Centro Nacional de Certificación de Productos Sanitarios

Technical Documentation Guidance:

Regulation (EU) 2017/746 (IVDR)

MINISTERIO DE SANIDAD

CNCPS CENTRO NACIONAL DE CERTIFICACIÓN DE PRODUCTOS SANITARIOS

Notified Body 0318

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1. Introduction

The application to the Notified Body for the CE certification of an *in vitro* diagnostic medical device is done once the manufacturer has verified that the device complies with the requirements of Regulation 2017/746 (IVDR).

The technical documentation of *in vitro* diagnostic medical devices must be in compliance with the requirements of the IVDR.

The IVDR introduces, for the first time, explicit provisions for the preparation and updating of such documentation in Annexes II and III.

The correct application of these provisions by the manufacturer is a determining factor for the success of the conformity assessment process and the maintenance of the CE marking.

This booklet provides additional guidance from this Notified Body to ensure that documentation is provided accurately and in line with the assessment criteria of the Centro Nacional de Certificación de Productos Sanitarios ("National Certification Center for Medical Devices", hereafter CNCps).

The CNCps takes the IVDR, as well as the harmonised standards, common specifications, pharmacopoeial monographs, European guidelines, applicable MDCGs and the current state of the art as a reference in its assessment.

The assessment of the technical documentation carried out as part of the application for certification under the IVDR is an initial assessment and not a transfer of information under Directive 98/79/EC (IVDD).

The technical dossier thus acts as a letter of introduction and information exchange between the company and Competent Authorities, Notified Bodies, potential customers, third country authorities or external experts.

This document is intended as a guide for manufacturers in preparing and submitting the technical documentation required for conformity assessment of their devices.

2. Characteristics of the Technical Documentation format

2.1. Previous considerations

The technical documentation is:

- MANDATORY for all *in vitro* diagnostic devices regardless of their risk class.
- CRITICAL for the conformity assessment procedure.
- PREREQUISITE to demonstrate compliance with the general safety and operational requirements of the IVDR.
- UPDATED AND MAINTAINED throughout the device life cycle.

As stated in the IVDR, technical documentation shall be presented in a clear, organised, easily searchable and unambiguous manner:

- CLEAR: The information should follow a coherent structure. The manufacturer should avoid repeating the same information on several documents, cross-references may be used instead. Explain the use of internal company jargon and abbreviations. If necessary, provide a glossary.
- ORGANISED: The manufacturer should name the documents in such a way that their content can be easily identified, and structure them in folders according to the table of contents. If the technical limitations of the CNCps platform do not allow for the creation of sub-folders, the manufacturer can use "zip" files to organize the documentation instead.
- EASY TO SEARCH: Scanned, non-searchable documents should be avoided. However, in certain cases, it may be necessary to provide a scan of a handwritten document or the signature page if the document has been signed manually (nonetheless the rest of the document must still be provided in searchable format).
- INEQUIVOCAL: The technical documentation should always use the same terminology and the same name for the device, for the reports or the manufacturing premises throughout the documentation.

To ensure documentary traceability it is important that the name of the technical documentation/technical dossier identifying each device is always entered in the same way in the CNCps application.

To avoid server problems, this name will be a maximum of 35 characters.

The device name shall match the name included in the form IVDR_DEX_04_Devices. The name should be unique as far as possible and identical to the name used on the labelling and in the technical documentation.

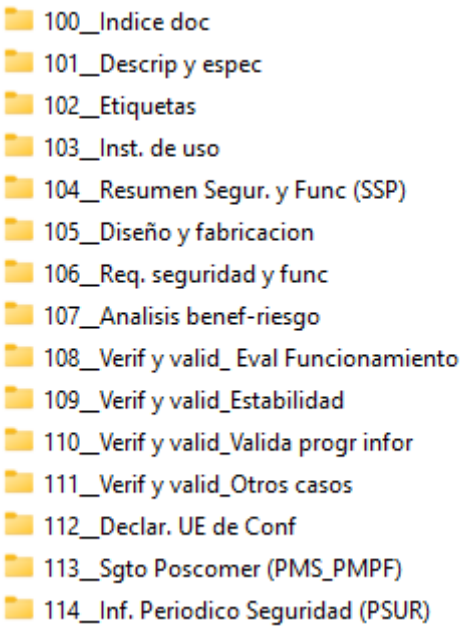
2.2. Language

The application documents shall be written in Spanish. However, the CNCps may accept the submission of technical, scientific or specialised documentation in English. In any case, the CNCps reserves the right to request the translation of any document into Spanish.

