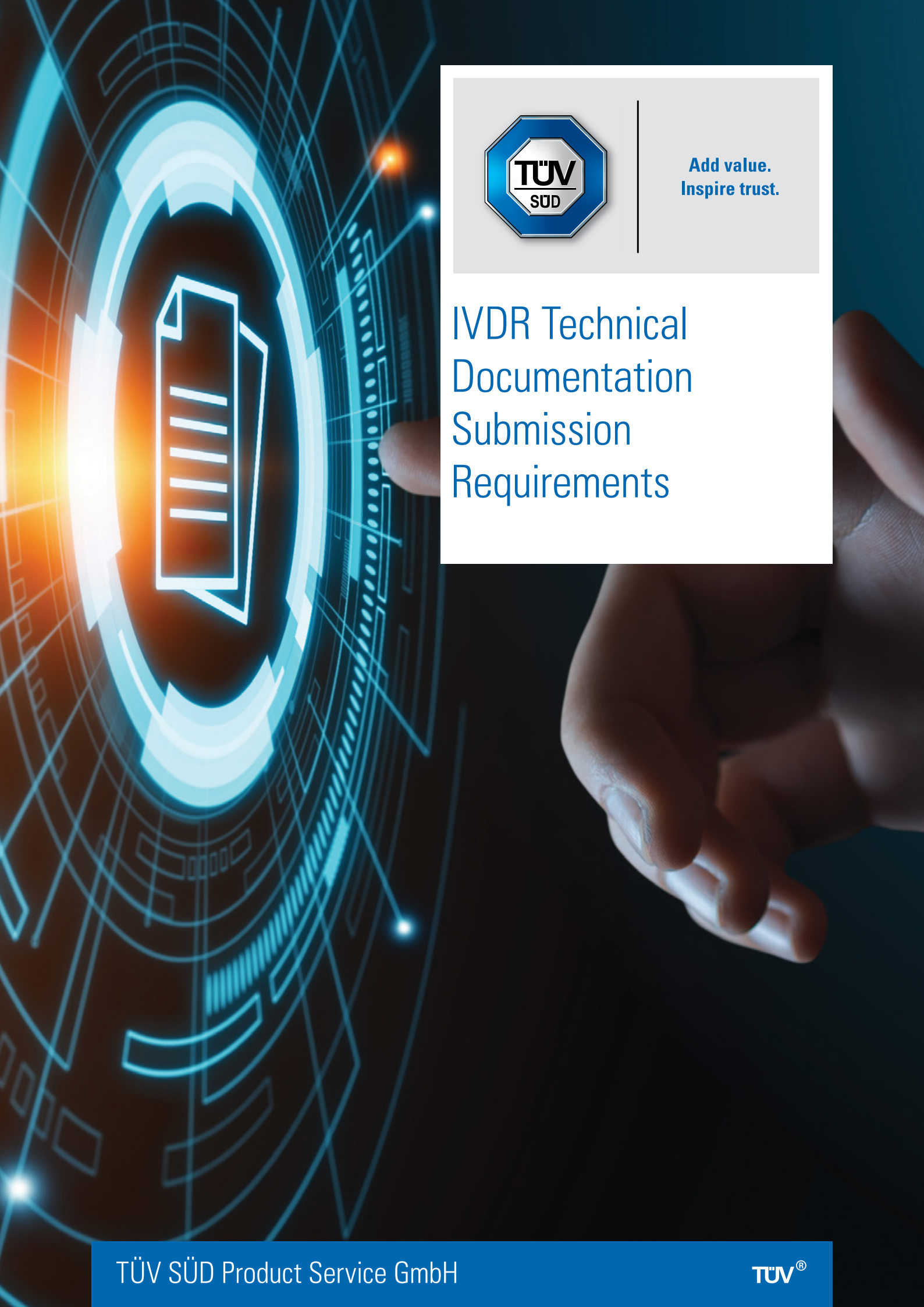

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IVDR Technical Documentation Submission Requirements

TÜV SÜD Product Service GmbH

I. Introduction

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL (IVDR) requires all manufacturers of In Vitro Diagnostic Devices to draw up and keep up to date a Technical Documentation as described in Annex II and Annex III of that Regulation.

Depending on the classification and Conformity Assessment procedure chosen, a Notified Body assesses the Technical Documentation and whether it complies with the requirements described in the IVDR.

This document provides an overview on how to submit a Technical Documentation, and what documentation can be expected. It does NOT give guidance on what the contents of the Technical Documentation should look like and how regulatory requirements are fulfilled. It is the sole responsibility of the manufacturer to comply with all requirements given in Annex II and Annex III of the Regulation.

