The European Association of Medical devices Notified Bodies

Team-NB Position Paper

Editor :	**Team-NB**	Adoption date	03/09/2025	Version : V2

Best Practice Guidance for the Submission of Technical Documentation under Annex II and III of In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746

Best Practice Guidance for the Submission of Technical Documentation under Annex II and III of In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746

Information to be supplied by the manufacturer –

a collaborative notified body approach.

Contents

Scope of Document 4
General Considerations 5
Device Description & Specifications - Including Variants, Accessories, Classification & Materials 7
1. Device description and specification details should include: 7
2. Reference to previous and similar generations of the device 10
Information to be supplied by manufacturer (Includes DoC, Labels, IFU, etc.) 11
Design & Manufacturing Information 13
Design Information: 13
Manufacturing Information: 14
Sites and Subcontractors 14
General Safety & Performance Requirements (GSPRs) 15
Benefit Risk Analysis and Risk Management 16
Product Verification and Validation 19
Performance Characteristics 19
Information on Performance of the Device 19
Stability (applicable to reagents) 22
Metrological Traceability 23
Usability 23
Chemical, Physical and Biological properties 24
Hazardous substances, CMR, endocrine disrupting substances 24
Sterilisation 24
Biological Material 25
Construction of devices and interaction with their environment 25
Devices with a measuring function 26
Protection against radiation 26
Software & Software Validation 26
Electrical Safety and Electromagnetic Compatibility (EMC) 29
Protection against mechanical and thermal risks 30
Protection against risk associated with devices intended for self-testing or near patient testing 30
Performance Evaluation (Includes SSP and labelling) 31
Performance Evaluation Plan. 31
Scientific Validity 32
Clinical Performance Study 33
Product verification by EURL 33
Common Specifications 33

Performance Evaluation Report.....33
Post Market Performance Follow Up.....34
Post Market Performance Follow Up (PMPF) Plan. 34
Post Market Performance Follow Up (PMPF) Evaluation Report. 34
Summary of Safety and Performance (SSP). 34
Post Market Surveillance 35
Companion Diagnostics.....36
Revision History 36

Scope of Document

This best practice guidance document has been developed by members of Team NB who have reviewed the best practice guidance documents 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.

Manufacturers of all Classes of IVD medical devices are expected to demonstrate conformity of the IVD medical device to the General Safety and Performance Requirements of the IVD Medical Devices regulation through the preparation and holding of technical documentation that shows how each IVD medical device was developed, designed, and manufactured together with the descriptions and explanations necessary to understand the manufacturer's determination with respect to such conformity. This technical documentation is intended to reflect the current status of the IVD medical device through application of the manufacturer's QMS.

The technical documentation reflects the status of the IVD medical device at a particular moment in time (e.g., at the moment of premarket submission or when requested for post-market purposes) and is prepared in order to meet the applicable regulatory requirements and more specifically the General Safety and Performance requirements (GSPR). Where the technical documentation is submitted to a NB, it should be in a language acceptable to the reviewing organization.

This technical documentation submission guidance is aligned to the requirements of In Vitro Diagnostic Medical Devices Regulation [IVDR] (EU) 2017/746, described in detail in Annexes II and III, and Article 29.

Disclaimer:
The content of the best practice guidance is based on the interpretation of the In Vitro Diagnostic Medical Device Regulation EU 2017/746 by Team NB and affiliated notified bodies. During a technical documentation assessment, it may be required that additional documentation/information needs 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. When EU Regulation 2017/746 is referred, this includes the latest amendments and relates to published EU Implementing Acts and EU Delegated Acts.

This guidance is intended to be comprehensive, but not exhaustive in its request.

General Considerations

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

- **Incomplete Submissions** – Insufficient or missing information that is required for the conformity assessment activities.

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

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 the IVDR, per Article 48 (12).
- ✓ Manufacturers should also contact their notified body to clarify the requirements related to documentation labelling and methods for submission to the notified body.
- ✓ Clear reference should be mentioned in the technical documentations regarding the submitted application and/or quotation that preceded to the technical dossier submission.
- ✓ General administrative information should be provided in the technical documentation about the manufacturer details: legal manufacturer name, legal manufacturer address, EU Authorized Representative and subcontractors location, EMDN coding and NANDO coding.
- ✓ In general, it is best to provide information about past compliance history of the device, placing on the market and whether the device is made available to the market through distance sales. This information could be made available in an accompanying cover letter.

Technical documentation submission

- ✓ The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular regulatory references to the applicable regulatory requirements of the EU IVDR.
- ✓ Where appropriate 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 shall document how the manufacturer ensures compliance to every applicable GSPR.
- ✓ 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 purpose, indications for use, contraindications, warnings, etc.).
- ✓ Ensure that 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.
- ✓ As part of the technical documentation referred to in Annex II, the manufacturer shall keep up to date a list of all UDIs that it has assigned.

Next Revision Date: (2 years from endorsement)

This document is subject to further revisions as experiences will be gained.

This document is the result of an initiative to compile existing guidance from several notified bodies, to harmonise expectations and facilitate manufacturer's tasks when drafting their technical documentation.

Team NB may decide to revise this document to adapt it to changes in the regulation, development of guidance documents (e.g., MDCG documents) and the change in interpretation over time.

List of Abbreviations

CAS	Chemical Abstract Services
CDx	Companion Diagnostics
CLSI	Clinical & Laboratory Standard Institute
CMR	Carcinogenic, mutagenice or toxic for reproduction
CS	Common Specifications
DoC	Declaration of Conformity
ELSA	Electrical Safety
EMC	Electrical Safety and Electromagnetic Compatibility
EMDN	European Medical Device Nomenclature
EURL	EU Reference Laboratories
GSPR	General Safety & Performance Requirements
IFU	Instructions for Use
INN	International Non-proprietary Name
NANDO	New Approach Notified and Designated Organisations
PMPF	Post Market Performance Follow-Up
SDS	Safety Data Sheet
SSP	Summary of Safety & Performance
UDI	Unique Device Identification

Device Description & Specifications - Including Variants, Accessories, Classification & Materials

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

1. Device description and specification details should include:

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

- Provide a table listing each variant/model/configuration/component/accessory that is subject of the submission. Include the identifier (e.g., bar code, catalogue, model or part number, UDI) and a statement of its name/description (e.g., Trade name, size, intended use)
- Provide details of the EMDN code
- Applicable IVDR codes (NANDO) as well as information whether device is for single use only or multiple use shall be included; (refer to Commission Implementing Regulation (EU) 2017/2185).
- The general device description should enable understanding of the design, packaging, sterilisation, or other characteristics of the device such as devices used in combination, single-use, multiple use, sterile devices. It should include details of the components and accessories where applicable. In the case of companion diagnostics, it should include the associated medicinal product(s), including International Non-proprietary Name (INN).
- The intended purpose and/or intended use shall provide enough detail to explain the specific medical purpose as defined by IVDR Article 2.
- Identify the intended users of the device (i.e., laboratory professional, healthcare professionals or lay persons). Intended users as claimed shall be substantiated by the clinical performance evaluation and in the risk management, usability file part of the design file.
- Device name must be the same (and in same language) as listed on the application document.