2.3. Structure of the technical documentation

The CNCps requires that the technical documentation is submitted in an orderly manner, according to a set folder structure that the manufacturer can download from the platform at the time of making an application. These folders are based on the sections of Annex II and III of the IVDR.

The CNCps technical documentation structure is made up of 15 folders:



The information contained in each folder is key to the evaluation of the technical dossier. The most common causes of delay in the evaluation are the submission of incomplete applications and poor documentation structuring. Technical documentation should therefore be presented in a clear, organised, easily searchable, unambiguous and complete manner. This will result in a faster review and reduce the time for the certification decision.

For initial applications, the complete technical file must be submitted with all relevant documentation to evaluate the device, regardless of whether the device has been previously certified under Directive 98/79/EC by the CNCps.

Depending on the characteristics and classification of the device, it may not be necessary to include documentation in all the folders; only when it is applicable. For example, it may not be necessary to provide the SSP in the "004_Resumen Segur. y Func. (SSP)" folder for Class A and B. However, in those cases, it is still necessary to introduce at least a document stating that such section is not applicable, to avoid reading errors by the CNCps platform.

For design modification requests, only the documentation affected by the change needs to be attached.

2.4. Format

The technical documentation must have been previously reviewed and approved in accordance with the documentation control procedure of each company. Nevertheless, draft versions of some documents such as the declaration of conformity or the safety and performance summary (SSP) may be accepted.

The following document formats will be accepted:

- Searchable PDF files.
- Microsoft Office files.

For graphical information will be accepted:

- Images in JPG, PNG, BMP, GIF or any other format that does not require special software.
- Videos in MP4, WEBM, AVI, WMV, MKV or any other format that does not require special software to reproduce.

3. Content of the Technical Documentation

This section includes some indications to be taken into account when preparing the technical documentation and placing it in the relevant folders. The tables included in each sub-section show a reference to the IVDR requirements and additional observations by the CNCps.

3.1. Table of contents and cover letter (Folder "100_Indice doc")

Folder	IVDR reference	Considerations
Folder 100: Indice doc	-	This folder should include: - Cover letter - Table of contents - Identification of documents in each folder

The cover letter shall include a summary of the following:

- The name, address and SRN of the manufacturer and, if applicable, the authorized representative. It must be consistent with the device labels, instructions for use and the declaration of conformity.
- The type of application (new device, design change, etc.) and the conformity assessment route requested. If it is a device previously certified under Directive 98/79/EC, include a reference to the IVDD certificate number.
- For requets of change certification conditions (design modifications, inclusion of new variants, changes in the quality management system, etc.), provide the certificate number concerned.
- Device name: name of the device as it appears on the label and associated documents.
- Brief description of the device, including classification (according to Annex VIII).

The table of contents shall list the documentation included on each folder, including the identification code of the document(s) provided, its date, version and/or edition.

If certain documentation is not applicable, this shall be expressly indicated.

Note: Table layout example for the table of contents (include one row per folder):

Folder	Applicable/ Not applicable	Documentation
Folder 1XX_*Folder Name*	Indicate in this column if the folder is applicable (A) or not (NA)	Include in this column the list of the documents included in each folder In case of design modifications: identify the documents that have been modified If deemed not applicable (NA), please include the justification in this column

3.2. Description and specifications (Folder "101_Descripcion y espec.")

Folder	IVDR reference	Considerations
Folder 101: Descripcion y espec"	Annex II, point 1	In addition to classification according to Annex VIII, describe the IVR, IVD, IVP, IVS and IVT codes applicable to the device, as well as the generic group according to the European Nomenclature (EMDN).

