packaging integrity and labelling integrity/legibility – accelerated aging and real time aging to be provided.
- Usability evaluation for aseptic presentation.
- IFU to evidence directions for visual inspection of the SBS for breaches of packaging integrity prior to use.

For Nonsterile packaging – if the shelf life is claimed:

- Certificates/COA - for the packaging materials used.
- Accreditation certificates for the testing facility.

- Protocol for the shelf-life studies covering product functionality – accelerated aging and real time aging to be provided.
- Reports for the shelf-life studies covering product functionality – accelerated aging and real time aging to be provided.

Transportation (transit) testing:

- Protocol/test report for transit testing covering the standard storage and shipping conditions, product functionality and packaging test post-transit testing etc.

6.1.5 Performance and Safety - Design Verification and Validations (including devices with a measuring or diagnostic function, MR Compatibility)

The manufacturer should provide the following documentation:

- Overview of all testing performed.
- Protocol and reports with evidence of compliance with design requirements including measurement accuracy and range, output generated, stability, functions, features, dimensions, accuracies etc.
- Testing to relevant standards (e.g. EN 60601/80601 series [essential performance] for Active medical devices) should be provided if compliance to these is claimed. Protocol & report should provide the evidence for all variants/configurations of the device, should cover interconnections to accessories and parts of the device. Only the latest or harmonised versions of the applicable standards or acceptable, unless a thorough gap analysis to the latest version is provided as a justification to compliance.
- Evidence should demonstrate compliance for the environmental conditions specified for the device and for the lifetime of the device (or service periods prescribed).

- If the device is to be connected to other device(s) to operate as intended, a description of this combination/configuration including proof that it conforms to the general safety and performance requirements when connected to any such device(s) having regard to the characteristics specified by the manufacturer.
- For tests conducted by a test laboratory, include the test reports, certificate and evidence of accreditation of the test laboratory for the test conducted at the time of testing.
- For in-house testing, evidence of the competency of the personnel involved is required as well as evidence of correct test methodology, calibration of test equipment/facilities and QMS procedures.
- MRI safety test protocols and reports, together with labelling relevant for MRI Safety, as relevant for the device.

6.1.6 Usability

Please provide the protocols, data and results for usability studies.

- The following is expected when compliance to the relevant European standards (EN62366 and EN60601-1-6) is claimed: Usability engineering file, including the following information: Use specification,

Identification of user interface characteristics related to safety and potential use errors, Identification of known and foreseeable hazards and hazardous situations, Identification and description of hazard-related use scenarios, Selection of the hazard-related use scenarios for summative evaluation, User interface specification, User interface evaluation plan, User interface design and implementation, Formative evaluation and Summative evaluation.

- The usability documentation should be in line with the risk management process.

- Usability engineering should cover the device (device design, user interface, displays, controls etc.), Information provided with the device (warnings, Instruction for use, maintenance manuals, instructions for cleaning etc.), Labelling information (including warnings, contraindications, symbols etc.)

- Specific for devices intended for use by lay persons: verification the device performs appropriately for the intended purpose considering the skills and the means available to lay persons and the influence resulting from variations that can be anticipated in the layperson's technique and environment.
- Accompanying documents include a concise description of the medical device, which includes the operating principle, significant physical characteristics, significant performance characteristics and the intended user profile.

- It is recommended to include a concise description of the sequence of steps performed by the user in the TD, including relevant preparatory steps as applicable (e.g. opening of packaging, aseptic presentation). Pictures and diagrams support understanding and ease of review.

- For devices which have a Patient Implant Card, please provide evidence of the evaluation of the instructions given to health professionals to ensure that they can complete the card correctly (see MDCG 2019-8 v2).

- An identification of any requirements for mandatory user training, or a justification for why no such training is required, is expected in the usability evaluation.

- Specific for devices intended for use by lay persons: the information and instructions are considered easy to understand and apply.

6.1.7 Common Pitfalls in Pre-Clinical and Clinical Data

Biocompatibility

- No evidence for qualification of biological evaluator and/or toxicological risk assessor provided.
- No evidence for laboratory qualification / test method validation provided.
- Cumulative exposure not considered for categorisation (duration of contact).
- Incomplete identification of applicable biological effects (for example, the biological effects "Genotoxicity", "Carcinogenicity" and/or "Reproductive/developmental toxicity" are not considered for devices that are known to contain CMR substances).
- Incomplete risk assessment of the identified endpoints (for example, especially for devices which were previously certified under the Directives, due to a combination of outdated biological testing, implausible references to the clinical experience, incomplete chemical characterisation).
- Test item representativeness not justified with respect to all relevant biocompatibility influencing factors.
- No justification provided for chosen extent of chemical characterisation, especially in case no analytical testing is performed.
- Selection of extraction conditions (e.g., solvents, time, temperature) used for chemical analytical testing not justified.
- Reporting threshold in analytical chemical (E&L) testing for organic and inorganic substances not documented/justified.
- Worst-case exposure dose not considered in the toxicological risk assessment (e.g., number/quantity of simultaneously applied devices).
- Lowest body weight of the intended target population not considered in the toxicological risk assessment.
- No documentation provided which biological endpoints are intended to be covered by the toxicological risk assessment.
- No evaluation provided for impacts on biocompatibility over the lifetime of the device (for example, from storage, transport, use, reprocessing).
- No sufficient justification for acceptability provided or no proper measures taken in cases where tests indicate a risk (e.g., cytotoxic test result or MOS < 1 in the toxicological risk assessment).
- No or implausible risk assessment for particles provided.
- No gap and impact assessment provided to demonstrate validity of evaluation/test when performed according to outdated standard.
- Unclear strategy for evaluation of changes.
- Post market surveillance activities do not address biological risks/are not suitable to monitor biological risks.

Software and Software Validation (Specifically AI/ML systems)

- Lack of transparency is the AI model (manufacturer cannot explain why the system gives the output with a given input).
- Insufficient data or poor validation of datasets: incomplete data sources, poor labelling of data, biased or unbalanced datasets.
- Clinical performance is expanded from the training datasets to new fields, excessive generalisation.
- Unbiasedness and fairness have not been validated for all patient groups.

Sterile Packaging Validation

- The packaging process validation does not test the boundaries of the process.
- Validation of only one sealing/forming/assembly machine from a pool of machines which are used in routine for sealing/forming/assembly. The stated “machine equivalence” is only a theoretical assumption based on the position that technically identical equipment performs identical without substantiation by data.
- Mechanical and/or climatic hazards to be expected during the routine transportation are not covered by the performed transport simulation.
- The worst-case constellation of product/packaging/sterilisation is not tested in the transport validation.
- In accelerated aging studies, the upper limit of the claimed storage temperature range is not covered by the calculation of the accelerated aging time.
- During accelerated aging, the relative humidity must be controlled or a rationale for exclusion of humidity control must be documented, which is frequently missed.
- Labelling integrity and readability after transport simulation as well as after aging is often not investigated.
- The applied test method is not validated at all, or the applied test method is not adequate for the packaging characteristic intended to be proven.

Design Verification and Validation

- A clear and traceable justification for the representative character of the tested samples is missing. For example, if two models of a device with different sizes are tested, it remains unclear why these specific models were chosen as the worst-case representatives for the entire device range (considering factors such as thickness, length, etc.).
- Relevant test reports are available for the manufacturer but not added to the technical documentation. If the manufacturer has identified any limitations or methodological flaws in the test reports or other documents, it is important for an efficient conformity assessment to address these issues as part of the pre-clinical evaluation. This includes explaining why the results are relevant for the demonstration of GSPR conformity, despite any limitations.
- The labelling includes claims regarding the performance of the device which are not supported by respective evidence. Provisions of existing standards may not cover all aspects, however any claim on the device must be proven.
- The technical documentation does not include a complete summary of the specifications of the finished device. Such list is crucial for understanding and assessment of the device. Technical drawings, or other documents in the TD may be referenced as appropriate.
- The technical documentation includes the test reports, but no executive summary report. It is in the interest of the efficiency of the conformity assessment procedure to provide such documents to the notified body. It should include in short, the information about the relevant tests, such as e.g. tested device, brief summary of the performed test incl. reference to the applied standard (if applicable), specifications, test results + min/max, mean, standard deviation, deviations to test protocol, together with a reference to the test report /documentation, and conclusion. The executive summary should include this information for all e.g. physical performance tests at t=0 including an overall conclusion. The same approach should be taken for an executive summary of physical performance test after aging up to shelf life, etc.
- Shortcomings in the demonstration of device stability:
    - An evaluation of whether the device is adversely affected during transport and storage is not provided.
    - The evaluation of the device stability over the time of claimed shelf life is focused only on the sterile barrier packaging but does not consider the stability of the device.
    - The stability of the device over the lifetime is not demonstrated.
- Interim time points for real-time aging and, where applicable, accelerated aging have not been defined. Nota Bene: Without a passing interim result, no shelf life can be supported (0 days), as it remains unclear at which point during storage the product may have failed.
- Furthermore, aging studies (real-time and accelerated aging) should commence simultaneously to ensure that the accelerated aging approach adequately reflects the effects of real-time aging on the device's characteristics and performance (including both the product and packaging).

6.2 Specific cases

6.2.1 Drug/Device Combination Products

- Devices incorporating as an integral part a substance, which if used separately, may be considered a medicinal product in the meaning of Directive 2001/83 EEC.
- The submission should clearly indicate whether the device utilises, or is used in conjunction with, any medicinal substances. If the device is a system and includes multiple components, then identify the components which incorporate these medicinal substances.
- Devices which incorporate medicinal substances may be subject to requirements of additional European Directives / Regulations. Additional review resources may be required, including external independent reviewers and/or Competent Authority consultation and/or a European Agency for the Evaluation of Medicinal Products (EMA).
- Please provide the following data:
    - Applicability of device including a medicinal substance(s).
      Recommendation: Explanation for classification of the product as device incorporating as an integral part an ancillary medicinal substance.
        - Intended purpose of the product.
        - Type of product, brief description and method by which the principal intended action is achieved.
        - Mechanism of action. Ancillary action to the device.
        - Indications, application of the device.
    - Justification for the use of medicinal substance(s).
      Recommendation: Background related to substance such as: How it is incorporated and the purpose for the incorporation of the medicinal substance.
    - Information and identification of medicinal substance(s).
      Recommendation: Presentation of the substance (quantitative and qualitative composition).
    - Regulatory status of similar products. Related risk assessment (either stand-alone or as a part of the risk management section) for use of medicinal product.
      Recommendation: Critical appraisal of the results of the risk assessment (either stand-alone or as a part of the risk management section for use of medicinal product). Please note that these documents should also be part of the Common Technical Document (CTD).
        - Description of production, processing, preservation, testing and handling of medicinal product.
        - Summary and test protocols/reports on the safety, quality and usefulness of the medicinal product taking account of the intended purpose of the device.

- Validation method and reports in the manufacturing process.

- Preclinical and biocompatibility data.

- Stability tests.

- Clinical Data (CER)
  - Clinical Evaluation of Literature data, including references.

  - Clinical pharmacokinetic testing.

  - Additional clinical investigation confirming the safety and usefulness (in accordance with EN ISO 14155).

- Usefulness: Evaluation of the usefulness in relation to the safety of the medicinal substance as part of the medical device considering the intended purpose of the device.
  Recommendation: The usefulness of the ancillary medicinal substance incorporated in the medical device should be addressed by clinical evaluation or by cross-reference to other sections of the dossier, as applicable.

For the Medicinal substance:

Recommendation: CTD including Modules 1-5.

To perform their assessment, the Competent Authorities (CA) prefer the documentation to follow the CTD structure [i.e., Non-eCTD electronic Submission (NeeS)]. Presentation of the data in line with CTD principles will facilitate an efficient assessment by the selected CA. A NeeS guidance document can be found on the eSubmission website. A CTD folder structure template is available for download on the ICH web site (note that this template lacks Module 1, which you will have to create yourself, preferably in line with the “File-Folder Structure & Names” tab in the EU NeeS Validation Criteria document). All study reports/literature references (full text) should be included in the documentation.