By following this document, you help to perform an efficient and timely assessment of the Technical Documentation. If this document or parts thereof is not followed, it will still be possible to conduct a successful assessment of the Technical Documentation, however, the time needed, and hence the costs associated, could increase.
We hope this document provides you with a helpful tool in submitting your Technical Documentation. Please do not hesitate to contact your personal client manager

II. Administrative Notes

Please submit your complete Technical Documentation, either via the TÜV SÜD DropOff fileshare portal, via USB drive or via CD. All documents should be readable and searchable PDFs and filenames used should be meaningful. All documents should be in a released state, exceptions can occur as for e.g. the SSP. All documents and records should be controlled by revision/version and/or date, approval by the respective responsible personnel should be traceable, if applicable. In case the Technical Documentation gets revised during the review process, please also update the text boxes within this document accordingly and resubmit it.

III. Technical Documentation

The Technical Documentation and the summary thereof shall be presented in a clear, organised,readily searchable and unambiguous manner and shall include in particular the elements listed in Annex II and III of the IVDR.
The complete Technical Documentation must be submitted in full. References to files from other products or previous submissions are not accepted.

To allow an efficient assessment of the Technical Documentation, the following chapter should be used to point us to the sections in the Technical Documentation, where the relevant information can be found.

Please complete each section below, by either entering the file(s) where the relevant information can be found, or by ticking the “Not Applicable”-box (n.a.). If a section is not applicable, please provide a reference to the location in the

Technical Documentation, where a rationale for non-applicability can be found. Please enter the filename, and the document title and version/date, in the respective fields. If information is to be found at multiple locations within the Technical Documentation, please indicate what information can be found where (be precise and specific).

1. Device description and specification, including variants and accessories (Regulation (EU) 2017/746 (IVDR), Annex II Section 1)

1.1 Product or trade name

The product name shall be consistent with the product displayed on the product's packaging and marketing brochures as well as the application.

n.a.

1.2 Basic unique device identifier

The Basic UDI device identifier attributed by the manufacturer to the device in question, as soon as identification of this device shall be based on a UDI system, or otherwise clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability.

n.a.

1.3 Intended purpose, intended user and general device description

Intended purpose of the device:

- what is to be detected and/or measured;
- its function such as screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction,companion diagnostic;
- the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate;
- whether it is automated or not;
- whether it is qualitative, semi-quantitative or quantitative;
- the type of specimen(s) required
- testing population;
- Intended user of the device: what is the intended user group of the device, such as self-testing,near patient and laboratory professional use, healthcare professionals;
- for CDx, the relevant target population with associated medicinal product;

n.a.

General device description:

- the description of the principle of the assay method or the principles of operation of the instrument;
- the description of the reactive ingredients of relevant components such as antibodies, antigens, nucleic acid primers; and where applicable:
- the description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use;
- for instruments of automated assays: the description of the appropriate assay characteristics or dedicated assays;
- for automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation;
- a description of any software to be used with the device

n.a.

1.4 Qualification of the product as a device

Rationale for the qualification of the product as an In Vitro Diagnostic medical device.

n.a.

1.5 Classification / risk class of the device

The rule(s) used for classification including the bullet point of classification rule shall be named, a justification shall be given.

n.a.

1.6 Configurations and variants of the device

If there are any configurations and variants of the device, this shall be laid down in the Technical Documentation, including any model numbers, names, constituents, sizes etc.

n.a.

1.7 Composition of the device

All components and ingredients of the device shall be shown, including, if applicable, CAS numbers, concentrations etc.

n.a.

1.8 Principle of action

What is the principle of action of the device. The description should be specific enough to allow the user to understand the functioning of the device.

n.a.

1.9 Accessories and device combinations

A description of all accessories, other medical devices and other products (generic, batteries, covers, bags…) that are not medical devices, which are intended to be used in combination with it.

If the device is to be connected to other device(s) in order 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.

Accessories provided separately need to have their own labelling, instruction for use, packaging and certification.

n.a.

1.10 Accessories / equipment required for use but not provided with the devices

A description of all accessories / equipment that is required for use, but not provided with the device. Must also be mentioned in the IFU.

n.a.

1.11 Reference to previous and similar Generations of the Device

An overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist; An overview of identified similar devices available on the Union or international markets, where such devices exist.

n.a.

2. Information supplied by the manufacturer (Regulation (EU) 2017/746 (IVDR), Annex II Section 2)

The label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in the case of specific management conditions, in the languages accepted in the Member States where the device is envisaged to be sold; The instructions for use in the languages accepted in the Member States where the device is envisaged to be sold.

n.a.