This folder will include a main document containing all the information related to point 1 of Annex II of the IVDR with the corresponding annexes such as drawings or device specifications, raw material and packaging material. This main document must clearly reference all the documents attached as annexes in the same folder.

- Trade name or commercial name and general description of the device.
  The trade name must be consistent throughout the technical documentation. The device description should allow the reviewer to understand the design, packaging, sterilisation, and component characteristics of the device.
  In the case of software devices, the device description must also include:
  - The version to be certified.
  - Description of all the ways in which it is intended to be used: software with local installation, mobile application, web access, etc.
  - A basic description of the user interface

- Basic UDI-DI assigned to the device by the manufacturer

  The basic UDI-DI shall be consistent throughout the technical documentation. In case of grouping of several devices, justification for such grouping shall be provided.

- Intended purpose

  The intended purpose must be consistent throughout the technical documentation (description, labelling, performance evaluation, risk analysis, post-market surveillance, etc.) and it shall include:

  - Identification of what is being detected or measured.
  - Wether it is a quantitative, qualitative or semi-quantitative measurement.
  - Purpose of the device: diagnosis, diagnostic aid, screening, predisposition, prognosis, prediction and determination of physiological status.
  - How the result relates to a diagnosis, including any specific disorder, condition, or risk factor of interest that is intended to be detected, defined, or differentiated.
  - Basic operating principles, i.e., the intended users and setting, whether or not it is automated, and the type of sample(s) required.
  - Intended patient population.
  - Intended user: laboratory professional, healthcare professional (point of care – PoC- testing) or lay user (self-testing).

- Description of the principle of the test method or principles of operation of the instrument

  - A description of the principle of the test method or principles of operation of the instrument according to Annex II 1.1(d) should be included, detailing whether it is established or novel, in which case the novel features should be explained.
  - If used in combination with other products, interactions with the various components should be included and the overall performance described.
  - For automated test instruments, include a description of the appropriate test characteristics according to Annex II 1.1(i).

- For automated tests, include a description of the characteristics of the instrumentation appropriate to perform the test.
- Description of the software to be used with the product according to Annex II 1.1 (j).

- Qualification of the device as an in vitro diagnostic medical device
  - Justification should be provided as to why the product is considered an "in vitro" diagnostic medical device in accordance with Article 2. Particular importance should be given in the case of software (MDCG 2019-11).
  - In the case of diagnostic tests in lieu of patient care, the definition should comply with IVDR art. 2(5).
  - In the case of self-diagnostic tests, it must comply with IVDR art. 2(6). For more information, please refer to MDCG 2024-11.

- Device classification
  - The application should include the classification of the device, the classification of the product, the applicable rules of Annex VIII, and the-not applicable rules of Annex VIII. If several rules are applicable, all of them should be identified indicating that the rule with the highest classification is the one that applies to classify the device.
  - If the device contains multiple tests, each test should be classified on its own but the highest classification is the one that applies to the product as a whole.
  - If the device is part of a set for a purpose other than those covered by the in vitro diagnostic medical device definition, it should be explicitly identified. For example, for in vitro diagnostic medical devices that are software, if the product incorporates several modules, these must be identified and it will be justified which of them is a medical device and which is not.
  - The classification of the device must be the same in all technical documentation, including the declaration of conformity.

In the event of a dispute between the notified body and the manufacturer regarding classification of the product according to Annex VIII, the manufacturer should provide evidence of the decision of the competent authority where the manufacturer has its registered place of business (Article 48 (2)). If the manufacturer does not have a registered place of business in the EU and has not yet designated an authorised representative, evidence of the decision of the competent authority of the Member State that has designated the notified body shall be required.