The available applicable guidance on the content of the CTD should be taken into consideration when collating the dossier. Also note that different Competent Authorities may have slightly different requirements, and the specific advice may be available on their websites and should be taken into consideration.

6.2.2 Human Origin Matter

Devices manufactured utilising derivatives of tissues or cells of human origin which are non-viable or rendered non-viable according to GSPR 13.1.

The submission should clearly indicate whether the device utilises or contains any human-based products. If the device is a system and includes multiple components, then identify the components which incorporate or utilise these substances.

Manufacturing subcontractors and sub-sub suppliers should be consulted, if appropriate, to establish if any such substances are used during manufacture, even if they do not feature in the final device.

Devices which incorporate human-derived substances may be subject to requirements of additional European Directives / Regulations especially **REGULATION (EU) 2024/1938**. Additional review resources may be required, including external independent reviewers and/or Competent Authority consultation and/or a European Agency for the Evaluation of Medicinal Products (EMA). In case the human tissue derivative is a medicinal product, the section for Drug Device Combination products also applies.

Devices may contain human origin material in the following cases:

1. When they are manufactured utilising derivatives of tissues or cells of human origin which are non-viable or are rendered non-viable.

2. When they incorporate a medicinal substance with ancillary function, which includes a human blood or plasma derivative.

In the 1st case, the scientific opinion of one of the competent authorities designated by the Member States, as described in MDR, Annex IX, section 5.3 may be required.

In the 2nd case, the opinion of EMA, as described in MDR, Annex IX, section 5.2 may be required.

Please provide the following data:

The provided data, apart from the relevant MDR sections, needs to demonstrate compliance with Directives 2002/98/EC (applies to human blood and blood components) or 2004/23/EC (applies to tissues or cells of human origin) until 07.08.2027 (depending on the used human origin material) and, after that date, with Regulation 2024/1938 (substances of human origin), which applies to all materials of human origin.

- Applicability of human origin material.
- Justification for the use of human tissue material based on a risk-benefit analysis demonstrating the usefulness of the human origin material incorporation.
- Explanation / justification of use of human origin material in comparison with alternative products.
- Description of the method which renders the human material non-viable.
- Identification of human origin material and/or composition for all components including coatings and surface treatments.
- Quantity of material in one device, number of treatments possible, route of administration.
- Information on the nature of the human starting tissue.
- Information regarding donation (sourcing, collection and testing) and procurement. This formulation is more accurate since for human origin the term donation is important.
- Information about the traceability of the human origin material.
- Information about the in-process controls of the manufacturing processes focusing on the safety of the material.
- Specifications of the human origin material.
- Microbiological safety (in addition to the point regarding viruses and transmissible agents).
- Shelf life & stability data of the material.
- Human origin material related risk assessment including microbial including parasites safety, virus and prion safety (either stand-alone or as a part of the risk management section).
- Description of sourcing, processing, preservation, testing and handling of human origin materials or their derivatives including information of the individual donors or the human cell bank development and establishing.

- Summary and test protocols/reports on the safety, quality and usefulness of the derivatives of the human tissues or cells, considering the intended purpose of the device.
- Validation method and reports of elimination or viral inactivation in the manufacturing process including possible inactivation / elimination processes regarding prions, as CJD and other TSEs are applicable for human tissues in general.
- Copy of labels and IFU submitted in Section 2, including relevant information related to the derivatives of the human tissues or cells utilised or contained in the device as per MDR Annex I GSPR 23.2 and GSPR 23.4(s).

6.2.3 Animal Origin Matter

- Devices manufactured utilising tissue or cells of animal origin or their derivatives, which are non-viable or rendered non-viable, according to MDR Annex I GSPR 13.2.
- The submission should clearly indicate whether the device is manufactured utilising any animal-based material/ substance and specify the type of the material/substance used including the animal species from which the material is sourced. Note: GSPR 13.2 is also applicable if the animal-based material/ substance is not a (functional) part of the final device but only utilised during manufacturing.
- If the device is a system and includes multiple components, then identify the components which incorporate or utilise these substances.
- Manufacturing subcontractors should be consulted, if appropriate, to establish if any such substances are used during manufacture, even if they do not feature in the final device. The manufacturer should request evidence of compliance to EN ISO 22442 series or EU 722/2012 or for any applicable exclusions (e.g., tallow species and processing method utilised) from the subcontractor.
- If the device is manufactured utilising any animal-based material/substance, specify the type of the material/substance used including the animal species from which the material is sourced. **Note**: GSPR
- 13.2 is also applicable if the animal-based material/ substance is no (functional) part of the final device but only utilised during manufacturing.

Please provide the following data:

Starting animal material

- Nature of starting tissue (e.g. tendon).
- Information on Tissue infectivity as per latest edition of “WHO Tables on Tissue Infectivity
- Distribution in transmissible Spongioform Encephalopathies” (for material from TSE susceptible species only).
- Animal species.
- Animal age.
- Evidence for veterinary controls appropriate for the animal species.
- Geographical sources including BSE status of source country as per Commission Decision 2007/453/EC (latest amendment; for material from TSE susceptible species only).
- EDQM Certificate (for material from TSE susceptible species only).

Animal material specifications

- Quantity of material in one device, number of treatments possible, route of administration.

Supply chain

- List of used slaughterhouse(s).
- List of (sub-tier) supplier(s).
- Technical Agreements with the supplier(s) of the animal material.
- Description of sourcing processes including rearing (where deemed necessary), slaughtering, transport and handling of the animal material at the slaughterhouse(s) and (sub-tier) supplier(s) with special focus on measures implemented to avoid cross-contamination between animals/species/tissues.
- Description of the processing steps at (sub-tier) supplier and/or manufacturer level with special focus on measures implemented to avoid cross-contamination and process steps with transmissible agents' inactivation or elimination capacity.
- Information on control over the supply chain (audits and further controls).

Description of the traceability system

Risk management documents in relation to utilisation of animal materials and in compliance to regulatory requirements such as Commission Regulation (EU) No. 722/2012 Annex I and EN ISO 22442-1.

PMS system to collect and evaluate production and post-production information regarding changes which may affect the assessment of the suitability of the applied processing steps.

- Literature review for zoonoses
- Literature review in relation to the TSE risk estimation (for material from TSE susceptible species only)

Justification for the use of animal tissue considering the clinical benefit of the device, the potential residual risk of the device and suitable alternatives.

Evidence for safety with regards to transmissible agents

- Identification of animal origin material, including TSE risk category according to WHO definition.
- Identification of process steps with virus and/or TSE inactivation or elimination capacity Note: only if the device does not withstand those rigorous processes, it is acceptable to omit them; a justification is required in these cases.
- An estimate of the TSE risk arising from the use of the product, considering the likelihood of contamination of the product, the nature and duration of patient exposure.
- Literature review in compliance with EN ISO 22442-3.
- Validation study protocol and report from a qualified laboratory covering i.e.
  - Selected model viruses/TSE agents
  - Information on scaling down
  - Virus/TSE log10 reduction capacity
  - Conclusion
- In case no validation study was performed, justification is required.
- Final report evaluating the overall virus/TSE risks.
- Summary and test protocols/reports on the safety, quality and usefulness of the tissues and

cells, considering the intended purpose of the device.
- Validation method and reports of elimination or viral inactivation in the manufacturing process. TSE inactivation / elimination is applicable for the processes. At the very least, a respective literature review for the entire processes should be applied, see EU 722/2012. An exceptional case is if the device does not withstand rigorous inactivation / elimination processes.
- Description of the avoidance of cross contamination during manufacturing steps up to the final packaged device and the measures taken; the amount of pooling, e.g., for biological heart valves, should be defined in case of TSE relevant material.
- Evidence on compliance with EU 722/2012 in case TSE relevant material is used.
- Copy of labels and IFU submitted in Section 2 including relevant information related to the animal tissues or cells or derivatives utilised or contained in the device as per GSPR 23.2 and GSPR 23.4(s).

6.2.4 Biological Origin Matter

For devices manufactured utilising non-viable biological substances other than those referred to in Sections 6.2.2 and 6.2.3, please provide the following data:

- Identification of non-viable biological substances utilised and the components where they are used. Include list of used raw materials (e.g. culture media, water quality, etc.)
- Characterisation and evidence for suitability of used materials (including the MCB)-e.g. CoA, etc.
- List of material suppliers, producers, and their possible certifications.
- Methods for identification of microbial production strain and for strain maintenance in master cell bank, working cell bank and production cell bank should be defined.
- Description of manufacturing processes including upstream (fermentation process, in-process control parameters, etc.) and downstream (purification steps, filtration steps, acceptance criteria for final product, etc.).
- Measures against cross-contamination during manufacturing and storage of the cell banks and the product.
- Description of preservation, testing and handling of those substances, sourcing, waste disposal chain, considering the composition of the master call bank, working cell bank, fermentation and media thereof.
- Justification that the materials used are safe for their intended use, for patients, users, and where applicable, other persons. (Note: this is assessed within the manufacturer's risk analysis).
- Safety regarding viruses and other transmissible agents using appropriate methods of sourcing.
- Microbiological safety (addition to point regarding viruses and transmissible agents).
- Validation report for elimination or inactivation during the manufacturing process.
- Consideration of fermentation / production residuals in the purified bulk substance, consideration of cell debris and residuals (DNA, RNA residuals) in the final purified bulk substance, including exotoxins released by bacterial strain.
- Shelf-life and stability data of the biological substance/material/product.
- Risk analysis of the manufacturer concerning use of the biological origin material and the risks stated above.

6.2.5 Substances absorbed or locally dispersed

Devices composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body to achieve their intended purpose (Rule 21, MDR Annex VIII).

MDR Annex I, GSPR 12.2 requires for devices that are composed of such substances to consider the relevant requirements of Directive 2001/83/EC in relation to absorption, distribution, metabolism, excretion (commonly referred to as ADME profile), local tolerance, toxicity, interaction with other devices, medicinal products or other substances and potential for adverse reactions.

Devices that are composed of such substances may be subject to requirements of additional European Directives / Regulations. Additional review resources may be required, including external independent reviewers and/or Competent Authority consultation and/or a European Agency for the Evaluation of Medicinal Products (EMA).

Please provide the following data:

- Applicability of such substances that are systemically absorbed or locally dispersed.
- Identification of such substances that are systemically absorbed by or locally dispersed in the human body.
- Address the specific aspects related to absorption, distribution, metabolism and excretion tests, toxicity (ADMET).
- In general, for devices consisting of substances in relation to Rule 21, tests for product characterisation, for proper qualification as a medical device (mechanism of action) and for establishing the right classification according to Rule 21 are deemed necessary.

- Information and/or test data related to these requirements should be included in the Technical Documentation. If evidence is based on published literature, manufacturers should rationalise the applicability of such literature data to their own device considering the nature of their device, intended purpose, contact with various body tissues and other substances, pertinence with the route of administration, the target population, and its associated medical conditions etc.
- Test protocols and reports for determining the absorption, distribution, metabolism, excretion of those substances.
- Test protocols and reports for determining the local tolerance of those substances (refer to biocompatibility).
- Test protocols and reports for determining the possible interactions of those substances, or of their products of metabolism in the human body, with other devices, medicinal products, or other substances.
- Test protocols and reports for determining the 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 (refer to biocompatibility)

- Justification in case above mentioned studies on absorbable or locally dispersed materials are not performed/provided. Please add a scientific based justification in case related tests on absorbable or locally dispersed materials are not performed/provided.