3. Design and manufacturing information (Regulation (EU) 2017/746 (IVDR), Annex II Section 3)

3.1 Design Information

Information to allow the design stages applied to the device to be understood.
Information on the specific design stages, the techniques that are used to control, monitor and verify the design of the device during these stages.

A summary on the design process with reference to the applied implemented documented procedure(s) and versions date shall be included. For CDx, the design with regards to suitability of the device in relation to the medicinal product concerned.

n.a.

3.2 Manufacturing Information

Manufacturing includes production, assembly, packaging, sterile packaging, sterilisation, final packaging (as applicable).

Flow Chart including operation steps, time points of in-process controls (monitoring) and final controls, reference of manufacturing procedures (ID numbers sufficient for traceability). A summary of manufacturing processes allowing an understanding of the critical process steps and utilities and process chemical required to product the device.
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 and corresponding control measures (e.g. references to verification and validation activities, copy of the certificate shall be included).

n.a.

4. General Safety and Performance Requirements (Regulation (EU) 2017/746 (IVDR), Annex II Section 4)

Fulfilment of all applicable General Safety and Performance Requirements must be shown. If this is done by a GSPR checklist, please make sure: Non-applicable General Safety and Performance Requirements shall have a justification as to why they are not applicable to the device.

Demonstration of conformity includes a precise identity of the controlled documents offering evidence of conformity with harmonised standards, common specification or other method employed to demonstrate conformity with the General Safety and Performance Requirements. A cross-reference to the location of such evidence is provided.

n.a.

5. Benefit-Risk Analysis and Risk Management (Regulation (EU) 2017/746 (IVDR), Annex II Section 5)

All relevant risk management files according to the current state of the art, including at minimum a plan and report.
If the plan and report are not self-explanatory, a copy of the relevant risk management procedure(s) should be provided.

n.a.

5.1 Specific Usability Risks (only for Self-Testing / Near-Patient Testing)

The risk files should specifically address risks with regards to usability related to self-testing or near-patient testing.
All known and foreseeable hazards associated with layman / near-patient use must be identified.

All risks associated with these hazards occurring during intended use and during reasonable foreseeably misuse must be estimated and evaluated.

Risk control measures related to use error conform to safety principles, taking account of the generally acknowledged state of the art. Risks related to the ergonomic features of the device and the environment in which the device is intended to be used must be reduced as far as possible.

The technical knowledge, experience, education, training and use environment must be considered.
The medical and physical conditions of intended users must be considered.

n.a.

6. Benefit-Risk Analysis and Risk Management (Regulation (EU) 2017/746 (IVDR), Annex II Section 6)

Note: All verification and validation documents in the sections below shall at a minimum comprise a plan, including acceptance criteria and a rationale for sample size, and a report that analyses and summarised the results.

6.1 Specimen Type / Handling

A description of specimen type and handling, including, where applicable:

- Different specimen types that can be analysed
- Determination of appropriate criteria for specimen collection and handling, stability, storage,transport
- Usage of different anticoagulants (EDTA, Citrate, Heparin, etc.)
- The influence of sample pretreatment
- The influence of sample storage and freeze and thaw cycles

n.a.

6.2 Analytical Performance

The analytical performance shall contain at a minimum, where applicable:

- Accuracy and precision of measurement
  The intra- and inter-assay-precision. The samples should be representative and cover different levelsof reactivity.
- Analytical sensitivity
  Specimen type, number of replicates, concentration tested, calculation of determination of sensitivity should be clear.
- Analytical specificity
  Interfering endogenous / exogenous substances investigated:
- Substances used for patient treatment (e.g. medicinal products)
- Substances ingested by patient (e.g. alcohol, food)
- Substances added during specimen preparation (e.g. preservatives, stabilisers)
- Substances encountered in specific specimen types (e.g. hemoglobin, lipids, bilirubin, proteins)
- Analytes of similar structure (e.g. precursors, metabolites)
- Typical interfering substances
- Metrological traceability of calibrator and control material values
- Measuring range of the assay
- Limits of detection and quantitation
- Measuring range (including high dose hook effect)
- Linearity
- Definition of assay cut-off

Including description of study design, populations studies, method / mode of specimen characterisation, statistical methods.

The results should be summarised in the analytical performance report. It shall contain a conclusion if the Safety and Performance requirements (including Common Technical Specifications / Common Specifications) concerning the

sensitivity and specificity are fulfilled. It shall demonstrate the analytical performance, taking into consideration the state of the art (e.g. CE-marked reference test applied).

n.a.