The following guidelines provide guidelines for the qualification and classification of medical devices and in vitro diagnostic medical devices:

- MDCG 2024-11 Guidance on qualification of in vitro diagnostic medical devices
- MDCG 2020-16 Rev.3Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746..
- MDCG 2019-11 Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 - MDR and Regulation (EU) 2017/746 -

The manufacturer must also correctly identify and justify the codes (IVR, IVS, IVT, IVP and IVD) applicable to his device as described in Implementing Regulation (EU) 2017/2185. This can be done with the help of MDCG 2021-14 "Explanatory note on IVDR codes".

The CNCps, during the application admission stage, reviews the codes assigned to the device to ensure their consistency with the design and intended purpose or the deviceion processes and technologies as declared by the manufacturer.

- Description and list of the different configurations and variants of the product intended to be marketed

  A complete description or list of the different configurations/variants of the product intended to be marketed should be included, including references, names, commercial presentations, constituents, volumes, etc.

  The application should include a detailed description of the components listed above, identifying all reagents that are part of the product. It should be noted that

it should be aligned with what is indicated in the device design and in the instructions for use.

- Where applicable, sample collection material and simple transport material supplied with the device, or recommended instructions for use

  Sample collection and transport materials should be detailed so that samples are kept in good condition, even during transport. Pre-analytical requirements such as analyte stability should therefore be considered.
- Description of accessories and those devices to be used in combination with the device

  A detailed description of all accessories, and other devices necessary for the product to function properly, e.g. buffers, extraction kits, whether included with the product or not, should be included.

  In the event that the device includes a medical device, such as a lancet, details of its regulatory status (declaration of conformity, MDR certificate in force) should be provided.

  If software is used with the device, a description of the software, including the version, should be included.

- References to previous or similar generations of the device

  The documentation must contain information on previous generations of the device.
  - If the device is new and has never been marketed in any market, state this clearly.
  - If the device has been previously marketed under IVDD by the manufacturer, provide a summary of the product's history in the market, indicating the nature and timing of any changes to the product.
  - Indicate whether the device intended to be marketed under IVDR is identical to it or has undergone any changes compared to the product on the market. In this case, the modifications that have been made, e.g., changes in classification or intended purpose, should be detailed.

- Include a summary of similar devices identified in the EU market or in international markets, if any, providing for each of them the key specifications on which you base the similarity to your product.
- Indicate any similar devices that have been used as comparator products in performance studies or have been used in scientific literature searches.

3.3. Labels (Folder "102_Etiquetas")

Folder	IVDR	Considerations
Folder 102: Etiquetas	Annex I, point 20.1, 20.2, 20.3 Annex II, point 2(a)	- If applicable, include the translation procedure - If there are different trademarks for the same device, include the labels for each trademark

The labeling must contain all the information contained in Annex I points 20.1, 20.2 and 20.3 applicable to the device.

This folder shall include a main document that identifies the codes of the documents, models, or arts that constitute the device labeling, including version and date, of all levels of packaging and forms of presentation.

Example models of each of these in approved and controlled versions shall be included as an annex to this folder.

For the preparation of labeling and instructions for use the manufacturer should ensure that all requirements of the common specifications and applicable standards are addressed, where necessary. Where symbols are used in the information supplied by the manufacturer, the harmonized standard EN ISO 15223-1 should be taken into account.

The information contained in this folder must be able to identify the content that is printed on the device (fixed data) and the content that is added to the device during the manufacturing process, e.g. during in-line printing (variable data), including the symbols used.

If the manufacturer intends to market the device in countries with accepted languages other than English (see document "IVDR - Language requirements for manufacturers"),

the languages accepted by the member states where the device is intended to be marketed shall be indicated and the translation procedure applied shall be attached to this folder.

Some specific label requirements must be taken into account, e.g. if it includes substances or mixtures considered as hazardous, in which case EC Regulation 1272/2008 applies, or in case the device is a self-diagnostic or a point-of-care diagnostic test.

For class C and D devices, the manufacturer shall mention on the label or in the instructions for use where the summary of safety and performance (SSP) according to Art. 29 IVDR is available, in the absence of EUDAMED.

In the case of software devices, specific information on where the label will be located and how to access it must be included.