Furthermore, the TD should contain complete, clear and coherent information about the MD and substances, such as:

- consistency in terms of name, pseudonyms, chemical nomenclature and role of the substances in all documents;
- available analytical and safety data, from external suppliers (e.g.; Technical Data Sheet (TDS) and Material Safety Data Sheet (MSDS));
- reported formulation study: rationales and studies to support the selected concentrations (e.g.; substances concentration for the considered route of administration given in bibliography; rationale for the substances concentration in the finished product; role and mechanism of the selected substances in the final formulation);

Please provide robust and reproducible information, to guarantee:

1) protocols and reports written in a readable and solid manner (e.g.; not redundant, but linked to analytical guidelines, or to the databases of the analytical methods; etc.)
2) validated and focused analytical methods, used to analyse MD and substances;

("Focused" means the method must be validated considering: the site of clinical application, the environmental matrix, any other elements that may generate perturbations and/or matrix effects on the analysis).

Please consider the requirements indicated in ISO 17025 for the test laboratory qualification.

Addressing this topic, manufacturers can refer to and/or consider internationally recognized databases, where suitable information on mechanisms of action, pharmacological effects, clinical sites of application, concentrations to be used and/or critical limits, toxicology, etc., can be found.

European Agency for Medicinal Products EMA (including EU monographs on Herbal Medicinal Products EMA monographs) https://www.ema.europa.eu/en/medicines

6.2.6 Hazardous substances, CMR, endocrine disrupting substances

Devices containing CMR or endocrine-disrupting substances referred to in GSPR 10.4.1 of MDR Annex I: GSPRs 10.4.1 - 10.4.5 describe specific requirements for devices that contain substances which are carcinogenic, mutagenic or toxic to reproduction and substances having endocrine-disrupting properties. Information and/or test data related to these requirements should be included in the Technical Documentation. This information may be provided either as a stand-alone section or incorporated into other relevant sections such as biocompatibility, labelling etc.

Please provide the following data:

- Applicability of CMR substances (carcinogenic, mutagenic or toxic to reproduction) substances having endocrine disrupting properties in a concentration of > 0.1% w/w acc. to GSPR 10.4.1.
- List substances in a concentration of > 0.1% w/w.
- If evidence is based on published literature, manufacturers should rationalise the applicability of such literature data to their own device considering the nature of their device, intended purpose, contact with various body tissues and other substances etc. Or, planning and overview as well as reports of tests performed, evaluation of data and test results. Evidence could also include safety datasheets or signed declarations from the vendors.
- Justification according to GSPR 10.4.2 for use of substances in a concentration of > 0.1% w/w including:
    - An analysis and estimation of potential patient or user exposure to the substance.
    - An analysis of possible alternative substances, materials or designs, including, when available, information about independent research, peer reviewed studies, scientific opinions from relevant Scientific Committees and an analysis of the availability of such alternatives.
    - Argumentation because possible substance and/ or material substitutes or design changes, if available, are inappropriate to maintain the functionality, performance and the benefit-risk ratios of the product; including considering if the intended use of such devices includes treatment of children or treatment of pregnant or nursing women or treatment of other patient groups considered particularly vulnerable to such substances and / or materials.
    - Where applicable and available, the latest relevant Scientific Committee guidelines (as per GSPR 10.4.3 and 10.4.4).
- Copy of labelling including the list of such substances in a concentration of > 0.1% w/w on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging.
- Copy of IFU: If the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials, information on residual risks for those patient groups and, if applicable, on appropriate precautionary measures is given in the instructions for use.

Note: a process to identify and regularly update CMR or endocrine disrupting substances using relevant standards: CLP regulation + ATPs (Adaption to Technical Progress), ECHA webpage, REACH, SVCH list, Commission Delegated Regulation (EU) 2017/2100, SCHEER guideline refers to ECHA's endocrine disruptor (ED) assessment list and ECHA list for Biocidal Products Committee opinions on active substances will be part of an audit.

6.2.7 Sterilisation validation of medical devices including devices that are intended to be (re-)processed before use (reusable or intended to be sterilised by the customer)

Sterilisation

Product supplied Sterile - Sterilisation

1- Confirm the applied (harmonised) standard(s) and claimed SAL used for the selected sterilisation method i.e.
   - ETO-EN ISO 11135.
   - Irradiation by Gamma/E beam -EN ISO 11137-1, EN ISO 11137-2, EN ISO 13004.
   - Steam- EN ISO 17665-1.
   - Aseptic processing – EN ISO 13408 series.
   - Others.

2- Name and address of the sterilisation facility and relevant documentation – if outsourced:

- Technical agreement with sub-contractors – device manufacturer and sterilisation company.
- Valid QMS ISO certificate confirming the sterilisation facility complies to perform sterilisation for relevant standard.

3- If performed in-house – IQ, OQ, PQ data.

4- Sterilisation parameters.

5- Example of IFU and Label.

6- Sterilisation validation and revalidation:
   - Procedure confirming the sterilisation controls i.e. validation, revalidation, routine release and frequency as per relevant sterilisation standard used.
   - Procedure confirming bioburden test controls, endotoxin test controls, clean environment test controls and frequency.
   - Product family assessment and selection of the product for sterilisation validation i.e. PCD.
   - Protocol and report for the original sterilisation validation - covering all data.
   - Protocol and report for the most recent sterilisation re-validation sterilisation validation - covering all data.
   - Sterility testing - validation of test method as per EN ISO 11737-2 and results.
   - Bioburden testing - validation of test method as per EN ISO 11737-1 and -2 most recent bioburden results.
   - Endotoxin test validation and two most recent results.
   - Results of environmental monitoring and validation of the controlled environment - clean room microbial monitoring and physical clean room validation - most recent results.
   - Annual or at least most recent sterilisation assessment to confirm changes within the sterilisation process, manufacturing process, packaging changes etc.
   - A statement that the product functionality tests were performed after representative or worst-case sterilisation conditions.
   - Additional information based on the sterilisation method used:
     Ethylene Oxide (ETO) documents to include:
       - PCD, IPCD, EPCD information, ETO residuals report, including a statement whether paediatric use applies and how this was considered regarding ETO limits, information on ETO gas specification and certificate, biological indicators and certificate.

Radiation documents to include:

- Calibration details/certificates of the dosimeters used.
- Dose setting/dose substantiation Method 1, VDmax. Method 2 original validation report and if conducted for a product family, rationale for the device being in the family.
- Dose audit data trend and two most recent dose audit reports, if frequency in dose audits reduced then a justification for reduction.
- Dose mapping for min-max dose range.

Steam – PCD, Biological indicators and certificate.

Aseptic – Justification for use of this method, Process simulation Original Validation reports, Media fills Initial PQ, Media fill Periodic Performance Requalification PRQ reports, as per applicable standards, Media Selection & Growth Support, certificate for the filter used and Validation of Fluid-Specific Microbial Retention by Filters.

Product Supplied nonsterile and to be sterilised by end user:

These products include both products intended for single use and to be processed before use, and reusable products which undergo reprocessing between their uses.

Please provide:

- Latest revision of IFU (or/and instruction of reprocessing if applicable) and Label Including:
- Sterilisation parameters and other processing parameters for cleaning and disinfection, if applicable.
- Validation of each claim identified in the IFU (i.e. washing, cleaning, disinfection, repackaging, sterilisation).
- Assessment of changes.
- Bioburden data if cleaning and disinfection by the user is not possible/foreseen.
- Residual tests if applicable for the disinfectants used.
- Accumulation of process residuals (cleaning/disinfection agents or even sterilizing agents such as ETO should be part of life cycle validation).
- If applicable, product family assessment and selection of the representative product for each validation.
- Reference to the section of the risk management file related to (re-)processing (as per EN ISO 17664-1, Chapter 5).
- Reference to the data collected as part of the Post-Market Surveillance (PMS) related to reprocessing.
- If applicable, rationale for the contamination and acceptance criteria based on risk analysis.
- If applicable, lifecycle test data including functional testing and biological evaluation under consideration of the end of lifecycle.
- For tests conducted by a test laboratory: test reports and evidence of accreditation of the test laboratory.
- For in-house testing: test method validation, evidence of the competency of the personnel involved is required as well as evidence of calibration of test equipment/facilities and QMS procedures.

Reusability/ Reprocessing - Class Ir - Reusable surgical instruments:

In line with MDR Article 52(7c), notified body involvement is required only for aspects to the aspects relating to the reuse of the device, in particular cleaning, disinfection, sterilisation, maintenance and functional testing and the related instructions for use.

Please provide:

- Name and description of the device.
- UDI.
- Intended use and classification.
- Declaration of conformity.
- GSPRs.
- Labelling and IFU.
- Applicable standards.
- Design, manufacturing and bench testing.
- Product functionality test covering maximum number of reuses as per IFU.
- If applicable - packaging, shelf-life and lifetime validations as per packaging shelf-life sections depends on product sold sterile or non-sterile or to be sterilised by end user.
- Disinfectant, cleaning, sterilisation - Protocol and reports for validations as per parameters listed within IFU.
- Reusable aspects only for below:
    - Risk assessment.
    - PMS.
    - Vigilance reports.
    - Complaints.
    - Biological safety.
    - Clinical evaluation.

6.2.8 Common Pitfalls in Devices Incorporating Medicinal and Biological Materials

Drug/device combination products

For medicinal substances approved in the EU included into the combination product:

- Reference to the drug master file (DMF) of the medicinal substance is not provided, including information on the competent authority, which approved the DMF. The related Letter of Access for DMF is not provided.
- The requirements of the competent authority regarding the drug dossier necessary for the consultation procedure are not considered.
- Pre-submission meetings with the relevant competent authorities are not considered.

Devices containing materials of animal origin material

- GSPR 13.2 is considered non-applicable in the case of devices that are manufactured with tallow derivates as a manufacturing aid, serving as a lubricant and having no (main) functional part in the final device.
- No information on traceability or about processing of the material is provided in case a manufacturing aid based on animal origin, e.g. tallow derivatives, is purchased from a supplier. However, the manufacturer must provide information regarding the supply chain and provide full evidence about the compliance of the material used, including evidence in case the tallow derivative was processed under a rigorous process as laid down in regulation (EU) 722/2012.

Substances absorbed or locally dispersed substances

- Thoroughly evaluate if MDS 1008 applies for the device under assessment and justify the decision accordingly.
- All MDS 1008 related characteristics which are stability-indicating need to be assessed after shelf-life. For example, ADMET characteristics and absorption kinetics could be affected during storage of the device, as per requirement of GSPR 6.
- Thoroughly evaluate the MDS 1008 relevant GSPRs if they are applicable for the device under assessment, considering the device's Intended Use. Provide a justification in case a GSPR is deemed to be non-applicable.
- Provide a justification in the absence of relevant MDS 1008 related studies, according to MDR Annex II Section 6.2c.
- If literature data of an equivalent device is to be used, thoroughly demonstrate the equivalence to the device under assessment, considering all relevant aspects such as technical, biological, and clinical characteristics.
- Especially for substance-based devices, a lot of times claims are made, which indicate that substances are included, which may be considered medicinal products. In such cases the rationale for the qualification of the product as medical device must be scientific based, traceable and robust (MDCG 2022-5).
- If the product qualifies as a medical device containing substances, which may be considered a medicinal product, the correct classification under Rule 14, i.e. Class III, must be applied. The resulting conformity assessment path considering that the device contains substance(s), which may be considered a medicinal product becomes relevant, i.e. consultation according to MDR Annex IX, 5.2.
- In case there is disagreement, clarification on the correct conformity assessment path under consideration of MDR Article 51 (2) is needed.