6.3 Clinical Performance

The clinical performance must be demonstrated based on:

- Clinical performance studies and/or
- Scientific (peer-reviewed) literature and/or
- Published experience gained by routine diagnostic testing

If Clinical Performance Studies are performed, a Clinical Performance Study Plan and Report shall be provided. The report shall include, where applicable:
Diagnostic sensitivity

- Diagnostic specificity
- Positive predictive value
- Negative predictive value
- Likelihood ratio
- Expected values in normal and affected populations

n.a.

6.4 Performance of self-testing devices / Near-patient testing devices

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.

n.a.

6.5 Scientific Validity

Scientific validity shall be demonstrated and documented in the scientific validity report
Scientific validity demonstrated based on:

- Relevant information of devices measuring the same analyte or marker and/or
- Scientific (peer-reviewed) literature and/or
- Consensus expert opinions / positions from relevant professional associations and/or
- Results from proof of concept studies and/or
- Results from clinical performance studies and/or

n.a.

6.6 Performance Evaluation Report

An overall Performance Evaluation Report shall summarise all performance evaluation results and shall contain at a minimum, where applicable:

- Justification for the approach taken to gather clinical evidence.
- Literature search methodology / protocol / report of literature review (or a reference to it).
- Technology on which the device is based, the intended purpose of the device and any claims made about the device's performance and/or safety.
- Scientific validity and analytical / clinical performance.
- Clinical evidence demonstrating the state-of-the-art of the device.
- New conclusions derived from Post-Market Performance Follow-Up (PMPF).

n.a.

6.7 Stability (REGULATION (EU) 2017/746 (IVDR), Annex II Section 6.3)

Demonstration of the claimed stability by appropriate studies, including plan(s) with predefined acceptance criteria and rationale(s) for sample size. Where appropriate:

Real-time stability, accelerated stability, on-board stability, open vial stability, shipping stability.

n.a.

6.8 Software Verification and Validation / Functional Safety / Cybersecurity (REGULATION (EU) 2017/746 (IVDR), Annex II Section 6.4)

Documents regarding validation of the software (verification, validation and testing performed in-house and in actual user environment. Documentation should demonstrate the product was developed and manufactured according to state-of-the-art taking into account the principles of development life cycle, risk management, information security, verification and validation.

n.a.

6.9 CHEMICAL, PHYSICAL AND BIOLOGICAL PROPERTIES (REGULATION (EU) 2017/746 (IVDR), Annex II Section 6.5)

6.9.1 Nanoparticle Technology

The documentation should demonstrate that the nanoparticles were designed and manufactured in such a way as to reduce as far as possible risks linked to the size and the properties of particles used.

n.a.

6.9.2 Hazardous Substances

A documentation of all hazardous substances that are incorporated in the device, and how they are controlled and labelled. Any risks should be addressed in risk management.

n.a.

6.9.3 Substances of Animal / Human / Microbiological Origin

A documentation of all substance of Animal / Human / Microbiological Origin. What component is affected, what control measures are performed. A validation should be available, if applicable. Any risks should be addressed in risk management.

n.a.

6.9.4 Sterile Devices or Devices with Defined Microbiological Condition

In the case of devices placed on the market in a sterile or defined microbiological condition, a description of the environmental conditions for the relevant manufacturing steps.

In the case of devices placed on the market in a sterile condition, a description of the methods used, including the validation reports, with respect to packaging, sterilisation and maintenance of sterility. The validation report shall address bioburden testing, and, if applicable, testing for sterilant residues.

n.a.

6.9.5 Constructional Safety

6.9.5.1 Mechanical Safety

A documentation that demonstrates that all relevant harmonised (if applicable) or state-of-the-art standards and IVDR provisions were followed, including minimisation of all identified risks.

n.a.

6.9.5.2 Electrical safety / electromagnetic compatibility

A documentation that demonstrates that all relevant harmonised (if applicable) or state-of-the-art standards and IVDR provisions were followed, including minimisation of all identified risks.

n.a.

6.9.5.3 Ionising and non-ionising radiation

A documentation that demonstrates that all relevant harmonised (if applicable) or state-of-the-art standards and IVDR provisions were followed, including minimisation of all identified risks.

n.a.

6.9.5.4 Environmental protection and safe disposal

A documentation that after use, the disposal of product and packaging in accordance with hospital, administrative and/or local government policy is safe. Precautions to be taken against any special, unusual risks related to the disposal of the device should be included in the labelling.

n.a.

6.9.5.5 Packaging

A description of the packaging including a documentation the demonstrates that packaging will not adversely affect the device characteristics and performances during the shelf life of the device. Validation of packaging with regards to integrity, cleanliness, and sterilisation, where applicable.

n.a.