NOTE: *In addition to the conformity assessment procedure requirements referred to in the IVDR, for companion diagnostics, the notified body shall consult a competent authority designated by the Member States in accordance with Directive 2001/83/EC of the European Parliament and of the Council (1) or the EMA, as applicable. It is therefore important for the Notified Body reviewer to know, as part of the technical dossier submission whether the drug has undergone a centralised procedure through the EMA, or a local procedure with competent authority designated by the Member States, that has approved the drug.*

(b) the Basic UDI-DI as referred to in Part C of Annex VI assigned by the manufacturer to the device.

- The Basic UDI-DI must be consistent throughout the technical documentation
- For devices grouped under one basic UDI-DI number please describe the differences to demonstrate how these falls under the same group.
- See MDCG 2018-1 for further guidance.

(c) the intended purpose of the device which may include information on:

(i) what is to be detected and/or measured;
(ii) its function such as screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic;
(iii) the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate;
(iv) whether it is automated or not;
(v) whether it is qualitative, semi-quantitative or quantitative;
(vi) the type of specimen(s) required;
(vii) where applicable, the testing population;
(viii) the intended user;
(ix) in addition, for companion diagnostics, the relevant target population and the associated medicinal product(s), including INN.

- The IVDR refers to Intended purpose and Intended Use. These are understood to have the same meaning.
- The Technical Documentation shall include intended patient population. If no specific testing population is stated in the intended purpose, it is understood that the device is to be used without limitation.
- Where there is a foreseeable risk that the tests may be misused, a clear limitation of use should be included in the IFU, e.g. "This test device is not intended to be a first-line device to be used for screening for transmissible agents". This information should be reflected in the technical documentation as well.
- If the application includes a change to the intended use, all sections of the file should be reviewed for potential impact.

Notes: The intended user and use environment should be clearly described within the technical documentation. The intended use, user, target population and clinical condition / physiological state must be supported by the results of the clinical performance evaluation.

(d) the description of the principle of the assay method or the principles of operation of the instrument.

- Provide a detailed description of the principle of the assay method.

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

- Per IVDR, Article 2, explain how the product qualifies as an IVD. This is especially important for software as a medical device since both can easily be qualified to fall under the MDR or IVDR. Refer also to MDCG 2019-11 for further guidance.
- IVD's that do NOT fall under the definitions per Article 2 IVDR are:
  - products for general laboratory use or research-use only products, unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination.
  - invasive sampling products or products which are directly applied to the human body for the purpose of obtaining a specimen,
  - internationally certified reference materials and materials used for external quality assessment schemes.
- On the other hand, specimen receptacles shall be deemed to be in vitro diagnostic medical devices.

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

- The classification of a device is defined by its *intended purpose,* as specified by the manufacturer. This covers the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use, in the performance evaluation or in promotional or sales materials or statements.
- Indicate the device classification and rationale per IVDR Annex VIII. The rationale should address each point of the selected classification rule. If multiple classification rules apply, all should be identified and the strictest rules resulting in the higher classification shall apply.
- The rationale shall not only address the reasoning why a particular rule applies but also reasoning why a particular classification rule is considered not to apply.
- If the device contains multiple tests each must be classified in their own right, note the highest classification shall apply to the overall device.
- Refer also to MDCG 2020-16 for further guidance.
- If the IVD is independent software, guidance for the qualification and classification of the software can be found in MDCG 2019-11.

(g) the description of the components and where appropriate, the description of the reactive ingredients of relevant components such as antibodies, antigens, nucleic acid primers.

- Please provide a detailed description of the listed components identifying the reactive ingredients including information on the presence of carcinogenic, mutagenic or toxic for reproduction (CMRs) substances and assessment against regulation (EU) 1272/2008 Consider the inclusion of CAS number

And where applicable;

(h) the description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use.

- This describes the specimen receptacle and transport materials that are used to collect the specimen and retain the specimen in good condition, even during transport. It also covers the devices that are recommended, when not delivered by the manufacturer.
- Consider the pre-analytical requirements, e.g., stability of the analyte.

(i) for instruments of automated assays: the description of the appropriate assay characteristics or dedicated assays.

- Evidence needs to be provided demonstrating the compatibility of the instrument with the appropriate or dedicated assays as part of the performance evaluation. This information is only needed for instruments of automated assays.

(j) for automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation.

- Describe the appropriate instrumentation and provide the application sheets for dedicated instrumentation. This information is only needed for automated assays.

(k) a description of any software to be used with the device.

- This would be a general description of the software that is supplied together with the device or is recommended to be used together with the device.
- Include the software version which drives the device or influences the use of the device.

(l) 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 and variants of the device to be made available on the market shall be detailed in the Technical Documentation, including any model numbers, names, constituents, sizes etc.

(m) 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 the device.

- Provide a description of all accessories, other devices, or generic products (e.g., buffers, extraction kits) required for the device to function correctly.
- If the accessory included in the kit is a medical device, per EU 2017/745 (MDR) such as a lancet, provide approval details (e.g., Certificate / DoC)
-

2. Reference to previous and similar generations of the device

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

What is expected is:

- an overview of the previous generation or generations of the device produced by the manufacturer.
    - For initial applications under IVDR, confirm whether the device has been previously marketed under IVDD as a self-declared or NB certified device. Indicate whether any changes have been made in comparison to any issued IVDD-certified device.

  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, state this explicitly.
    - Ensure that a market history is provided indicating the nature and timing of any changes.

Market history should include EU and approvals in other geographies.

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

What is expected is:

- Provide an overview of identified similar devices available on the EU or international markets if such devices exist. Provide a comparison of the key specifications.

Information to be supplied by manufacturer (Includes DoC, Labels, IFU, etc.)

Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user or any other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, Article 10(10) IVDR.

Labelling

Provide the label or labels on the IVD for all variants; this includes device labelling, any sterile packaging labelling, single unit packaging labelling, sales packaging labelling or transport packaging labelling, in the final approved version (print layout).

IVDs 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.

If possible, provide drawings/images with the packaging configuration (showing placement of all labels) and label specifications (layout, size).

The position of labels on the finished device should be clear. If the device has a sterile package, 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 GSPR 20.2 and Article 18.

Ensure that any specific requirements of relevant harmonised standards or Common Specification (CS) are addressed in the labels and information for use.

In the case of devices containing a substance or a mixture which may be considered as being dangerous, relevant hazard pictograms and labelling requirements of Regulation (EC) No 1272/2008 shall apply.