(Re-)processing

- The manufacturer did not evaluate the national and European requirements for (re-)processing (e.g. Hygiene Requirements for the Reprocessing of Medical Devices (KRINKO BfArM 2012, Germany), DS 2451-13: Infection control in the health care sector - Part 13: Requirements for reprocessing of reusable medical equipment (Denmark), Good practices for the sterilisation of medical devices. Revision of the recommendations on sterilization (SHC 7848 - 2006 / SHC 9256 – 2017, Belgium).
- The rationale for the selection of the worst-case product for validation could not be followed (not all critical design aspects are covered).
- No evidence for the validation of the test methods at the timepoint of testing was provided (e.g. accreditation certificate with the respective scope).
- In the risk analysis provided by the manufacturer, not all relevant points regarding reprocessing are determined (e.g. water quality of the final rinsing step).
- The instruction for (re-)processing could not be identified by date of issue or identifier of the latest revision of the instructions for re-processing.
- A specification of the maximum time between end of use and start of the initial treatment of the device could not be found in the instructions for reprocessing.
- In the instruction for (re-)processing provided by the manufacturer, no automated cleaning and/or disinfection process is specified, although the product could withstand such a process.
- The microbiological water quality (incl. endotoxin limit, if applicable) for the final rinsing is not specified in sufficient detail (the terms deionized water or contaminant-free do not describe the microbiological water quality, according to an international standard or pharmacopeia). A disinfection procedure is not specified in the instructions of (re-)processing.
- The instructions for (re-)processing do not take the processing equipment and processes commonly available to the processor in the EU into account.
- Gravity displacement procedures for moist heat sterilization are specified in the instructions for (re-)processing. However, gravity displacement procedures are not considered state of the art.
- A limitation of the number of processing cycles is not provided in the IFU. However, for medical devices with critical design features such as, cavities and holes or sensitive materials an impact of repeated processing on product safety, e.g. accumulation of detergent residues or material alterations, should generally be assumed. Therefore, the number of reprocessing cycles should be limited unless such alterations are ruled out by testing.
- More than two observation time points are considered necessary to establish product safety with unlimited service lifetime for products with critical design features.
- In the provided documentation by the manufacturer, no evidence could be found that the labelling of the devices will be readable throughout the intended lifetime of the device.

6.3 Clinical Evaluation (Includes SSCP labelling)

In line with MDR Article 61 (1): *Confirmation of conformity with relevant general safety and performance requirements set out in Annex I under the normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects and of the acceptability of the benefit-risk-ratio referred to in Sections 1 and 8 of Annex I, should be based on clinical data providing sufficient clinical evidence, including where applicable relevant data as referred to in Annex III.*
The manufacturer should specify and justify the level of clinical evidence necessary to demonstrate conformity with the relevant general safety and performance requirements. That level of clinical evidence should be appropriate in view of the characteristics of the device and its intended purpose.

To that end, manufacturers should plan, conduct and document a clinical evaluation in accordance with this Article and Part A of Annex XIV.

As part of their submission, manufacturers should provide the final and approved versions of the following documents at a minimum:

Document	Class IIa and IIb Non-Implantable Devices	Class IIa and IIb Non-Implantable (Article 61.10) Devices	Class IIa and IIb Implantable Devices	Class III Non-Implantable Devices	Class III Implantable Devices
Clinical Evaluation Plan (CEP) including a clinical development plan	Yes	Yes	Yes	Yes	Yes
Clinical Evaluation Report (CER)	Yes	Yes	Yes	Yes	Yes
Literature search documents*	Yes	Yes	Yes	Yes	Yes
CVs and Declaration of conflict of Interest for persons involved in clinical evaluation	Yes	Yes	Yes	Yes	Yes
Clinical Investigation documentation per Annex XV	Yes, if applicable	Not Applicable	Yes, if applicable	Yes, if applicable	Yes, if applicable
SSCP	Not Applicable	Not Applicable	Yes	Yes	Yes
PMS Plan	Yes	Yes	Yes	Yes	Yes
PSUR	Yes, if available	Yes, if available	Yes, if available	Yes, if available	Yes, if available
PMCF Plan	Yes	Yes	Yes	Yes	Yes
PMCF Study Plan	Yes, if applicable	Typically, Not Applicable	Yes, if applicable	Yes, if applicable	Yes, if applicable
PMCF Report**	Yes, if available	Yes, if available	Yes, if available	Yes, if available	Yes, if available

*Literature search protocols and reports covering the objectives to systematically evaluate the State of Art and to find all available clinical evidence supporting the device under evaluation can be provided as stand-alone documents or included as part of CEP or CER. A full text copy of key articles included in the analysis in the CER should also be provided. A copy of other articles referenced in the CER may also be requested as part of the conformity assessment process.

**PMCF evaluation report can be provided as a stand-alone document or included as part of the CER

For additional information on specific device types please refer to the notes below:

Note 1: Where an opinion has been provided by the expert panels on the clinical strategy of the device(s) per Article 61 (2), the manufacturer should also provide a copy of the opinion and reference.

Note 2: In the case of orphan devices and devices with an orphan indication, the manufacturer must provide a justification for the orphan status, and any views expressed the European Expert Panels (if consulted). For guidance on orphan status criteria and the justification for orphan status, refer to MDCG 2024-10.

Note 3: In the case of devices which fall under Article 54 (Class III Implantable and Class IIb Active devices intended to administer and/or remove a medicinal products), the notified body must determine if any of the exemptions provided for in Article 54.2 are applicable. To facilitate this decision-making process, it would be helpful if manufacturers provide documentation to support any applicable exemptions (e.g. as applicable a description of all changes between a legacy device and the MDR-applied device).

Note 4: In the case of breakthrough (BtX) devices, the manufacturer must provide evidence of the expert panels decision regarding designation of BtX status, and any views expressed by the expert panel regarding the clinical development approach. For guidance refer to MDCG 2025-09.

Whilst not exhaustive, the following section will discuss the common pitfalls identified during the notified body assessment of the manufacturer's clinical evaluation documents.

6.3.1 Clinical Evaluation Strategy

Pitfall: The strategy chosen for clinical evaluation or the rationale for applicability of MDR Article 61 requirements, are not clearly presented in the clinical evaluation documentation.

Guidance: MDR Article 61 describes different options for gathering clinical evidence to support conformity of the device. The level of clinical evidence selected by the manufacturer is dependent on several factors including risk classification of the medical device and its regulatory status.

Based on the clinical evaluation strategy that is deemed most appropriate and as described in the clinical development plan, manufacturers have the option to generate and collect clinical data from a variety of sources including clinical investigations on the subject device or equivalent device and/or scientific literature and reports on clinical experience with the subject or equivalent device. Clinically relevant information derived from Post market surveillance (PMS) and post market clinical follow up (PMCF) activities can also provide a source of clinical data.

For higher-risk devices (Class III and Implantable) the requirement is that the clinical evaluation should, at a minimum, be based on clinical data generated by means of a properly designed clinical investigation(s) performed with the subject device. Exceptions to this rule are prescribed by Articles 61 (4-6) with further guidance provided in MDCG 2023-7.
For legacy devices, irrespective of risk classification, manufacturers may rely on the hierarchy of clinical evidence presented in MDCG 2020-6 Appendix III when justifying the sufficiency of their evidence.

For devices which are new to the market, the manufacturer must consider the need for a clinical investigation as part of its clinical development plan and provide a justification if a pre-market clinical investigation is deemed to be not required.

For devices which intend to leverage clinical data from equivalent devices, manufacturers should consider the guidance provided in MDCG 2020-5 and use the provided comparison table template for demonstration of equivalency. In the case of Class III and Implantable devices which are intending to rely on equivalence, the manufacturer should refer to MDCG 2023-7 which provides guidance on how to demonstrate sufficient level of access to the technical documentation of the equivalent device.

In the case of certain class IIa and Class IIb non-implantable devices, it may not be appropriate to demonstrate conformity based on clinical data. For these exceptional cases, manufacturers may avail of the clinical data exemption provided by Article 61.10. In this case the manufacturer must provide an adequate justification supporting its determination that clinical data are not appropriate for demonstrating conformity with the applicable GSPRs. The justification must consider the outputs of the devices risk management (e.g. residual clinical risks), the specifics of the interaction between the device and the human body including but not limited to consideration of type and duration of contact, anatomical location, novelty of the interaction etc. The justification must also consider the intended clinical performance including whether the device could influence the clinical outcome of a procedure or treatment, and any claims made by the manufacturer. If there are any clinical claims, these must be supported by clinical data rendering article 61 (10) not applicable. It is important that the manufacturer provides a robust justification with reference to supporting evidence as this will be a key focus of the notified bodies assessment. If clinical data are available for similar or equivalent devices, a clinical evaluation based on the application of article 61 (10) is unlikely to be accepted by the notified body. Further, the planning of specific PMCF activities in the post market phase is typically considered to be in direct contradiction to a statement that the generation of clinical data in the pre-market phase is inappropriate.

Note: Article 61(10) shall not be used for class III devices and implantable devices or for devices that have insufficient clinical data (lack or absence of clinical data). Per Article 61.1. the minimum expectation is that clinical data is required to support safety and performance requirements. Reliance on non-clinical data alone, including performance evaluation, bench testing, pre-clinical testing, usability assessments etc., is for exceptional cases only where there are no clinically relevant endpoints to measure in the intended patient population and sole reliance on pre-clinical data including bench testing is justified to be valid to predict the clinical performance and safety of device use.
In the case of devices that do not provide a direct clinical benefit, manufacturers should consider the role of the device in the overall procedure and its criticality to procedural success, when determining the applicability of Article 61.10. For example, clinical data may not be considered appropriate for low-risk generic surgical instruments such as scalpels and forceps. However, if a surgical instrument is

designed to be used with a specific implantable device, for example, it may be more appropriate to leverage indirect clinical data from the implant to demonstrate that the instrument does not have a negative influence/impact on the clinical outcomes (Refer to MDCG 2020-6 Section 1.1 and section 6.5a for further guidance)

6.3.2 Clinical Evaluation Plan (CEP)

Annex XIV Part A specifies the elements that must be included in the clinical evaluation plan. Manufacturers must ensure that ***all*** requirements specified in Annex XIV Part A are clearly addressed, otherwise they can expect to be challenged by the notified body.

Note: A legacy device may have a clinical evaluation plan that is different to a new device under MDR. MDCG 2020-6 Appendix II describes the expected content of a legacy device clinical evaluation plan. Whilst not explicitly stated in MDCG 2020-6, a clinical development plan is required for legacy devices, however as discussed later in this document, the level of detail will differ to that of a new medical device.

Note: For Orphan and BtX devices, manufacturers should consider the specific aspects detailed in MDCG 2024-10 Section 7.1 or MDCG 2025-09 Section 7.1, as appropriate, when developing the CEP.

The following are the **common pitfalls** identified by the notified body when assessing the **CEP**:

a) General safety and performance requirements (Annex XIV Part A, 1a – first indent)

Pitfall: GSPRs requiring clinical data are not identified or incomplete, and/or do not align with those identified in other parts of the technical documentation. Example: The sufficient accuracy, precision and stability of a device with measuring function is supported by clinical evidence from a clinical study, but GSPR 15.1 is not mentioned in the CEP.

Guidance: The manufacturer should ensure that references to GSPRs which require supporting clinical data are aligned across the technical documentation. According to MDR Article 61(1), at least GSPR 1 and 8 are required, but exceptions may apply in case of a performance-based evaluation according to MDR Art. 61(10) without clinical data. Other GSPRs which typically require clinical data include GSPR 5 and 6, however the manufacturers should consider the relevance of ***all*** Annex I GSPRs within the context of the characteristics of the specific medical device.

b) Intended purpose and Indications (Annex XIV Part A, 1a- second and third indent)

Pitfall: Intended purpose is vague or incomplete and the documentation does not clearly differentiate between the intended purpose and the indications.

Guidance: A clear, unambiguous and specific intended purpose which fulfils the definition in MDR Article 2(12) must be provided. As the intended purpose is critical for accurately determining that the device is a medical device and further the devices risk classification and clinical data requirements, it is subject to scrutiny by the notified and will be challenged if vague or incomplete.

The CEP should clearly differentiate between the indications and the intended purpose. In the absence of a MDR definition, manufacturers are directed to MDCG 2020-6 which defines indications as *"the clinical condition that is to be diagnosed, prevented, monitored, treated, alleviated, compensated for, replaced, modified or controlled by the medical device. It should be distinguished from 'intended purpose/intended use', which describes the effect of a device".* If the device does not have a specific indication, for example a steriliser or general use surgical equipment. (or contraindications), a justification should be provided.

Pitfall: Lack of consistency in the intended purpose and indications for use across the device's technical documentation.