6.9.5.6 Devices with connection to other device(s)

Information how to obtain a validated and safe combination (including key performance characteristics).

A demonstration that the whole combination (including the connection system) is safe and does not impair the specified performances. Information given on known restrictions to combinations. If device needs to be connected to other equipment, description of combination given including proof that it conforms to the general safety and performance requirements.

n.a.

6.9.6 Devices with a Measuring Function

Measurements should be expressed in legal units conforming to provisions the respective regulatory requirements. Metrological traceability of values assigned to calibrators and control materials must be shown.

n.a.

7. Summary of Safety and Performance (SSP) (only class C and D devices) (Regulation (EU) 2017/746 (IVDR), Article 29)

A summary of Safety and Performance should be documented. It should:

- be written in an understandable language for the intended target group.
- include the identification of the device, including the basic UDI DI and the single registration number.
- include the intended purpose of the device and any indications, contra-indications and target populations.
- include a description of the device, as well as a description of the accessories, other medical devices and combination with other devices, and a reference to previous generation(s) or variants.
- include the summary of the performance evaluation report and relevant information on the post-market production follow up.
- include references to harmonised standards and common (technical) specifications.
- include metrological traceability of assigned values.
- include suggested profile and training for users.
- include information on any residual risks and any undesirable effects, warnings and precautions.

n.a.

IV. POST-MARKET SURVEILLANCE (REGULATION (EU) 2017/746 (IVDR), Annex III)

1. Post-market surveillance plan

The post-market surveillance plan shall address the collection and utilisation of available information, in particular:

- information concerning serious incidents, including information from PSURs, and field safety corrective actions,
- records referring to non-serious incidents and data on any undesirable side-effects,
- information from trend reporting,
- relevant specialist or technical literature, databases and/or registers,
- information, including feedbacks and complaints, provided by users, distributors and importers,and
- publicly-available information about similar medical devices.

The post-market surveillance plan shall cover at least:

- a proactive and systematic process to collect any information referred to above. The process shall allow a correct characterisation of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market;
- effective and appropriate methods and processes to assess the collected data;
- suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;
- effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field;
- methods and protocols to manage the events subject to the trend report as provided for in Article 83, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period;
- methods and protocols to communicate effectively with competent authorities, notified bodies,economic operators and users;
- reference to procedures to fulfil the manufacturers obligations laid down in Articles 78, 79 and 81;
- systematic procedures to identify and initiate appropriate measures including corrective actions;
- effective tools to trace and identify devices for which corrective actions might be necessary; and
- a PMPF plan as referred to in Part B of Annex XIII, or a justification as to why a PMPF is not applicable.

n.a.

1.1 Periodic Safety Update Report (PSUR) (only class C and D devices)

The results and conclusions of the analyses of the gathered post-market surveillance data according to Annex III together with a rationale and description of any preventive and corrective actions taken shall be gathered in a PSUR, all PSURs are part of the Technical Documentation.

Throughout the lifetime of the device concerned this report shall set out:

- the conclusion of the benefit risk determination;
- the main findings of the Post Market Performance Follow-up Report and
- the volume of sales of devices and an estimate of the population that use the device
- and, where practicable, the usage frequency of the device.

Manufacturers of class C and D devices shall update the report at least annually and it shall be part of the technical documentation as specified in Annexes II and III.

n.a.

2. Post Market Performance Follow-Up (PMPF)

PMPF Evaluation reports analysing and concluding results of activities performed according to the PMPF plan shall be part of the Technical Documentation.

It should include. at least items according to Annex XIII part B 5.2. Conclusions of the PMPF evaluation reports shall be taken into account for the performance evaluation and in the risk management. Performance evaluation report shall be updated as per the PMPF plan.

n.a.

V. Proposed Perimeters for Products Verification Program (only class D devices)

Description of the final Quality Control release testing protocol (specification of samples / panels used, final release criteria). The information must match with the document provided to the Notified Body with the request to release the respective batch of class D product.

n.a.

Thank you for using this submission requirements document.

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TÜV SÜD is a trusted partner of choice for safety, security and sustainability solutions. It specialises in testing, certification, auditing and advisory services. Since 1866, the company has remained committed to its purpose of enabling progress by protecting people, the environment and assets from technology-related risks. Through more than 24,000 employees across over 1,000 locations, it adds value to customers and partners by enabling market access and managing risks. By anticipating technological developments and facilitating change, TÜV SÜD inspires trust in a physical and digital world to create a safer and more sustainable future.

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