Note: packaging which maintains the sterile condition of a device (“sterile packaging”), will require additional information and particulars. Labels for devices intended for self-testing and near-patient testing also requires bearing additional information. For class C and D devices the manufacturer shall mention on the label or instruction for use where the summary of safety and performance (SSP) is available as per Art. 29 IVDR, in absence of EUDAMED.

Instructions for use/Device Operating Manual(s)

Provide the instructions for use (IFU) in the language required by the specific Notified Body performing conformity assessment of the device. Indicate within the technical documentation all countries in which the device is intended to be sold and summarise the process for translation. Translation of IFU to all languages required in the target markets is required before product launch, however, only one language (that required by the NB) is acceptable in the initial submission, as long as the translation procedure is effective.

Manufacturers must ensure that the information within the IFUs, especially related to intended purpose, indications, contra-indications, and other safety related information, warnings is aligned with similar information from other sections such as risk management, performance evaluation, usability etc.

IFUs must contain all the information required as per applicable requirements specified within GSPR 20.4 and Article 18.

Ensure that any specific requirements of relevant standards or CS are addressed by the instructions for use.

For instruments, provide user manual, installation and service manuals if applicable.

Note: for surveillance reviews a list of all countries in which the device has been sold and all translated labelling including the IFU must be submitted. Instructions for use for self-testing devices also needs to bear additional information and requires additional validation on a lay user population.

Electronic IFU (e-IFU) information (if applicable)

If electronic IFU will be utilised, E-labelling information as provided on the device or on a leaflet must be included. Provide details / reference to risk management in relation to e-labelling.

Safety Data Sheet

If a safety data sheet (SDS) is provided for the device, the SDS is part of the Technical Documentation in the respective translations in accordance with EU member state requirements.

Note that instructions for obtaining the SDS shall be included on the label or instruction for use. The provisions of Regulation (EC) No 1907/2006 and EC) No 1272/2008 on the safety data sheet shall apply, unless all relevant information, as appropriate, is already made available in the instructions for use.

Copies of promotional materials (that mention that the device fulfils the requirements of CE marking) including any that make specific claims related to the device

Only marketing literature that mention that the device fulfils the requirements of CE marking or includes the CE mark itself is required to be provided.

Claims made in the marketing literature must be consistent with the IFU and consistently displayed in the submitted technical documentation.

Note: EN ISO 15223 is harmonised to the IVDR and provides details of approved harmonised symbols. EN ISO 18113 and EN ISO 20417 provide guidance on the content of labels and IFUs. Refer to Regulation (EC) No 1272/2008 for the content and supply of SDS.

Declaration of Conformity

The EU declaration of conformity (DoC), referred to in Article 17, is the procedure whereby the manufacturer, who fulfils the obligations imposed by Article 48, declares that the devices concerned fulfil the requirements of the IVDR which apply to them. The declaration of conformity will contain as a minimum all information referred to in Annex IV and will be available to the CA. The manufacturer will continuously update the EU declaration of conformity and will translate it into an official union

language or languages required by Member States in which the device is made available. If, in addition to the IVDR, a device is covered by other Union legislation which also requires an EU declaration of conformity, the manufacturers will elaborate a single EU declaration of conformity where all the Union legislation applied to the device are referred to. By drawing up the EU declaration of conformity the manufacturer assumes the responsibility for the regulatory compliance of the device with all Union legislation applicable to it. Before affixing a CE mark, the manufacturer will have an EC certificate issued by NB according to the Annex IX, Chapter I and III, or to Annex X in combination with XI. As part of the Notified Body technical documentation submission, where no final DoC is made available, the Notified Body will accept a DRAFT DoC.

The DoC should include the device intended purpose if this is necessary for the identification of the device and if it cannot be clearly and unambiguously concluded from the name of the device

Design & Manufacturing Information

Design Information:

The documentation should contain information to allow a NB reviewer to obtain a general understanding of the design applied to the IVD medical device. Also, provide information on the design stages applied to the device. Consider the methods used to control, monitor and verify the design during stages of development. For example, traceability matrix etc.

For devices already marketed, include a history of any major changes to its design, including the reason for design changes and the impact on the performance evaluations conducted. Where no new performance evaluation has been undertaken, the documentation shall incorporate a rationale for that decision.

- For IVDs which are reagents provide a description of the critical ingredients such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the device. The description must include at least a reference number of the critical materials.
- For devices incorporating instruments and/or software, provide an overview of the entire system. Indicate the transition steps and whether manual handling/manipulation are required.
- For instruments, provide a description of the major subsystems, analytical technology and any dedicated computer hardware and software.
- Where the device uses software for objective data interpretation or the device is a software, provide a description of the data interpretation methodology i.e., analysis algorithm. State whether this is automated or manual. Full lifecycle management must be demonstrated and provided as appropriate for the risk class of the software.
- If the software is qualified as a medical device (MDSW) as per MDCG 2019-11; provide evidence to demonstrate this.
- For devices intended for self-testing or near-patient testing, manufacturers must include a description of the design aspects that make them suitable for self-testing or near-patient testing.
- Typically for a Class D IVD medical device detailed information on material specifications would be provided and the batch release process / criteria. This section is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. If design takes place at multiple sites, a controlling site must be identified.

- For devices containing raw materials of human, animal or microbial origin, a Certificate of Analysis (CoA) must be submitted with information to fulfill Annex II, 6.5.b

Manufacturing Information:

The manufacturer shall include a detailed overview of the manufacturing processes and used technologies to enable understanding of the finished device. Manufacturing includes incoming inspection, production, assembly, packaging, sterile packaging, sterilisation, final packaging (as applicable). Indicate any special processes required to manufacture the device.

The detailed overview may be provided as manufacturing flowchart(s), including relevant information on incoming inspection of raw material to final product testing and packaging, etc. The main work instructions and DMR should be identifiable, also to serve as an input for the audit. More detailed information may always be provided for the audit of the quality management system or other applicable conformity assessment procedures. Reference can be made to the Device Master Record (DMR) and Quality Plan of the devices covered in the document.

Provide detailed information on:

- Incoming inspection of critical raw materials/active ingredients
- Specifications and final concentrations/quantities of critical raw materials/active ingredients (subcomponents for instruments) in the finished device
- In-process QC, a clear description of the test method and acceptance criteria and include results from a sample batch.
- Final release QC, a clear description of the test method and acceptance criteria and include results from a sample batch with the CoA.

In case of sub-contracted (outsourced) processes:

- For non-critical component suppliers (e.g., bulk) identification of supplier only.
- For critical component suppliers (e.g., outsourced manufacturing of sterile device) overview of manufacturing processes, used technologies and corresponding control measures (e.g., references to verification and validation activities, copy of the certificate shall be included).

As a general principle if any of the information requested in the Manufacturing section is not available in the requested language of the Notified Body, 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 translations of relevant words within the reports.