Guidance: Manufacturers are advised to cross-check the intended purpose statement and indications for use for alignment across the technical documentation prior to submission, during the review as applicable, and in the final approved version.

c) Clinical Benefits (Annex XIV Part A, 1a- fourth and sixth indent)

Pitfall: The clinical benefit (*role of the device in improving the health of the patient or patient management or public health*) is not clearly described

Guidance: Accurately defining the clinical benefit is an important starting point in the clinical evaluation process as the MDR requires the manufacture to demonstrate that the benefits associated with use of the device outweigh the potential risks to patient safety. When defining the clinical benefits, the manufacturer should consider the role of the device in the diagnosis, monitoring, prevention, treatment, alleviation etc. of a disease, injury or disability and the subsequent positive impact. For software devices, the role of the software in the overall clinical workflow should be carefully considered.

Dependent on the clinical performance of the device, the clinical benefits may be direct or indirect. Indirect clinical benefits are typically associated with devices which enable a procedure to be performed, or a therapy to be delivered or they may enable another device to achieve its intended purpose. In these cases, whilst the device itself may not have a direct positive impact, the manufacturer should consider if the devices performance will influence the clinical outcome of the patient/procedural success.

Typically, direct clinical benefits must be supported by clinical data pertaining to the device itself or another equivalent device, whereas for indirect clinical benefits, the manufacturer may choose to rely on evidence sources such as pre-clinical data or clinical data pertaining to another device which does have a direct clinical benefit and is used together with the device under evaluation. A suitable rationale must always be provided for appropriateness of the selected data source. For further information, refer to MDCG 2020-6 Section 6.5 and MEDDEV 2.7/1 Rev 4.

Pitfall: The CEP does not clearly provide an indicative list and specification of parameters to be used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device.

Guidance: To determine acceptability of the benefit-to-risk ratio of the device, performance and safety outcomes, the methods used (e.g. objective clinical tests, validated PROMs questionnaires, etc..), and the acceptance criteria must be defined based on state of the art, including product-specific standards if available. The goal is to demonstrate that by meeting the pre-defined acceptance criteria for each performance and safety outcome, and considering the overall relation of benefit to risk, the device under evaluation is a clinically acceptable option for patients in the light of any other currently available alternatives. Notably, cost considerations, reimbursement, efficiency in health care and similar objectives are only a target for the clinical evaluation under the MDR if they are directly related to clinical benefits for patients (e.g. enabling faster diagnostic pathways may have clinical benefits in the emergency situation, e.g. in acute stroke ("time is brain"), but facilitating higher patient throughput to save costs in elective hospital situations is not a clinical benefit in the MDR definition).

Note: The acceptance criteria (or thresholds) are usually defined in the CEP, however this is not explicitly stated in the MDR; thus, it may also be acceptable to define these acceptance criteria in the CER.

Note: Depending on the intended purpose, especially for some low-risk devices, it may be difficult to determine quantitative acceptance thresholds for performance and safety. For example, a digital healthcare software application for mobile phones that allows the communication between a patient and a physician may have only indirect clinical benefits like a positive medical supply effect (ensuring structural and process improvements - See article „Digital Health and Digital Treatments: The New Reality" by Imre M, Linke J, Gernert D. Published in PM QM 2020, 22. 3, November), with the outcome parameters e.g., that a patient is informed and can participate through the respective application, which leads to detection or monitoring of a disease or side effects during a specific treatment. Parameters to determine performance and safety based on the SOTA (if a reliable SOTA is available for such a device at all) may include a high rate of patient adherence to the device and a low imbalance rate between the electronically submitted findings and the clinical findings upon direct patient contact.

d) Specification of methods and parameters (Annex XIV Part A, 1a- fifth indent)

Pitfall: The CEP does not clearly specify the methods to be used for examination of qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and side-effects

Guidance: This requirement is asking the manufacturer to describe the methods that will be used to collect information and data for the purposes of identifying clinical risks, side-effects and residual risks associated with use of the device (for example: literature search, clinical trial data, PMS data, PMCF activities, risk management), and to specify how the data will be analysed both qualitatively and quantitatively (for example: the manufacturer may choose to adopt descriptive and inferential statistics to determine safety).

e) Clinical Development Plan (CDP) (Annex XIV Part A, 1a- final indent)

Pitfall: The manufacturer does not provide a CDP for legacy devices.

Guidance: According to MDR, Annex XIV for new medical devices a CDP describing the progression from exploratory investigations through to confirmatory investigations is expected. However considering the regulatory status of legacy devices, this level of detail is not expected and rather the CDP may focus on the strategy to obtain clinical evidence in line with MDR Article 61 requirements, and the planned PMCF activities. This is also reflected in Annex II of MDCG 2020-6. If applicable, the CDP should also include a justification for any deficiencies in relation to previously conducted first-in-man studies, feasibility and pilot studies, confirmatory investigations, such as pivotal clinical investigations, noting any reference to PMCF activities that are ongoing or reference to the PMCF Plan as described in Annex XIV.

6.3.3 Clinical Evaluation Report (CER)

Per Article 61 (12): *The clinical evaluation, its results and the clinical evidence derived from it shall be documented in a clinical evaluation report as referred to in Section 4 of Annex XIV, which, except for custom-made devices, shall be part of the technical documentation referred to in Annex II relating to the device concerned.*

Note: A Clinical Evaluation Report is always required for the device, including devices where the clinical evaluation is based solely on non-clinical data.

The Clinical Evaluation Report should be written in a clear and structured manner and contain sufficient information to enable an independent body (e.g. Competent authorities responsible for notified bodies or the notified body itself) to read and understand the document.

The following information should be provided at a minimum:

- Clear and comprehensive description of the device under evaluation including all relevant particulars (e.g. all device models/variants, description of the technical and clinical differences between the models/variants, a description of the clinical purpose of design characteristics, if any accessories are required to use the device, if the device is part of a system/ procedure pack, how the device is used in the context of the clinical diagnostic/treatment pathway, the use environment, etc.…).. The description should be sufficiently detailed to facilitate ease of understanding by persons not directly involved in the design, development and manufacturer of the device. For guidance refer to MEDDEV 2.7/1 Rev 4 Appendix 3. For devices which require consultation with the CECP as per Annex IX.5.1/Article 54, the description is expected to be part of the CER. For other devices, a clear reference to existing documents in the TD, such as the CEP, may be sufficient.

- Specification of the frequency of clinical evaluation updates and provision of this rationale.

- CVs and Declaration of Interests of all individuals conducting / approving the clinical evaluation and ensure these are appropriate for the device under evaluation (e.g. including an end user of the device, e.g.

medical professional with sufficient experience in the relevant device technology).

- 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, ensuring these have been performed within appropriate timelines.

- The literature searches should include a state-of-the-art literature identifying benchmark/similar devices and where appropriate other treatment/diagnostic alternatives. This data should form part of the performance and safety objectives for the device under evaluation.

- A second literature search should be conducted on the device under evaluation (or claimed equivalent) when the device has been previously marketed. The intention of this search is to identify any favourable or unfavourable clinical data that the manufacturer does not hold.

- A third literature search may be required to identify any pre-clinical aspects, particularly where there are unanswered questions from the clinical evaluation that can be supported by pre-clinical data and scientific evidence.

If clinical investigations have been performed, the following documentation is required:

- Clinical investigation plan(s), including any amendments. A summary of the sequence of amendments, and their approval by the competent authorities, may be helpful in complex investigations. For guidance refer to MDCG 2024-3. For orphan devices, manufacturers should consider the specific considerations detailed in MDCG 2024-10 Appendix A2 when planning a clinical investigation.
- Completed clinical investigation report, signed by the principal investigator(s).
- Evidence of communication and no objections with the ethics committee.
- All regulatory approvals of the clinical investigation and amendments, if any (from all countries, including outside of EU).
- Investigator's brochure. For guidance refer to MDCG 2024-5.
- Sample of the informed consent template.

If any deviations to the protocol have been applied, then justifications/acceptance of these deviations should be provided with copies of original and changed protocols.

If a pre-market clinical investigation has been conducted, please ensure: the final report demonstrates that requirements for all safety and performance endpoints have been met; there are no open clinical investigations relevant to your devices with endpoints related to safety or performance claims; study locations that were used in the pre-market clinical investigation are identified.

When clinical investigations are conducted outside the EU: provide an analysis whether results are transferable to the European population, consider the relevance of EN ISO 14155 and whether the results are publicly available.

Statistical Analysis Plans (SAPs) - a clear description must be provided of the statistical tools,

techniques, analyses used in the design and conduct of clinical investigations, and analysis of clinical data within the overall clinical evaluation.

The rationale if clinical investigation has not been performed for Class III and implantable devices per Article 61 (7). For guidance refer to MDCG 2023-7.

Information on public registration in EUDAMED of clinical investigations conducted. In the absence of EUDAMED, refer to MDCG 2021-1.

With respect to Regulation (EU) 2017/745, including EUDAMED single registration number, when available, or a rationale if clinical investigations are not performed under Regulation (EU) 2017/745 and are not publicly registered or published. Please include information about registration in any other public study register. If the study has not been registered, please provide justification.

All Competent/Regulatory Authority correspondence (from all countries, including outside of EU).

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 in accordance with MDR Annex XIV Part A (3) and MDCG 2020-5.

Justifications for allowable differences should be presented with scientific evidence, and this evidence should be provided separately.

For Class III and implantable devices: in case of applicability of MDR Article 61(5), 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 should be provided and evidence that the equivalent device is MDR certified. In the other cases, as per MDCG 2023-7, please provide evidence for the sufficient level of access to device equivalence data.

For devices incorporating medicinal substances/ non-viable tissues / cells from animal or human origin, 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.

Note: MEDDEV 2.7/1 Rev. 4 Section A9 'Clinical evaluation report - proposed table of contents, examples of contents' provide a helpful layout on the expectations of the content of a clinical evaluation report.

Note: For Orphan devices, manufacturers should consider the specific aspects detailed in MDCG 2024-10 Appendix A1 when generating the CER

Whilst not an exhaustive list, the following are the **common pitfalls** identified by the notified body when assessing the **CER**:

a) Frequency of Updates

Pitfall: The frequency for updating the clinical evaluation is not defined or the rationale for supporting the defined frequency does not consider all relevant and foreseeable circumstances that could trigger an update

Per MDR Article 62 (11): *The clinical evaluation and its documentation shall be updated throughout the life cycle of the device concerned with clinical data obtained from the implementation of the manufacturer's PMCF plan in accordance with Part B of Annex XIV and the post-market surveillance plan referred to in Article 84.*

Guidance: The clinical evaluation must be updated throughout the life cycle of the device with clinical data from the PMS and PMCF processes, however there is no defined update schedule requirement in the regulation. The expectation is that manufacturers align the frequency of clinical evaluation updates with the guidance currently available from MEDDEV 2.7/1 Rev 4.0. Based on this guidance the clinical evaluation should be updated at a minimum:

- When the manufacturer receives PMS including PMCF information with potential to change the current evaluation.
- at least annually if the device carries significant risks or is not yet well established.
- every 2 to 5 years if the device is not expected to carry significant risks and is well established,
- For Class III and Implantable devices: an annual update should be considered.

The manufacturer is expected to justify the defined frequency for performing periodic updates of the clinical evaluation, considering factors such as:

- Whether the device carries significant risks
- The likeliness of the new information becoming available on the device or state of the art
- Whether there are risks and uncertainties or unanswered questions, in the medium or long-term, that would influence the frequency of updates
- Whether design changes or changes to manufacturing procedures have been made (if any) which could impact the safety and/or performance of the device
- Whether significant changes to the state of the art have occurred which may affect the benefit-risk conclusion of the device
- Whether significant new or unanticipated device risks have been identified through the post-market surveillance
- Whether design or manufacturing changes have been made.

b) ***Defining State of the Art (SOTA)***

Pitfall: The state of the art is not clearly defined and/or is incomplete and it is not clear how the acceptance criteria for each safety and performance outcome have been established based on SOTA.