3.4. Instructions for use (Folder "103_Inst. de uso")

Folder	IVDR	Considerations
Folder 103: Inst. de uso	Annex I, point 20.4.1 and 20.4.2 Annex II, point 2(b)	- If applicable, it shall include the translation procedure. - Inform if there are electronic IFUs (eIFUs). - If applicable, include promotional material.

The instructions for use (IFU) must contain all the information required in Annex I points 20.1, 20.4.1 and 20.4.2 applicable to the device.

For the preparation of the instructions for use, it is essential to take into account the conclusions obtained from other documents in the technical dossier, such as the risk analysis and the performance evaluation, since they must be aligned with the purpose, indications, contraindications, warnings, etc.

In the case of instruments, the user manual, installation manual and service manuals must be provided if applicable.

IFUs of self-testing devices must include all the necessary information for the device to be safely used by lay users. In these cases, an additional validation with lay users is also required.

The ISO 18113 series of standards specifies the requirements for information provided by the manufacturer of IVD devices. It consists of five parts, which address the specific needs of professional users and users for self-testing. It also has specific parts for reagent and instrument requirements.

If the manufacturer intends to market the device in countries with languages other than Spanish, the languages accepted by the member states in which it intends to market it shall be indicated and the translation procedure applied shall be attached to this folder. In the case of the use of IFUs in electronic format, it is recommended that the provisions of Commission Implementing Regulation (EU) 2021/2226 be used as a reference.

In the event that it is decided not to accompany the product with IFUs, a justification must be provided in line with what is indicated in the risk analysis.

3.5. Summary of Safety and Performance (Folder "104_Resumen Segur. y Func. (SSP)")

Folder	IVDR	Considerations
Folder 104: Resumen Segur y Func (SSP)	Article 29 MDCG 2022-9	Only applicable for Class C and Class D devices

For Class C and D devices, the Safety and Performance Summary (SSP) must be provided to the Notified Body, regardless of whether or not the EUDAMED module is available.

This must be written in a clear and understandable way for the intended user and for the patient (if applicable) and must contain all the elements listed in IVDR Article 29 (section 2).

MDCG 2022-9 Summary of safety and performance shall be used as a reference.

The SSP must be provided at least in Spanish for validation by the notified body. If the manufacturer intends to market the device in countries with languages other than Spanish, the languages accepted by the member states where the device is to be marketed must be indicated and the translation procedure applied must be attached to this folder. In any case, the SSP shall indicate in which language it has been validated by the notified body.

The SSP shall be updated as indicated in Article 56 at least once every year during the lifetime of the device, and the updates must be defined in the Post-market Surveillance Plan (PMS).

3.6. Design and manufacture (Folder "105_Diseño y fabricacion")

Folder	IVDR	Considerations
Folder 105: Diseño y fabricacion	Annex II, point 3	- If the devices were IVDD certified, history of design modifications. - The design procedure must be included

The technical file must include sufficient information to allow the reviewer to understand the design and manufacturing of the device. This is necessary to confirm that the risk analysis and performance evaluation are appropriate for the device, as well as to assess RGSF compliance.

Design documentation and manufacturing documentation shall be provided in separate sub-folders.

3.6.1 Design information

- Materials and components:

A description of all the components that are part of the device should be included, identifying those components considered critical, such as antibodies, antigens, enzymes, nucleic acid primers, etc.

If applicable, it shall include the Material Safety Data Sheet (MSDS).

- Design stages and design information:
  - Manufacturers should provide an overview of key design inputs and outputs, as well as a design traceability matrix.
  - Documentation should include the design steps applied to the device, including verification and validation protocols and reports of critical processes (methods, acceptance criteria), as well as verification of compliance with requirements when connected to other devices.
  - In the case of self-diagnostic and NPT products, a description of the design aspects that make the device suitable for use, considering usability, complexity, safety, test technology, etc., shall be included.
  - In the case of instruments, information on subsystems, analytical technology, hardware and software shall be provided.
  - Manufacturers should clearly indicate whether the device is software in itself or whether it is required for proper operation as intended. The submission should include a description of any software to be used with the device, either as an integral part of the device or associated with the device to ensure its safe use. Manufacturers should include a checklist to demonstrate compliance with EN 62304.
  - For in vitro diagnostic medical devices that are software this shall also sinclude:
    - System architecture, with an explanation of how the software components use or enhance each other and how they are integrated into the overall processing; the computing resources used to develop the system.
    - Type of versioning, programming language, external libraries/dependencies, modules or framework technologies used, as appropriate. - Identification and analysis of software requirements (functional and non-functional).