Sites and Subcontractors

The manufacturer shall provide the following documentation at a minimum:

- Site and local manufacturer details (address and contacts)
- European representative, if applicable (Article 11)
- Site with design responsibility
- Site(s) performing production, assembly, final product testing, and packaging of the finished device.
- Where sterilisation is performed, if applicable.

- Where a service or production is outsourced provide the name and address of the critical subcontractors or suppliers (as per Commission Recommendation 2013/473/EU), along with the service or product supplied by each.
- Copies of critical subcontractor and suppliers ISO 13485 certificates or other relevant certificates based on the product / service they provide. If a critical subcontractor and/or suppliers does not have an ISO 13485 certificate from a certification body, then other satisfactory evidence to the Notified Body shall be provided, e.g., additional supplier audits to be arranged by the manufacturer.
- For critical suppliers and /or subcontractors satisfactory evidence that the purchase critical products or service meet the specified requirements shall be shown (e.g., EN ISO 13485 certificate, records of supplier audits, 100 % incoming inspection or any other control)
- Based on the provided information the notified body will then assess if an audit at the premises of the critical supplier and/or subcontractor is necessary. Relying on solely the supplier certification may not be considered sufficient.

Information about sites and subcontractors must be also included in the application.

In general, this section would also contain a general explanation of the subcontractor control system that is applied by the manufacturer, including reference to the documented (purchasing) procedures.

General Safety & Performance Requirements (GSPRs)

The manufacturer should provide documentation that includes the following:

a. Each GSPR of IVDR 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 IVDR, Annex I. A "rationale" column on each clause/sub-clause of IVDR, Annex I, that apply to the device, with an explanation as to why others do not apply.
    - GSPR that have different sub-sections, these must be addressed independently.
b. 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 IVDR Annex I
c. Harmonised standards, Common Specification (CS), generally acknowledged state-of-the art guidelines or other solutions applied (refer to the specific edition).
    - EXAMPLE: A column "applied standards, CS or others", for each clause/sub-clause of IVDR, respectively.
    - *NOTE 1 to (4): This is usually accomplished by means of a list of applicable standards and CS, as well as by reference to appropriate standards and CS in the appropriate documents (e.g., test reports).*
    - *NOTE 2 to (4): 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 & conclusion of acceptability of any compliance gaps.*

- *NOTE 3 to (4): Refer also to additional applicable standards, and/or Directives – e.g., Machinery, EMC, RoHS, scientific opinions, guidance as necessary to show state of the art.*

d. 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.
   - *NOTE 1 TO (4): This shall include a cross- reference to the location of that document within the full Technical Documentation. The more specific the references are to documents supporting compliance, the faster the review can be conducted.*

Example of such a table:

IVDR ID.#	**Requirement**	**Applicable Y/N**	**Method of conformity applied (i.e., harmonised/ international standard, others)**	**Justification**	**Documentation (reference)**
	ANNEX I **GENERAL SAFETY AND PERFORMANCE REQUIREMENTS**				
	CHAPTER I **GENERAL REQUIREMENTS**				
1	Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.	**Y/N**	**…**	**…**	**…**
2	The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.	**Y/N**	**…**	**…**	**…**
Etc.	Etc.	Etc.		Etc.	Etc.

Benefit Risk Analysis and Risk Management

For risk management refer to the IVDR requirements as stated in Annex I, clauses 1-8 and Annex II, section 5. Clearly indicate whether the risk management process is based on EN ISO 14971, and which version of the standard is implemented.

The interface between risk management process and performance evaluation performed by the manufacturer must be clear and noticeable (refer to Annex VII, 4.5.4); and the results of risk management shall provide information about the appropriateness of the performance evaluation.

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.

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.

Note that risk management documentation shall comprise all parts / components of a device.
Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating.

The requirements also apply in case of outsourced processes.

Risk management plan

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.
- Description of the life cycle phases of the device.
- Assignment of responsibilities and authorities for risk management, including details of the risk assessment team.
- Identification of requirements for review of risk management activities.
- The system used for qualitative or quantitative categorization 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.

Risk analysis / risk control measures

The documentation shall contain information on:

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

The documentation shall include:

- Design risk assessment: documented risk assessment for the design aspects of the device.
- Production/process risk assessment: documented risk assessment for the production / manufacturing process aspects of the device.
- Application/Product risk assessment: documented risk assessment for the application aspects of the device.
- Information about the health-related harm(s) to the patient derived from the hazards and hazardous situations identified.

For design risk assessment, an assessment shall 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 shall cover the requirements set out in section 5 of IVDR Annex I. For usability evaluation refer to the IVDR requirements stated in Annex I, clauses 9.4, 13.7, 19, 20.1a, as well as to EN 62366-1.

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

- All known and foreseeable hazards associated with each device are identified and analyzed (i.e., estimation and evaluation of risks for each hazardous situation).
- All known and foreseeable risks, and any undesirable side-effects, are minimized 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, sterilization, performance, 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 device(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 residual risks and the overall residual risk.
- 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 according to Annex I (4).

The risk analysis shall address all known and foreseeable hazards, including but not limited to:

- Hazards related to all device components.
- Hazards related to intended use and reasonably foreseeable misuse.
- 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 intended users, especially for self-testing or near patient testing
- Hazards related to the manufacturing process.

Note: additional hazards are also given in EN ISO 14971.

<u>Risk management report</u>

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 shall 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 (IVDR, Annex I, 1).

Note: For devices based upon existing devices, the manufacturer may conclude that pre-existing risk management documentation is applicable. However, there are always risks associated with even small changes, and a summary to demonstrate that these risks have been considered (and have been adequately mitigated) should be provided.

Product Verification and Validation

Performance Characteristics

The manufacturer should provide the following documentation:

- An overview of the design inputs and key outputs for the device. Including a design traceability matrix where appropriate.
- Overview of all testing performed to demonstrate compliance to applicable parameters described in Annex I GSPR 9.1(a) and (b), 9.3 and 9.4. Where a parameter is not applicable, provide a rationale within the performance evaluation plan.
- Protocol and reports with evidence of compliance with design requirements.
- Testing to relevant standards shall be provided if compliance to these is claimed.
- Evidence for all variants/configurations of the device, shall cover interconnections to accessories and parts of the device.
- Evidence shall 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.
- Test reports documenting results of studies carried out with the intended user. *(Note: for self-test devices a sample of the device may be requested)*
- For tests conducted by a test laboratory, include the test reports, certificate and evidence of accreditation of the test laboratory

Information on Performance of the Device

Specimen type:

- Data must be provided to demonstrate performance with all specimen types indicated in the intended purpose.
- Consideration shall be given to conducting performance evaluation within the intended patient population age and demographic.
- Where applicable mention any sample pre-treatments e.g., preservatives, fixatives, anticoagulants etc
- Where applicable, include a description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use.