Guidance: Evaluation of the device within the context of the state of the art is essential for demonstrating that when used as intended, the benefits outweigh any potential safety risks. As a starting point to this analysis, manufacturers must define the SOTA for their device. A comprehensive analysis of the SOTA is critical as it facilitates characterisation of the expected clinical performance (and the resulting clinical benefit), and the clinical safety profile for the device under evaluation.

SOTA is not defined by the regulation however other sources provide guidance to develop a harmonised understanding:

- Per IMDRF/GRRP WG/N47: *Developed stage of current technical capability and/or accepted clinical practice in regard to products, processes and patient management, based on the relevant consolidated findings of science, technology and experience*
- Per MDCG 2020-6: The state-of-the-art embodies what is currently and generally accepted as good practice in technology and medicine. The state-of-the-art does not necessarily imply the most technologically advanced solution.

Considering these definitions, it is generally accepted that defining SOTA within the CER involves describing the medical field, including best clinical practices e.g. based on guidelines issued by medical expert societies, within which the device under evaluation is intended to operate. The medical field includes the clinical condition including its epidemiology and natural progression, that is intended to be treated, managed, diagnosed etc. by the device. Discussion of currently available alternative treatment options (including conservative, surgical, medicinal) should be addressed, considering the appropriateness of patient selection criteria/ targets groups as an input for the intended use specification. In addition, similar and benchmark devices should be identified and a discussion of their safety and performance profile provided. When defining SOTA, the manufacturer must ensure coverage of the full intended purpose. The manufacturer must describe and evaluate the degree of novelty of the device, in the light of the current SOTA and consider novelty in the specification of the sufficient level of evidence.

It is expected that a comprehensive SOTA analysis will lead to the identification of the safety and performance objectives and acceptance criteria which will be used to compare the device with similar/benchmark devices and other alternative treatments, in accordance with MDR Annex XIV Part A, 1a indent #6. The purpose of this comparison is to demonstrate an acceptable benefit-to-safety profile of the device under evaluation considering existing products or therapies. Alternatively, the outcome of the SOTA analysis may demonstrate an unmet clinical need, for which the device under evaluation is intended to address.

Clinical data and if appropriate non-clinical data, will be used by the manufacturer to demonstrate achievement of the performance and safety acceptance criteria and that the benefit of the device outweighs the risks.

In summary, the two most relevant outputs of the SOTA review are:

- the identification of alternative treatment options, and

- the identification of relevant performance and safety outcome parameters together with their acceptable ranges for similar devices and alternative treatment options. These acceptance thresholds as identified in the SOTA should be fed into the CEP during the planning phase (see section CEP above) and be compared to the available device-specific (clinical) data in order to conclude about the acceptability of the benefit-risk ratio for the device under assessment.

c) Sufficient Clinical Evidence

Pitfall: Sufficient clinical evidence to support the applicable annex I GSPRs *(specifically to support the claimed intended purpose)* and any clinical claims made within the technical documentation including the labelling, instructions for use, any promotional or marketing materials is not provided by the manufacturer.

MDR Article 2(51) defines clinical evidence as: *clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer.*

Guidance: Clinical data providing sufficient evidence is required to demonstrate that a medical device is safe for use, performs as intended and that the benefits outweigh any potential residual risks. Sufficient clinical evidence relates to the quantity and quality (e.g. completeness, scientific validity, reliability) of clinical data that is needed to support conformity.

It is up to the manufacturer to specify and justify within the clinical evaluation plan or report, what types of clinical data are required and why the resulting clinical evidence is sufficient. The role of the notified body is to verify that, in view of the characteristics of the device and its intended purpose, the conclusions presented in the clinical evaluation are robust and fully supported by sufficient clinical evidence. It should be noted that there are several factors that influence the regulatory expectations for providing high quality clinical data, such as risk classification of the device, novelty, safety concerns relating to the device family on the market, market history (new vs. legacy device), etc. Per MDR Art. 61(1): The level of clinical evidence shall be appropriate in view of the characteristics of the device and its intended purpose.

If the intended patient population has no exclusions, the clinical data must cover all age categories: neonates, infants, children, adults, and the elderly.

As part of their assessment, the notified body will look for evidence that the manufacturer has applied a scientific and logical approach to determining the sufficiency of their clinical evidence. In accordance with MEDDEV 2.7/1 Rev 4.0, recommended steps are as follows:

Step 1: Identify Clinical Data

Clinical data refers to any safety or performance related data/information generated from use of the subject device and/or an equivalent device in the intended patient population per the manufacturers intended use. For further guidance including sources of clinical data, refer to MEDDEV 2.7/1 Rev 4.0, Section 8.0 identification of Pertinent Data and MDCG 2020-6 Section 6.2.

Note: If the clinical evaluation covers multiple device models/variants, manufacturers should consider stratifying their data for ease of interpretation and review by the notified body.

Note: If the manufacturer intends to use clinical data that is generated outside of the EU, they must demonstrate that the resulting data can be extrapolated to the target EU population – consideration should be given to relevant differences in clinical practices, surgical procedures, differences in the epidemiology of target disease, physiological and genetic differences between regions and their ethnicities, appropriateness of model training and validation data in AI based devices, etc.

Note: For Orphan indications, manufacturers should consider the guidance provided on clinical data extrapolation in MDCG 2024-10 Appendix A3.

Note: For medical device software, MDCG 2020-1 describes three key components that must be considered when compiling clinical evidence: Valid Clinical Association/Scientific Validity, Technical performance/Analytical performance, and Clinical performance.

Note: The notified body assessment of the literature search protocol typically focuses on (1) Search databases selected and justification for use, (2) Search method to be applied e.g. PICO, PRISMA etc., (3) Search terms – coverage of the intended purpose and all indications, (4) Search date and justification for search date ranges, (5) Inclusion and exclusion criteria and rationale for their use, (6) Process for identifying information from other sources such as internet searches for unpublished information, (7) Approaches taken to identify best practice industry and medical practices/guidelines and (8) Data collection plan to ensure reliability and completeness of results, including the identification of duplicate data. For further guidance refer to MEDDEV 2.7/1 Rev 4.0, Appendix A4 and A5.

Note: The notified body assessment of a clinical investigations typically focuses on (1) Ethics and competent authority approval (2) Study design, including the adherence to acknowledged principles of good clinical practice (e.g. EN ISO 14155) (3) Study locations, (4) Patient population including the in-/exclusion criteria in the light of the target groups specified in the IFU (5) Patient numbers – this number should be statistically justified, (6) Objectives and Endpoints (7) Appropriateness of length of follow up and intervals, in particular in implantable and long-term invasive devices, (8) the efficacy results and how they support the clinical evaluation, (9) the safety results and how they align with the risk management of the manufacturer. Notably, any device deficiencies observed in the study are expected to be evaluated as part of the CER. (10) any deviations from the study protocol and how they have been considered, (11) any remaining open scientific questions and how they have been considered for setting up the PMCF plan.

Note: If the manufacturer intends to support certain aspects of the intended purpose based on clinical data generated from the use of the device in other uses (for example leveraging clinical data pertaining to adult patients to adolescents or children), a detailed justification must be provided demonstrating

the relevance of the clinical data to the specific intended purpose aspect (e.g. patient sub-populations, device variants etc.).

Step 2: Appraise Clinical Data

Manufacturer must provide evidence that they have appraised the clinical data derived from peer reviewed scientific literature and any other relevant reports or publications. Data appraisal requires consideration of at the least the following elements:

- Relevance to the device under evaluation or the equivalent device (if applicable), (Refer to MEDDEV 2.7/1 Rev 4.0, Section 9.3.2).
- Scientific validity and reliability (Refer to MEDDEV 2.7/1 Rev 4.0, Section 9.3.1 and Appendix A6).
- Coverage of the target patient population covered by the intended purpose and all indications.
- Coverage of the device variants included in the clinical evaluation.
- Clinical claims made by the manufacturer.

Ultimately the goal of data appraisal is to identify datasets that provide the strongest evidence to support the manufacturers conclusions regarding device safety and performance. For guidance refer to MEDDEV 2.7/1 Rev 4.0, Section 9.0 and Appendix 6 and MDCG 2020-6 Section 6.3.

Step 3: Analyse Clinical Data

The final step is to analyse the appraised datasets and determine if collectively and within the context of the SOTA, they provide sufficient evidence, to demonstrate that, for the duration of its lifetime:

- the expected clinical benefit of device use has been demonstrated and
- does not cause unacceptable levels of harm to the users or patients, when weighed against the clinical benefits.

The notified body will look for evidence that the manufacturer has completed a comprehensive analysis of the appraised data including consideration of all datasets which provide unfavourable results and that the analysed data supports the manufacturers conclusion regarding conformity to the applicable GSPRs.

Consistency in performance and safety outcomes across different datasets provides greater confidence in the reliability and validity of the data. However, if different results are identified across the datasets or there is a particular outlier dataset, the manufacturer should discuss these differences and if possible, explain the reasoning behind them. If a decision is made that a specific dataset does not add value to the evaluation, a rationale should be provided.

Based on this analysis, the manufacturer should conclude:

- If sufficient evidence (quality and quantity) is available to support the intended use including indications and target populations for all variants covered by the clinical evaluation.

- The manufacturer should also consider the minimum level of clinical data that is needed based on the regulatory requirements of Article 61. For example, Class III and Implantable devices require clinical data generated from a pre-market clinical investigations unless the manufacturer can avail of any of the exemptions provided for in Article 6 (4-6).
- For legacy devices, manufacturers should refer to the guidance provided in MDCG 2020-6 Appendix III and may consider applying the hierarchy of clinical data types to their device.
- As part of the assessment, the notified body must verify adequacy of the evidence to support any claims that are made by the manufacturer. To facilitate this verification, tabulation of the clinical and non-clinical claims within the CER including a clear reference to the data which supports each claim is advised.

- If there is a need to conduct pre-market clinical investigation or other studies to address any identified gaps in the data.
- If specific Post Market Clinical Follow Up activities are required to generate real world data to further support safety and performance outcomes (e.g. long term follow up post implantation, data on rare indications, rare populations, rare complications, address any uncertainties etc.).
- If there is a need to narrow the intended purpose and claims due to lack of sufficient supporting evidence.

For guidance refer to MEDDEV 2.7/1 Rev 4.0, Sections 10 and 11 and Appendix 6 and MDCG 2020-6 Section 6.5 and Appendix III.

d) Benefit-Risk Analysis

Pitfall: Conclusions regarding acceptability of the benefit to risk ratio do not consider all available data.

Guidance: The clinical benefit refers to the positive impact of the device on the health of the patient expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), or positive impact on patient management or public health. It is acknowledged that the clinical benefit can be achieved directly by the medical device or indirectly whereby the device itself does not directly achieve a positive impact but may influence the clinical outcome of the patient. The risks refer to the residual clinical related harms which have the potential to negatively impact on patient health. The expected clinical benefits and clinical risks should be identified as part of the SOTA analysis, and the clinical risks including likelihood of occurrence and mitigations, considered via the devices risk management.

In the CER, a clear description of the benefits and the key clinical risks including actions taken to reduce them to an acceptable level should be provided. This information is expected to be traceable to and aligned with the records in the risk management file. E.g., for a clinical risk described to be mitigated by information for safety in the IFU in the CER, a related line in a FMEA provided in the risk management file, systematically evaluating this risk and the effective implementation, is expected.

Considering all the available data, the manufacturer must demonstrate that the benefits of using the device outweigh the risks for all medical conditions and target populations covered by the intended purpose, and for all device variants. This may be achieved through comparison of the performance

and safety profile of the device with the currently available treatment options, alternative therapy options, benchmark and similar devices, identified as an outcome of the State-of-the-Art analysis.

Three possibly acceptable scenarios may be detected:

(1.) performance and safety for the device under evaluation are comparable with or outperforming the current SOTA.

(2.) performance is lower than SOTA, but also the risks are reduced compared to SOTA to a level that justifies the lower performance.