- IVD software lifecycle documentation and related procedures (e.g., software development plan, software requirements specification, risk management and problem resolution).
- Information on system requirements where it will be installed, if applicable.
- IT security measures adopted.
- Release procedure and record.
- Statement in case the software is based on artificial intelligence. In addition, in these cases, the design information should include information on:
  - Type of learning of the AI model used.
  - Information on the data set used: origin, percentage of data used for training, testing, validation, information on who has done the labeling of the data, etc.
  - If applicable, the use of previously trained systems or tools provided by third parties and the way in which they have been used, integrated or modified.

- Design facilities:

  Information on the facilities where the device was designed should be included.

3.6.2 Manufacturing information:

All facilities, including those of critical subcontractors and suppliers, where the manufacturing process of the device is carried out should be identified, specifying the activity performed at each site.

The manufacturer should include a detailed description of the manufacturing stages to provide an understanding of the production process. An overview can be provided in the form of manufacturing flow diagrams.

The documentation shall also include information on the manufacturing steps, checks and controls, carried out including packaging and any special processes required to manufacture the device:

- Work instructions. Sufficient information on the manufacturing processes as well as a clear identification of the required equipment shall be included.
- Incoming inspection of raw materials/critical components.
- In-process quality control: Testing and acceptance criteria.
- Final product quality control: Tests and acceptance criteria.
- Specifications and final concentrations/quantities of raw materials/critical active ingredients in finished product.
- Batch release criteria for the device.
- Other records as deemed applicable.

Manufacturing records of at least one commercial scale batch of the device shall be provided.

3.7. General Safety and Performance Requirements (GSPR) (Folder "106_Req seguridad y func")

Folder	IVDR	Considerations
Folder 106: Req seguridad y func	Annex II, point 4	- The "IVDR_DEX_14_Tabla de requisitos de seguridad y funcionamiento IVDR" form must be provided -For instruments, justification of conformity with the provisions of Directive 2006/42/EC shall also be included.

The "IVDR_DEX_14_Safety and Performance Requirements Table IVDR" form available at the CNCps website shall be submitted, with dated and versioned references to the documents evidencing compliance. The reference to the documents demonstrating compliance shall be sufficiently direct to clearly identify the relevant document. A general reference or a reference to an entire folder is not valid.

This table shall also include the harmonized standards, common specifications and application guides declared by the manufacturer.

The manufacturer must indicate if the compliance with the each harmonized standard is complete or partial. If the manufacturer declares partial compliance, the parts of the standard that have been considered non-applicable must be identified and justified.

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3.8. Benefit-risk analysis (Folder "107_Analisis benef-riesgo")

Folder	IVDR	Considerations
Folder 107: Benefit-risk analysis	Annex II, point 5	This folder shall include: - Risk management procedure - Risk management plan - Risk management report

The interrelationship between the risk management process and the manufacturer's performance evaluation of the device should be clearly identifiable (Annex VII, 4.5.4). The results of the risk analysis should provide information on the adequacy of the performance evaluation.

Risk management should be understood as a continuous iterative process that encompasses the entire life cycle of the device and requires continuous updating. Evidence should be provided that this concept has been properly implemented.

The information contained should be aligned with the current EN ISO 14971 standard. Annex H of the ISO/TR 24971:2024 application guide provides guidelines for risk management oriented risk management for in vitro diagnostic medical devices.