- Provide the protocol and data for the determination of appropriate criteria for specimen collection and handling, stability (including freeze/thaw cycles), storage and transport.
- Detail any time-critical methods. These must be clearly defined in the IFU, with supporting data in the Technical Documentation.

Accuracy of measurement:
- May be demonstrated through trueness and precision separately.
- Trueness can only be demonstrated if a certified reference material or method is available.
- Where trueness cannot be demonstrated through a certified reference material or method, other approaches may be used such as method comparison to other well-documented methods.
- Precision: reproducibility and repeatability (as defined in state-of-the-art guidelines such as CLSI EP05 A3:2014) shall be demonstrated separately. The study protocol should include a description, where appropriate, of the operator, sample type and concentration, replicates per sample, number of lots / runs per day and the device and associated instruments.

Analytical specificity:
- This section shall describe interference and cross reactivity studies performed to determine the analytical specificity in the presence of other substances/agents in the specimen.
- Information shall be provided on the evaluation of potentially interfering and cross-reacting substances or agents on the assay, on the tested substance or agent type and its concentration, specimen type, analyte test concentration, and results. Interfering factors and cross-reacting substances or agents, which vary greatly depending on the assay type and design, could derive from exogenous or endogenous sources.
- Requirements in Annex II, 6.1.2.3 shall be addressed, all applicable and non-applicable interferents and cross-reacting substances or agents must be justified.

Measuring range:
- This section shall include information on the measuring range regardless of whether the measuring systems are linear or non-linear, including the limit of detection and describe information on how the range and detection limit were established. For quantitative assays, the measuring range must be defined by the LoQ and linearity data to the upper limit of the range.
- This information shall include a description of specimen type, number of specimens, number of replicates, and specimen preparation including information on the matrix, analyte levels and how levels were established. If applicable, a description of any high dose hook effect and the data supporting the mitigation such as dilution steps shall be added.
- The study protocol should describe the method used including the operator, sample type, sample number, number of replicates, how levels were established and were applicable associated devices.
- Data should include the detection capability (LoB, LoD and LoQ), information on Linearity/Non-Linearity, Hook effect and dilutions recovery. If these are not applicable, provide a rationale.

Cut-off:
- Provide details of the study design including:
    - Specify the population studied. This should align with the claimed target population within the technical documentation.

    - Provide the method for characterising the specimens.
    - Detail the statistical methods used for determining the assay cut-off (Receiver Operator Characteristic (ROC) to generate results and if applicable, define grey zone/equivocal zone).
- The results should align with claims in the IFU.

Analytical Sensitivity:

- Analytical sensitivity may be expressed as the limit of detection, i.e., “the smallest amount of the target marker that can be precisely detected“. For LoB, LoD and LoQ, the term detection capability is preferred (CLSI EP-17 A2:2012/ED2IG-2021).
- Should provide a description of specimen type including surrogate samples, matrix, analyte levels and how the levels were established. If a surrogate sample is used, manufacturer needs to provide a commutability study.

Demonstrate and document the analytical performance in a separate analytical performance report with a summary of the results including final claims in the instructions for use, including a rational for the acceptance criteria and sample sizes used.

Stability (applicable to reagents)

Claimed shelf-life:

- Provide details on the claimed shelf-life and storage conditions.
- Provide a study report which details the study protocol, the acceptance criteria and testing intervals. The report must include data on at least 3 lots of the device. Confirm if these are manufactured lots. If possible, also include the study protocol.
- Accelerated studies or extrapolated data from real time data are acceptable for initial shelf-life claims but shall be followed up with data generated from real time stability studies.
- In case accelerated aging data is used initially, the respective storage temperature needs to be considered for calculation (e.g., for room temperature the ambient temperature is 25 °C).
- Estimated dates by which the related real time aging data will be available need to be provided, including interim time-points, where applicable.

In-Use Stability:

- Provide details on the claimed in-use stability and storage conditions.
- Provide a study report which details the study protocol, the acceptance criteria and testing intervals.
- The study protocol needs to represent routine use, automated and manual processing needs to be addressed separately
- The study must include data on at least 1 lot of the device reflecting the actual routine use of the device, e.g., open vial stability, on-board stability, calibration stability.
- Data can be generated using real or simulated conditions.
- Indicate if the studies have been conducted at the start or end of the device shelf-life

Shipping and Transport:

- The transport of the product to the end user shall not adversely have any effect on the quality, safety or performance of the product.
- Shipping and transport studies should be planned.
- Provide details on the packaging types used - primary, secondary etc.
- Provide details of the specified shipping conditions.
- Provide a study report which details the study protocol, the acceptance criteria and shipping conditions assessed. Shipping conditions may be real or simulated but must include variable conditions such as extreme heat and or cold.

- Provide the packaging validation study report detailing the study protocol and acceptance criteria.
- If packaging/stability/shelf-life is being leveraged from another device, a detailed rationale should be provided on why this is appropriate.

For sterile packaging:

- Provide any applicable certificates/COA - for the packaging materials used to ensure the packaging is suitable for the sterilisation method used.
- Provide accreditation certificates for the testing facility.
- 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.
- Provide the protocol and report for the shelf-life studies covering device functionality as well as packaging integrity – accelerated aging and real time aging to be provided.

Note: EN ISO 23640 and the CLSI EP25-A Guidance provide instruction on conducting stability studies.

For Instruments:

- Provide details of the claimed lifetime of the instrument.
- Provide details of any parts that require replacing throughout the lifetime of the device or service periods required.

Metrological Traceability

- Provide details of the reference measurement procedure and or reference materials through which the assigned values of calibrators or controls are assured.
- If no international reference standard exists, an explanation must be also given about how the assay is standardized (e.g., how internal standards are prepared, what SOTA device is used as reference, etc.).
- Provide details of the calibration hierarchy and measurement uncertainty.
- Provide details of value assignment and validation of assigned values.
- Provide details on how traceability is maintained throughout the device lifecycle.
- Indicate the maximum allowable expanded measurement uncertainty for all the analytes in compliance with EN-ISO 17511:2020, section 4.3.1.

Note: EN ISO 17511 provides guidance on establishing metrological traceability

Usability

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 shall be in line with the risk management process.

Specific attention shall be paid to:

- Verification the device performs appropriately for the intended purpose considering the skills and the means available to user and the influence resulting from variations that can be anticipated in the user's technique and environment.
- Verification of the information supplied with the device also considering any training material provided to the intended user.
- Specifically for self-test devices – the accompanying documents should include a concise description of the device, which includes the operating principle, physical characteristics, significant performance characteristics and the intended user profile. The information and instructions are considered easy to understand and apply.