(3.) risk are higher than SOTA, but also the performance is higher than the current SOTA in a way that justifies higher risks. At some point, a mathematical counterbalancing of what kind of benefits justify what kind of risks will not be possible anymore but rather must be assessed based on the clinical expertise of the evaluators.

e) Device Lifetime

Pitfall: The lifetime of the medical device is not defined or is claimed to be indefinite or undefined.

Guidance: Manufacturers must define the lifetime or expected lifetime or expected service life for the medical device. The lifetime can be specified in terms of minutes/days/years/months or other appropriate quantitative terms such as number of uses etc. or relative terms such as e.g. time to next update for software, etc. In case of implants, which are not intended to be removed, the lifetime of the device is equal to the remaining lifetime of the patient after implantation. This fact must be duly considered in the evaluation of risks, with a view of the earliest age at which the patient may receive the implant (e.g. device for adults: 18 years) versus the life expectancy in the target market.

A clear specification of the device lifetime enables the notified body assessor to ensure that the clinical data and/or PMCF plan is appropriate to meet the requirements of Annex XIV. For further guidance refer to Team NB Position Paper on Medical Device Lifetime

6.3.4 Post Market Clinical Follow-Up (PMCF) Plan and Evaluation Report

Per Article 61 (11): *The clinical evaluation and its documentation shall be updated throughout the life cycle of the device concerned with clinical data obtained from the implementation of the manufacturer's PMCF plan in accordance with Part B of Annex XIV and the post-market surveillance plan referred to in Article 84. For class III devices and implantable devices, the PMCF evaluation report and, if indicated, the summary of safety and clinical performance referred to in Article 32 shall be updated at least annually with such data.*

PMCF is a continuous process that is used to proactively collect and evaluate clinical data generated from actual use of the CE marked device in the target population per the approved intended purpose and in accordance with a predefined plan. In accordance with MDR Annex XIV Part 6.1, the purpose of PMCF is to confirm the safety, performance and continued acceptability of benefit to risk for the duration of the devices expected lifetime, detect any new/emerging risks and to identify possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct. The data and information generated from implementation of the PMCF plan, is fed back into and updates the devices clinical evaluation and risk management. This is an important step in the process as it allows the manufacturer to continuously evaluate their device within the context of the current SOTA and safety and performance profile of benchmark/similar devices.

The **common pitfalls** identified by the notify body during the assessment of the **PMCF plan and report** are as follows:

a) PMCF Plan and Report content

Pitfall: The PMCF plan does not include all elements required by Annex XIV Part B.

Guidance: MDCG 2020-7 has been developed to assist manufacturers demonstrate compliance with the regulatory requirements for developing a PMCF plan (MDR Annex XIV Part B, Section 6.2). Whilst not mandatory, it is highly recommended that manufacturers follow this guidance when generating the PMCF plan for their device and provide as much detail as possible to facilitate verification by the notified body. Manufacturers should avoid generic PMCF plans. Rather it should be clear to the notified body how the findings and conclusions from the devices clinical evaluation has been considered in the establishment of the proposed PMCF Plan.

It should be noted that per MDR Annex XIV 6.2, PMCF is not exclusively related to clinical studies. If the manufacturer determines that PMCF clinical studies are not required, a PMCF plan is still required, as the manufacturer is expected to at least perform general PMCF methods.

If the manufacturer determines that specific activities such as studies or surveys are required, the plan should clearly indicate their timings/durations and relevant endpoints in respect of the SOTA. It is also important to confirm the quality and quantity of evidence that will be generated from the activity. If appropriate, the manufacturer may refer to supporting documentation such as study/survey protocols in the PMCF plan, however these documents cannot be submitted in place of the PMCF plan.

The PMCF plan can be generated as a stand-alone document or incorporated as part of the PMS plan. Irrespective of the approach taken, the manufacturer is responsible for demonstrating how each requirement of Annex XIV Part B 6.2 has been addressed.

Pitfall: The PMCF report in incomplete and lacks details on status of activities.

Guidance: MDCG 2020-8 has been developed to assist manufacturers demonstrate compliance with the regulatory requirements for generating the PMCF evaluation report. It must be clear from the report if specific PMCF activities are on track or if there have been any variations from plan. The report should also clearly state the reporting period and whether the data presented in historical or newly generated during the reporting period. Evidence of off-label use should be clearly documented and discussed with the report and consideration given to the need to update the clinical evaluation and risk management documentation.

Analysis of the data generated from the PMCF activities should be clearly presented within the PMCF report and the findings and results discussed in relation to the specific objectives defined by the PMCF plan and within the context of the SOTA.

The status of the PMCF activities defined in the PMCF plan should be clearly described in the PMCF report including a justification for any delays or deviations, including consideration of the impact if any on achievement of the objectives and whether changes require notification to and approval by the notified body. Where activities are ongoing and data is incomplete, specifically for PMCF studies, it is still expected that some level of analysis will be undertaken, even if this is limited to an analysis of adverse events, for example. Where applicable, interim analyses should be provided, as these provide evidence that activities are progressing appropriately.

The PMCF evaluation report may be generated as a stand-alone document with appropriate discussion and reference in the CER, or it can be fully integrated into the CER. Irrespective of the approach taken, the manufacturer may consider using the outline provided by MDCG 2020-8 when presenting and discussing the PMCF data

b) General and Specific PMCF methods

Pitfall: The PMCF plan does not clearly differentiate between general and specific PMCF activities, and/or a justification is not provided for not performing specific PMCF, when appropriate

Guidance: MDR Annex XIV Part B 6.2 describes both general and specific methods of PMCF. General PMCF methods include activities such as literature reviews, solicited user feedback/focus groups, review of regulatory device databases and level 8 surveys (based on recall of multiple device usages). Whereas specific methods refer to activities such as retrospective/prospective clinical studies, registry studies, other real world data studies and level 4 high quality surveys (one survey per patient chart or device use or case). As part of the PMCF plan, the manufacturer is required to provide a rationale for the appropriateness of the chosen methods

Note: In the PMCF report general and specific activities should be discussed and presented separately in terms of rationale for the activity, sample size, objectives etc.

General PMCF activities are applicable to all types of devices, however, they may be particularly suited to devices where:

- the long-term safety and performance are known, or the device is standard of care.
- devices have a long history of use on EU market, with no identified trends or safety concerns and the manufacturer has sufficient (quality and quantity) clinical data to support their claims.
- the risk-benefit ratio is acceptable.

For devices that meet these criteria, specific PMCF activities are typically not required. Nevertheless, general PMCF activity should still be planned, have clear objectives and be conducted systematically and a justification for not performing specific PMCF provided.

Specific PMCF activities are appropriate for devices where uncertainties remain from the clinical evaluation and additional clinical data is required to support long term safety and performance of the device or rare indications or specific target populations or specific device variants or to address new concerns arising from vigilance, literature and other PMS data for example.

Specific PMCF is usually required when the devices are:

- Novel technologies or have a new or novel intended use.
- Higher-risk device and use scenarios.
- Devices approved with clinical data from equivalent devices
- When urgent market access has been granted in public health emergencies.
- Specific questions may remain open from the clinical evaluation. E.g. lifetime data for longer term implants.

PMCF studies are conducted to address uncertainties and gaps in clinical data. This can be due to needing to address unanswered questions of long-term safety, clinical performance and/or effectiveness or to address new concerns arising from vigilance, literature and other PMS data.

Registry studies are a means of organised data collection for a specific type of device. Whilst they can be sponsored by the manufacturer of the device, they may often be organised at a national population level, with the aim to improve knowledge of safety and performance of a device or device type. Registries are based on real world experience and particularly suited to tracking long term outcomes and follow up. However, the data collected may be prone to bias, due to retrospective input of data, burden on inputters and compliance.

High quality surveys – Level 4

High quality surveys are generally at the patient level whereby one questionnaire/survey is completed per medical chart. The survey should have clearly defined primary and secondary endpoints. Validating the questionnaire to be used and ensuring the sample size is statistically calculated is vital. Methods to analyse the data received should be appropriate to the data gathered. During planning the manufacturer must consider how many surveys need to be conducted and received to ensure statistical applicability of any findings. If these factors are not considered and put into practice, the survey data loses its quality though may still provide useful information, but it will unlikely meet requirements of specific PMCF, rather it would be considered general PMCF.

Note: If specific PMCF activities are not to be conducted in EU countries a supporting rationale/justification must be provided.

Note: Objectives/endpoints set in the PMCF specific activities should be consistent with those on the clinical evaluation.

c) Changes to PMCF Plan

Pitfall: In the case of devices on a product certificate, significant changes to previously reviewed and accepted PMCF activities are not communicated to the notified body in advance of implementation.

Guidance: Proposed changes to the PMCF plan should be considered via the manufacturers change management process to determine the potential impact on product safety and performance, and on regulatory compliance. Per the MDR, significant changes require notification to the notified body for approval prior to implementation. Changes that may be considered significant include Removal or ceasing of any ongoing or planned specific activities, Delays or deviations to study protocol/timelines, Reduction in sample sizes or number of participating sites, Changes to study objectives or endpoints, Changes to statistical analysis plan. Typically, administrative changes or changes to general methods are not considered to be significant.

6.3.5 Summary of Safety and Clinical Performance (SSCP)

Per Article 32 of the MDR, all Class III and Implantable devices (excluding custom made devices) require an SSCP.

The content of the SSCP should be aligned to guidance provided in MDCG 2019-9 and should consider the following aspects:

- All information provided in the SSCP must be traceable to the technical documentation.
- Please confirm with your notified body the languages preference for validation of the SSCP.
- The SSCP should be in pdf format, printable and searchable and follow the template provided in MDCG 2019-9.
- The SSCP should be reviewed at least annually, coinciding with the annual update to the PMCF Evaluation report and the PSUR. As an outcome of this review and if required, the SSCP should be updated to ensure that any clinical and safety information remains correct, complete and continues to align with the most current version of the technical documentation. As an output of the update, consideration should be given to the need to inform healthcare professionals and patients/laypersons of any updates.
- For Class IIa implantable and Class IIb implantable WET (Well-Established Technologies) devices, the MDR allows notified bodies to choose representative devices from each device category or generic device group, respectively, for the assessment of Technical Documentation. The SSCPs for such devices chosen as the representative samples will be validated by the notified body as part of the technical documentation assessment for those devices. MDCG 2019-9 requires that notified bodies also upload the unvalidated SSCPs of the devices that were not chosen as representative devices (but are part of the same device categories or generic device groups) to EUDAMED and, therefore, these will need to be provided before certificate issue.

For Class III devices that are intended to be used directly by a patient or implantable devices that require an implant card (per article 18) then a patient/layperson version of the SSCP is always required. For all other devices the availability of a patient/layperson version SSCP should be considered. If it is still decided that a patient version/layperson is not applicable, then a robust justification must be provided.

For the patient/layperson version SSCP ensure:

- Appropriate patient/layperson terminology is used throughout the document in addition to stylistic recommendations.
- Evidence is provided of an appropriate readability assessment
- The layout template and guidance provided for the patient/layperson in MDCG 2019-9 is applied and the provided example statements have been considered.

Common pitfalls in SSCP

- Manufacturers do not include the quantification for risks in section 4 of the SSCP.
- The wording of the lay persons section is not adapted to the typical reading skills of persons without formal medical education.
- SSCP is written using regulatory and/or quality systems language, which may not be fully understood by the healthcare professional or the patient.
- Specific information requested in MDCG2019-9 is not provided.
- Incomplete summary of the clinical evidence, where the objective evidence provided is insufficient in terms of quantity and/or quality to support the conclusions drawn in the clinical evaluation.
- Incomplete or lack of information on alternative treatments.