Chemical, Physical and Biological properties

Hazardous substances, CMR, endocrine disrupting substances

- Provide details of all hazardous substances incorporated into the device and the final concentration of the substance. In the case of a device with multiple components, details of which component the hazardous substance is included, see Regulation (EC) No 1272/2008 and Article 59 of Regulation (EC) No 1907/2006.
- GSPRs 10.3 describes specific requirements for devices that contain substances which are carcinogenic, mutagenic or toxic to reproduction and substances having endocrine-disrupting properties. Any risks should be addressed in risk management
- The technical documentation should provide information documenting the means of control of exposure to the device and contamination of the device.
- 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 labelling etc. The provisions of Regulation (EC) No 1907/2006 on the safety data sheet shall apply, unless all relevant information, as appropriate, is already made available in the instructions for use.

Sterilisation

If the device is intended to be supplied sterile or in a defined microbiological condition, provide a description of the environmental conditions for the relevant manufacturing steps.

In the case of devices placed on the market in a sterile condition provide:

- a description of the methods of sterilisation used including the environmental conditions for manufacturing,
- the validation protocol(s) and report(s)

The validation report shall address

- packaging
- sterilisation
- maintenance of sterility
- bioburden testing,
- pyrogen testing
- testing for sterilant residues (if applicable)

If the device is placed in a primary/secondary package that is intended to be the sterile barrier, provide the following:

- Microbial barrier integrity of materials and seals for packaging
- Packaging validation reports reflecting all seals
- Maintenance of sterility up to the labelled shelf-life (refer to EN ISO 11607-1)
- Packaging system performance testing (handling, distribution, storage)
- Where accelerated aging data is used initially, the respective storage temperature needs to be considered for calculation (e.g., for room temperature the ambient temperature is 25°C). Estimated dates by which the related real time aging data will be available need to be provided, including interim time-points, where applicable.

Biological Material

The submission should clearly indicate whether the device utilises or contains any human, animal or microbial based products. If the device includes multiple components, then identify the components which incorporate these substances.

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

Provide the following data:

- Identification of the biological material and/or composition for all components.
- For animal source material identify the conditions in which the material was collected, and the information about the (geographical) origin of the animals.
- Biological material related risk assessment
- Description of sourcing, processing, preservation, testing and handling and control procedures.
- Description of the transmissible agent inactivation performed, if applicable.

For devices containing raw materials of human, animal or microbial origin, a CoA must be submitted with information to fulfil Annex II, 6.5.b

Construction of devices and interaction with their environment

For devices used in combination with other devices and/or electrical equipment, the manufacturer must demonstrate safety of the entire combination, including safe calibration, maintenance and disposal. The submission should include a description of the total combination including proof this conforms to the requirements set out in GSPR 13 to maintain the specified characteristics.

- Specify the equipment or accessories that have to be connected with the device for its intended use, such as analysers/instruments or devices for sample preparation or purification.
- Provide evidence that the combination(s) in question are validated and covered by the performance evaluation.
- Equivalence studies might be provided for further combinations, e.g., same assay on new instrument. These should provide a rationale to justify this approach.
- In case of “open systems” where the combination is not limited to a specific device, product specifications and characteristics need to be defined.
- Provide details of the operating conditions that affect the device’s safety and the control measures to reduce associated risks.
- Provide details for safe disposal of device and packaging including precautions to be taken against any special, unusual risks related to the disposal of the device.

Devices with a measuring function

- Mostly applicable to IVD instruments, IVD Medical Device Software (mobile apps that carry out measurements) and general measurement devices (ESR tubes, haematocrit measurement).
- In the case of devices placed on the market with a measuring function, the submission should include a description of the methods used in order to ensure the accuracy as given in the specifications.
- Units of measurements must conform to the provisions of Council Directive 80/181/EEC.

Protection against radiation

- Provide details of the source of radiation and quantity that may be emitted.
- Provide evidence that exposure levels are appropriate for the intended purpose and have been reduced as far as possible.
- Specify the design characteristics to reduce exposure to emissions
- Provide details of the risk assessment conducted.
- Indicate what visual displays or audible alarms are in place to warn of emissions.
- Necessary detail must also be captured in the IFU especially guidance on user protection and avoidance of misuse.

Software & Software Validation

A clear statement and documented rationale as to why the product is an IVD Medical Device Software (IVD MDSW) is required. Consider the following Team-NB position paper on software qualification.

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 shall be provided that explains how the requirements of the harmonised version have been met or exceeded shall be provided along with the evidence, considering state of the art.

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

The Software system safety classification shall be provided and the justification for it shall be clearly identified in the technical file. The software version under application shall be clearly identified in the application.

Traceability matrices that contain 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 review. 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.

Software

Common required documentation

Across the notified bodies selected, the following common documented evidence is required at a minimum in the technical document. 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 shall be demonstrated in the file. All required activities of any applied (harmonized) software standard for compliance shall be demonstrated in the file, including supporting checklists.

Software development plan

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

Software with Software System Safety Classification Class B and C should include documentation describing the development environment used (tools, elements, settings, etc.).

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 IVDR Annex II 16.4, 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.

Software detailed design

For Software with Software System Classification 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 shall 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 16.3 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 shall 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 shall 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 shall clearly state the harmonised or SOTA standard(s) of compliance used for conformance to the relevant GSPRs.

The manufacturer shall 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 shall align with the principles of Confidentiality, Integrity, and Availability (reference MDCG 2019-16 Guidance on Cybersecurity for medical devices).

The manufacturer shall 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.

Electrical Safety and Electromagnetic Compatibility (EMC)

This GSPR is only relevant for IVDs connected or equipped to an electronic energy source.

The manufacturer should provide the following documentation:

- Electrical safety test protocols & Electrical safety test reports.
- EMC test protocols & EMC test reports. Test protocols may be embedded as part of the test report.
- Provide an 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, provide a description of requirements related to the periodic tests and tests after repairs

- 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.
- 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 shall be included.
- The technical documentation should include identification of associated risks.

Notes:

- *Relevant standards for ELSA*
  - *EN 61010 series, EN 61010-1 in conjunction with EN 61010-2-101 and eventually further particular standards like e.g., EN 61010-2-081*
- *Relevant standards for EMC*
  - *EN 61326-1 in conjunction with EN 61326-2-6*
  - *IEC 60601-1-2: FDA requirement for IVD EMC (IEC 61326 not harmonized)*

- *The safety of devices emitting ionising radiation and electrical devices in relation to these characteristics must be considered.*
- *For Performance Evaluation of (IVD) Medical Device Software, reference is made towards MDCG 2020-1.*

Protection against mechanical and thermal risks

This section is relevant only to devices with moving parts or those that generate heat.

Manufacturers must show evidence of the device is able to withstand stresses in the planned work environment(s). Any risks associated with moving parts, substance leakage/carryover, vibrations, noise and temperature of accessible parts must be considered.

The technical documentation should include identification of associated risks.

Protection against risk associated with devices intended for self-testing or near patient testing

Layperson studies/near-patient studies shall demonstrate the performance for the intended user population, taking into consideration the skills and means available to users, the environment, errors related to handling of device / specimen and interpretation of results.

For near patient testing and self-tests, the IFU should make it clear the level of training, qualifications and or experience required by the end user (GSPR 19.1, 19.2, 19.3).

For self-testing devices the IFU should make it clear the level of training, qualifications and or experience required by the end user.

Especially, requirements mentioned in Annex I, section 19.1, 19.2 and 19.3 shall be demonstrated.

Performance Evaluation (Includes SSP and labelling)

In line with IVDR Article 56 (1): *Confirmation of conformity with relevant general safety and performance requirements set out in Annex I, in particular those concerning the performance characteristics referred to in Chapter I and Section 9 of Annex I, under the normal conditions of the intended use of the device, and the evaluation of the interference(s) and cross-reaction(s) and of the acceptability of the benefit-risk ratio referred to in Sections 1 and 8 of Annex I, shall be based on scientific validity, analytical and clinical performance data providing sufficient clinical evidence, including where applicable relevant data as referred to in Annex III.*

The manufacturer shall specify and justify the level of the clinical evidence necessary to demonstrate conformity with the relevant general safety and performance requirements. That level of clinical evidence shall be appropriate in view of the characteristics of the device and its intended purpose.

'PERFORMANCE EVALUATION (IVDR) 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.'

To that end, manufacturers shall plan, conduct and document a performance evaluation in accordance with this Article and with Part A of Annex XIII.

Refer to MDCG 2022-2 for further guidance on the general principles of clinical evidence for IVDs and MDCG 2022-9 for a safety and performance template. Refer to MDCG 2020-1 for performance evaluation of (IVD) medical device software.

The following documents should be provided for the performance evaluation assessment and when not provided a suitable justification should be provided for their absence. Results and conclusions that are contained in these documents will feed into the main technical document that is used to demonstrate conformity with requirements in Annex II and Annex III of the IVDR.

Performance Evaluation Plan.

A performance evaluation plan (PEP) is required to be able to continuously update the performance evaluation. The plan should align to Annex XIII Part A.

- The Performance Evaluation Plan shall provide details for each indent specified in Annex XIII Part A section 1.1. Where an indent is not applicable a justification must be provided.
- It should be clear how scientific validity, analytical performance and clinical performance will be demonstrated.
- Details of which parameters from GSPR 9 are applicable and not applicable must be provided.
- Qualification of external study sites (e.g., for clinical performance studies) needs to be demonstrated.
- A description of what is considered state of the art must be included.
- If the intention is to rely on evidence generated for an existing device, provide a rationale as to how the data is considered current.
- The PEP shall be provided as a single document that should contain enough information to stand on its own.

Note: Please note that every PMPF supplementary study will trigger an update in the PEP.

Scientific Validity

The scientific validity shall demonstrate the association of an analyte with a clinical condition or a physiological state. Independent demonstrations may be required if more than one claim is included in the intended purpose. It must not necessarily include data obtained with the particular device being assessed. For companion diagnostics, the scientific validity should include supporting information on the medicinal product specified in the intended purpose.

For scientific (peer-reviewed) literature searches, the methodology, the protocol, and report of the literature review must be included in the scientific validity report.

Where conduct proof of concept studies and/or clinical performance studies are conducted study protocols and reports must be provided. Clinical performance studies that are conducted must meet the requirements of Annex XIII, section 2.

Analytical Performance

The regulation defines analytical performance as – *'the ability of a device to correctly detect or measure a particular analyte.'*

The analytical performance should describe the studies conducted to demonstrate the device correctly and consistently detects the intended analyte(s). Refer to the product verification section above. The analytical performance must be documented in the analytical performance report.

For performance data generated on earlier versions of the device, include a justification for why the changes do not impact the validity of the data collected and how the data is considered to meet state of the art requirements.

Clinical Performance

The regulation defines clinical performance as - *'The ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user.'*

Clinical performance shall demonstrate the characteristics listed in Annex I 9.1.b., although the list is not exhaustive and other characteristics may apply depending on the clinical function (e.g., agreement tables, patient outcome measure and interaction analysis (CDx), hazard ratio, odds ratio). All non-applicable characteristics must be justified. Additional evidence of clinical performance may be necessary if more than one claim is given in the intended use / intended purpose.

Clinical performance studies shall be performed unless due justification is provided for relying on other sources of clinical performance data. If other sources of clinical performance data are used to demonstrate clinical performance, this shall be made clear in the technical documentation provided. Ethical considerations shall be always demonstrated in the clinical performance study report when a clinical performance study has been carried out.

The clinical performance shall be documented in a Clinical performance report (CPR). Demonstration of clinical performance shall be based on the sources listed in Annex XIII, 1.2.3.

- Where clinical performance is demonstrated by a clinical performance study, an overview of the study protocol and results should be provided in the CPR. The clinical performance study plan and report should be referenced.

- Studies performed using diagnostic left-over samples are not affected by requirements described in Article 58 and Annex XIV.
- Where clinical performance studies have not been conducted a rationale must be provided for relying on other sources of data.
- Where clinical performance is demonstrated by scientific peer reviewed literature/published experience:
  - Full text copies of the relevant published literature that have been selected for review
  - Literature search protocols and reports
  - Full list of retrieved articles
  - Full list of excluded articles, with reasons for exclusion

Clinical Performance Study

Clinical Performance Studies are intended to establish or confirm the devices claimed clinical performance characteristics.

A clinical performance study plan must be provided which documents all elements listed in Annex XIII Section 2.3.2. A rational must be provided for any element which is not applicable to the device or study.

A clinical performance study report must be provided, when clinical performance studies are used to support clinical evidence. It must be signed by a medical practitioner or other authorised responsible person. It shall confirm the study plan was followed and document the results including any negative findings. The conclusion shall be free of bias and clinically relevant.

Product verification by EURL

- Provide details of any applicable common specifications.
- Provide test release criteria.
- Provide re-test procedures and supporting documentation.
- If the device is currently on the market, provide QC release trends for last 20 batches or last 3 years, whichever is greatest.

Common Specifications

For all devices, for which Common Specifications (CS) are published, clearly identify the specific applicable requirements and provide evidence for compliance, e.g., by means of a correlation table and references to the details in the study plans and reports within the performance evaluation. Devices that are in conformity with the common technical specifications set out in Decision 2002/364/EC shall be presumed to be in conformity with the requirements regarding the performance characteristics set out in Section 9.1, points (a) and (b), Section 9.3 and Section 9.4, point (a), of Annex I to Regulation (EU) 2017/746.