ANNEX III TECHNICAL DOCUMENTATION ON POST-MARKET SURVEILLANCE

7 Post Market Surveillance

Per MDR Article 83 (1): *For each device, manufacturers shall plan, establish, document, implement, maintain and update a post-market surveillance system in a manner that is proportionate to the risk class and appropriate for the type of device. That system shall be an integral part of the manufacturer's quality management system referred to in Article 10(9).*

The PMS system is a critical component of the manufacturers quality management system (QMS), as it continuously and systematically generates safety and performance related data and information from actual use of the medical device from the market. The data and information are fed back into and used to update the other QMS processes including but not limited to feedback and complaint handling, improvement, design and development, risk management and clinical evaluation. An effective feedback loop between these processes is essential for demonstrating a full lifecycle approach to ensuring safety and performance of the device and that the benefits continue to outweigh the risks for the duration of its lifetime.

A PMS plan which clearly address all requirements listed in Annex III, is required for all device risk classifications. The data generated from implementation of the plan must be periodically analysed and the results and conclusions documented in the Post-Market Surveillance Report for Class I devices (Article 85) or the Periodic Safety Update Report for Class IIa, IIb and Class III devices (Article 86). These reports are subject to scrutiny by the notified body and the competent authority, and therefore the manufacturer must ensure that they are being updated and maintained per the frequency defined by the MDR (See Article 85 and 86).

Note: In the absence of EUDAMED, refer to MDCG 2021-1 and your notified body for further guidance on submission arrangements for PSUR evaluations.

Whilst not an exhaustive list, the following are the **common pitfalls** identified by the notified body when assessing the manufacturers **PMS documentation**.

7.1 Post Market Surveillance Plan

Pitfall: The PMS plan is not specific to a particular type of medical device.

Guidance: When establishing the PMS plan, it is important to clearly define the scope of the plan or in other words clearly what device or if relevant, what category or group of devices will be covered by the plan. A device is associated with one Basic UDI-DI and may include different variants or sizes. A category or group of devices will include multiple Basic UDI-DIs, and a justification should be provided to explain the relevance of grouping the devices together. The residual risks and market history associated with the device should drive the objectives of PMS Plan and each planned activity is expected to bring meaningful data for the specific device type.

The planned PMS activities should be proportionate to the risk associated with the device(s). To incorporate this concept into the PMS plan, consider the following:

- Develop the plan based on residual risks identified from the clinical evaluation.
- Link PMS activities to risks identified in the risk management file and clearly outline how data collection addresses specific risks.
- The plan should provide a justification for why certain risks do not require additional PMS activities.

Note: Manufacturers may refer to ISO/TR 20416:2020 Medical Devices – Post market surveillance for manufacturers, for additional guidance on scoping the PMS plan.

Pitfall: The level of information provided in the PMS plan lacks detail and is incomplete.

Guidance: The PMS plan must clearly and comprehensively address each of the requirements prescribed by Annex III 1.1(b). Any missing or poorly described requirements will be challenged by the notified body.

The PMS information that must be generated from the PMS system is described by Annex III 1.1 (a). This information can be derived from reactive or proactive data sources. Reactive is considered as a passive activity whereby the manufacturer waits for the information to be provided to them before assessing and if necessary, taking corrective action. A typical example is complaints, whereby the manufacturer finds out that there has been an issue after the fact, when they are notified by a customer or representative. Proactive is considered as an active approach, whereby the manufacturer goes out to the market and actively seeks performance and safety related data for the purposes of identifying and mitigating potential issues before they can occur and cause harm. An example of different reactive and proactive data sources is presented below:

<table>
<tr><th>Reactive Data Sources</th><th>Proactive Data Sources</th></tr>
<tr><td rowspan="2">▪ Complaint and vigilance data analysis
▪ Serious and non-serious incidents
▪ Service reports / Maintenance reports
▪ Feedback/Observations from the sales and marketing teams (e.g. social media, online patient forums, customer meetings etc.)
▪ Screening of scientific literature to identify device specific events
▪ Notified body communications/feedback
▪ Corrective actions (CAPA System)</td><td>General PMCF Methods:
▪ Level 8 Surveys
▪ Feedback / Interviews (Users, distributors, importers)
▪ Screening of scientific literature to identify new data and information. For example, in the case of similar or equivalent medical devices
▪ Publicly available information about similar medical device</td></tr>
<tr><td>Specific PMCF Methods:
▪ Level 4 Surveys
▪ Medical device registries
▪ PMCF study (retrospective or prospective)</td></tr>
</table>

Considering the scope and objectives of the PMS plan, the manufacturer should consider the following when developing their device specific PMS plan:

- Data collection
  - What data sources are you planning to use and why are these data sources suitable for the device.
  - How will you collect the data and who is responsible.
  - When will the data be collected and how much do you need (e.g. sample size).
  - Note: Notified bodies will look for evidence that the manufacturer has carefully considered which information is relevant to the specific device covered by the plan.
  - Note: Consideration should be given to ensuring that the data needed to generate the PSUR is collected (Refer to MDCG 2022-21).
- Data Analysis
  - How will you analyse the collected data (For example: Qualitative or quantitative (statistical), descriptive, transcription, codification etc.).
  - What type of data analysis is required to allow for comparison of the subject device to similar products available on the market.
  - Who is responsible for analysing the collected data and when will this analysis occur.
  - What methods and tools will be used to investigate complaints and analyse market-related experience collected in the field.
  - How will you differentiate between serious and non-serious incidents and what will you do if a serious incident is identified.
  - How will you determine if there is a trend or statistically significant increase in the frequency or severity of non-serious incidents or expected undesirable side effects (MDR Article 88).
- Acceptance Criteria
  - What indicators/thresholds and associated acceptance criteria will be used to identify the need to trigger an action including reassessment of the benefit to risk.
  - Are these indicators/thresholds appropriate to the device covered by the PMS plan considering the SOTA.
- Link to other QMS processes
  - If a corrective action or field safety corrective action is needed, how will this be triggered and managed.
  - How will you ensure that you can identify and trace any devices that require corrective actions.
  - What is the method for communicating with competent authorities, notified bodies, economic operators and users, as required.
  - What processes/procedures/methods are in place to ensure that relevant data and information is fed back into the relevant QMS processes such as design and development, risk management and clinical evaluation.
- Reporting
  - What processes/procedures/methods are in place to ensure that results of the analysed data and conclusion are available to generate the PMSR or PSUR per the defined schedule for generating these reports.
  - Note: Consider how the data is to be presented (Refer to MDCG 2022-21, Annex II).

Note: Manufacturers should refer to MDCG 2025-10, specifically sections 4 and for further guidance.

Note: Manufacturers may refer to other QMS procedures in their PMS plan. For example: trending, data analysis, complaint handling etc. However, the manufacturer should provide a summary of the relevant aspects of the procedure in the PMS plan and ensure that any device specific requirements are adequately addressed.

Pitfall: The PMS plan does not provide an adequate justification as to why PMCF is not applicable.

Guidance: The purpose of PMCF is to proactively collect new clinical data to address any gaps identified as an output of the clinical evaluation and to identify if there are any new/emergent risks that need to be considered. PMCF includes both general and specific methods per Annex XIV Part B.6.2 (a & b). Specific PMCF methods such as registry studies provide a means to collect new clinical data to address unanswered questions and unknowns regarding device safety and performance. Whereas general PMCF methods such as feedback, literature screening, regulatory database searches provide a simple yet effective proactive method for identifying new or emergent risks even for devices with a long history of safe use. It is generally accepted that if the clinical evaluation concludes that there are no unknowns or gaps in the clinical evidence, a justification for not performing specific PMCF methods may be appropriate, and this should be provided in the PMS plan.
Regarding general PMCF, per Annex III (1a), manufacturers should collect and utilise information from various sources such as specialist or technical literature, user feedback and publicly information about similar devices. This is aligned with the expectations of Annex XIV Part B, 6.1(a) on general PMCF methods and procedures. To demonstrate compliance to these requirements and to continually evaluate the state of the art (SOTA), it is widely acknowledged that general PMCF methods are expected for all devices including those that make use of Article 61.10.

7.2 Periodic Safety Update Report (PSUR)

Per MDR article 86, a PSUR must be generated for Class IIa, IIb and III devices. The purpose of the PSUR is to summarise the results and conclusions from the PMS data analysis and any follow up preventive and corrective actions that were taken, and to confirm continuing acceptability of the benefit: risk determination for the duration of the lifetime of the device. For Class IIb and Class III devices the PSUR must be updated at least annually. For Class IIa devices, the PSUR should be updated when necessary or at least every 2 years. The PSURs are part of the technical documentation.

In addition, and as part of the surveillance, the PSURs for Class III and implantable devices must be made available to the notified body for evaluation. For Class IIa and IIb non-implantable devices the PSUR is typically reviewed by the notified body as part of surveillance activities but must also be submitted to the notified body upon request.

The review period should be clearly stated at the start of the PSUR. The timeframe during which the data discussed within the PSUR was collected should be aligned with the review period (time frame) covered by the PSUR. Any gaps should be justified, and historical data clearly differentiated from new data. For guidance refer to MDCG 2022-21.

In addition to the guidance provided in MDCG 2022-21, manufacturers should consider additional points when assessing the data to draw meaningful and verifiable conclusions regarding continued acceptability of the benefit to risk, as:

- Comparative data analysis should be used to clearly demonstrate whether there is a change in the benefit: risk profile compared to previous years or if there are any emerging trends. This is especially important if the PSUR communicates unfavourable data for the current reporting period.
- Data for different devices under the same Basic UDI-DI should be stratified by model/variants/size for ease of interpretation or a rationale provided.

It is important to note that the aim of the PSUR is not to duplicate all the PMS data and reports but to summarize and discuss the results and provide a conclusion related to changes of risk/benefit of the concerned device(s).

Pitfall: Actions taken as feedback of relevant data into Risk Management, Clinical Evaluation and other elements of the TD, whenever relevant, is not reflected in the PSUR. Decision for not updating the SSCP based on information and data presented in the PSUR is not traceable.

Guidance: Per MDR Article 61.11 and Article 83.3 (a-c), the manufacturer must consider the need to review and update the clinical evaluation, risk management and other elements of the technical documentation such as labelling and Instructions for Use, based on the data discussed within the PSUR and the resulting conclusions. As the PSUR shall present actions taken the information on updates to the technical documentation as well as SSCP should be reflected in the PSUR and could be presented in a table format.

Per Article 83.3 (d), the SSCP must be reviewed based on the outcome of the PSUR. It needs to be ensured that clinical performance and safety information summarized in the SSCP remains correct, complete and current. If the PSUR concludes that the clinical performance and safety remain unchanged and thus no update to the SSCP is needed, a respective justification should be available in the PSUR.

Revision History

Version No.	Date	Brief description of main changes
1	05 October 2022	Initial release.
2	19 April 2023	Reference to MDCG and other guidance documents. Requesting manufacturers to inform the Notified Body where and when the subject device was previously assessed. Language considerations. e-IFU requirements. Design stages. Literature search requirements. Clarifications in wording and improved formatting.
3	09 April 2025	Various section updates to bring content up to date. Addition of common pitfalls observed by NBs. Significant rewrite of Clinical and PMS sections. Clarifications in wording and improved formatting (including table of abbreviations).
4	09 April 2026	Clarification on use of harmonised standards added to Scope, reasons for TD delay and tips for communication with NB expanded and abbreviations table updated. Comprehensive updates across all sections to incorporate new MDCG documents, updated standards (including ISO 10993-1:2025), and recent regulatory developments (e.g., updated e-IFU Regulation 2025/1234, AI Act considerations). Significant additions of *common pitfalls* observed by notified bodies across all technical documentation domains (device description, GSPRs, risk management, V&V, biocompatibility, software, packaging, sterilisation, SSCP,). Expanded guidance on leveraging prior conformity assessment evidence, documentation structuring, translation expectations, and alignment of duplicated information across TD. Updated content on high-impact areas such as AI/ML devices, cybersecurity, chemical characterisation, CMR/ED substances, human/animal/biological origin materials, and substance-based devices. Clarifications and enhancements throughout to improve consistency, completeness, and clarity of requirements for manufacturers, including improved formatting and additional explanatory examples.