Performance Evaluation Report

A Performance Evaluation Report (PER) is always required for the device per Article 56 (6). The PER should be a stand-alone document. The PER should provide the information as listed in Annex XIII 1.3.2. The report should include:

- The manufacturers assessment of the scientific validity, the analytical and the clinical performance to confirm the performance characteristics as planned in the PEP and the clinical

evidence. A justification for the chosen approach to gather clinical evidence needs to be provided.

- Conclusion as to the requirements of PMPF.
- Specification of the frequency of PER updates and provision of this rationale.
- For novel class D, where performance evaluation consultation procedure is required by Expert Panel according to IVDR Article 48(6), the PER should be marked "SENSITIVE and RELEASABLE to EXPERT PANEL (EXPAMED)" on front page.

Post Market Performance Follow Up

Post Market Performance Follow Up (PMPF) Plan.

PMPF is an integral part of the Post Market Surveillance system of the manufacturer. The content of the PMPF plan should consider at a minimum the requirements of Annex XIII Part B by providing the following information:

- General PMPF methods and procedures to be applied (or justification for absence of any activities as mentioned in Annex XIII Part B 5.2 (a)).
- Specific PMPF methods and procedures to be applied (or justification for absence of any activities as mentioned in Annex XIII Part B Part B 5.2 (b)).
- If the PMPF plan includes a PMPF study, then the full detailed study protocol should be provided with statistical analysis plans, and a clear statement from the manufacturer indicating commitment to the PMPF plan.
- If the PMPF plan does not include a PMPF Study, then a justification should be provided per Annex III of the IVDR.
- If a PMPF study is not required a rationale should be provided in the performance evaluation report.

Post Market Performance Follow Up (PMPF) Evaluation Report.

The content of the PMPF Evaluation Report should consider the following points:

- Include any information and reports from PMPF activities previously carried out.
- The PMPF evaluation report should include all general PMPF methods and procedures applied (Annex XIII Part B 5.2 (a)) and specific PMPF methods and procedures applied (Annex XIII Part B Part B 5.2 (b)).
- The report should identify the PMPF studies and stratify the data to the applicable indication of use and further stratified to the models/variants that have been included. In cases with multiple indications, sizes and variants - tabulated data is preferable.
- A PMPF Evaluation report may typically not yet be available at the time of the initial dossier submission with a Notified Body.

Summary of Safety and Performance (SSP).

Per Article 29 of the IVDR, all Class C and D devices require an SSP.

The content of the SSP Report should be aligned to the layout template and guidance provided in MDCG 2022-9 and should consider the following aspects:

- All information provided in the SSP must be traceable to the technical documentation.
- Confirm with your notified body the languages preference for validation of the SSP.
- The SSP should be in pdf format, printable and searchable and follow the template provided in MDCG 2022-9.

- The SSP should be updated as soon as possible (as per Article 56), where necessary.

For devices that could be considered to have a more direct impact on an individual patient, a second part dedicated to patients/lay persons should be added to the SSP. If it is decided that a patient version/layperson is not applicable, then a justification must be provided.

For self-test devices a patient/layperson version must be provided.

For the patient/layperson version SSP ensure:

- Appropriate patient/layperson terminology is used throughout the document in addition to stylistic recommendations.
- Evidence is provided of an appropriate validation technique of the patient/layperson test.
- The layout template and guidance provided for the patient/layperson in MDCG 2022-9 is applied and the provided example statements have been considered.

Post Market Surveillance

The submission should contain the following documentation on post-market surveillance:

- The post-market surveillance plan (in line with IVDR Article 79 and Annex III), including the search terms used in the search for serious incidents, field actions, relevant specialist or technical literature
- The post-market surveillance report (in line with IVDR Article 80) for Class B devices, if available.
- Periodic safety update report (in line with IVDR Article 81) for Class C and D devices, if available.
    - For Class D devices the PSUR should be submitted to the Notified Body (Article 81). These documents must be updated at least annually.
    - Periodic safety update report should be stand-alone document, per MDCG 2022-21.
- PMPF plan (as detailed in Part B of Annex XIII), PMPF study protocols and PMPF evaluation report (or a justification as to why a PMPF is not applicable).
- A copy of the Post Market Surveillance procedure and the procedures put in place to ensure compliance with the obligations resulting from the provisions on vigilance set out in Articles 82 to 87.

The manufacturer should also provide the following post market surveillance data for the last 5 years:

- Market History.
- Worldwide and EU sales volumes.
- Complaint data and trend analysis.
- Vigilance data and trend analysis (include details of any adverse incidents, recalls or FSCA)
- Publicly available information about similar medical devices.
- Modifications made and/or corrective actions taken following the incidents reported and revisions made to the risk management file.

Notes: *MDCG 2022-2, Appendix II includes a summary of the required frequency for updates of reports.*

Multiple devices can be addressed in a combined PMS plan. However, it needs to be ensured that the specific regulations/aspects applying to an individual device (Basic UDI-DI) are traceable in the PMS plan. Where applicable, manufacturers must also include a post-market performance follow- up plan

(Annex XIII, Part B), or a justification of why this is not applicable. The outcome of this must be documented in the post-market performance follow-up report.

For the PMS report, complaints data should be evaluated rather than just listed. Full details of vigilance issues should be provided, including the status of any Field Safety Corrective Actions or Notices, the associated CAPAs and patient outcomes. This data should include FSCA or FSN outside the EU, if related to a device which is sold in the EU. Ensure that all PMS data at the time of submission is up to date.

Already available data can be submitted and may be requested for legacy devices i.e., devices sold under the IVD Directive.

Companion Diagnostics

Devices classed as companion diagnostics:

- Must be essential in developing or generating the supporting information for the corresponding medicinal product.
- Must have a corresponding medicinal product. In some instances, a single device may be linked with multiple medicinal products, e.g., panel tests.

The Technical Documentation requirements for a companion diagnostic are the same as other devices. Additional requirements include:

- The International Non-proprietary Name (INN) of the associated medicinal product for which it is a companion test.
- The relevant target population and the associated medicinal product(s).
- A draft Summary of Safety and Performance (SSP and draft instructions for use (IFU need to be part of the application, as a basis for the consultation process between the Notified Body and the designated competent authority for the medicinal product (e.g., European Medicines Agency (EMA) to seek a scientific opinion. The provided information should enable the determination of the suitability of the device in relation to the medicinal product concerned.
- The suitability of the device in relation to the medicinal product will be reviewed by one of the CA designated by the Member States or EMA for the Evaluation of Medicinal products. This will be triggered by the NB reviewer and a scientific opinion made available within the timelines set forth in Annex IX (Section 5.2 (d)).
- An EU Technical Documentation certificate will not be issued until a scientific opinion has been received from the relevant CA or EMA.
- Additional resources may also be required for external independent reviews and/or software review.

Revision History

Version No	Date	Brief description of main changes
1	25th February 2023	Initial release
2	3rd September 2025	Various section updates to bring contents up to date Clarification in wording and improved formatting (including table of abbreviations).