This folder shall include the following documents:

- Risk management procedure describing the risk analysis and management system.
- Risk management plan for each device or for each group of similar products. It must include, at least, the scope of risk management activities, assignment of responsibilities for their execution, risk acceptability criteria, as well as the activities to be carried out to collect post-production information.
- Risk management report: this report should include:
    - Evidence of the competence of the team involved in risk analysis and risk management.
    - Identification and analysis of known and foreseeable hazards associated with each device related to the design, manufacture, use of the device, harms related to patient safety and health, and information that may come from post-marketing follow-up.
    - Estimation and evaluation of risks associated with and occurring during intended use, as well as reasonably foreseeable misuse.

- Elimination or control of identified risks (see IVDR Annex I, Section 4). The manufacturer should determine whether the measures applied (i.e., process validations, performance evaluation, stability, usability engineering, or other key verification/validation tests) have reduced all risks to the minimum possible, i.e., to levels acceptable considering the state of the art.
- Information to be provided to the user regarding the safe use of the device or the existence of residual risks, which should be communicated to the user as recommendations, warnings, cautions, symbols, legends, etc.
- The different symbols and/or legends of warnings/recommendations for the correct use of the device that appear on the labeling and in the instructions for use must be justified, and included among the risk managament measures.
- The impact of information from the post-marketing surveillance system, on hazards and their frequency of occurrence, on their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability should be considered.
- Demostration that all known and foreseeable risks, as well as any undesirable effects, have been minimized and are acceptable when compared to the evaluated potential benefits to patients and/or the user arising from the expected performance of the device during normal conditions of use.
- Conclusions of the analysis verifying that the risk management plan has been properly implemented, the overall residual risk is acceptable and that the appropriate methods are in place to collect and review information in the production and post-production phases.
- Planned frequency of review of the report.

3.9. Device verification and validation

The verification and validation of the devices comprises several aspects, including performance evaluation, stability, software validation, among others.

3.9.1 Device Verification and Validation. Performance Evaluation (Folder "108_ Verif y valid_Eval Funcionamiento")

Folder	IVDR	Considerations
Folder 108 "Verif_y_valid_Eva l Funcionamiento"	Article 56 Annex II, point 1.1 Annex II, point 6.1 Annex XIII, part A, section 1, 2 ,3	This folder shall include: - Information on the types of samples - Performance Evaluation Plan (PEP) - Performance Evaluation Report (PER) - Scientific validity report - Analytical performance report - Clinical Performance Report

Performance evaluation is a continuous process by which data are evaluated and analyzed to demonstrate the scientific validity, analytical performance and clinical performance of the device in terms of its intended purpose.

This process should be planned, comprehensive and objective, considering both favorable and unfavorable data, and should be proportionate and appropriate to the characteristics of the device, including its risk class, performance and intended purpose.

The common specifications published for each type of device and the MDCG 2022-2 Guidance on general principles of clinical evidence for In Vitro Diagnostic medical devices (IVDs) should be used as a reference. In the case of devices that are software, consider MDCG 2020-1.

The Performance Evaluation shall be conducted in accordance with Article 56 and Part A of Annex XIII to demonstrate the following:

- Scientific validity Art. 2 (38): Association of an analyte with a clinical or physiological state.
- Analytical performance Art. 2 (40): Ability of a device to correctly detect or measure a particular analyte.

- Clinical performance Art. 2 (41): Ability of a device to produce results correlated with a particular clinical condition or with a particular physiological or pathological process or state based on the reference population and intended user.

The information should be arranged in a consistent manner and, if necessary, may be organized in sub-folders.

Class D devices shall be tested at an EU reference laboratory (EURL) to verify their performance. A positive opinion from the EURL will be required for certification of the device (IVDR Annex IX section 4.9).

In the case of Class D devices without common specifications and this is the first certification of such a device, the CNCps will consult the European Commission's expert panel on the performance report (PECP procedure, IVDR Article 48.6).

- Information on the type of sample (Annex II 1.1.)

- The manufacturer shall specify the type of sample to be used for the proper functioning of the device, e.g. urine sample, capillary blood, tissue, etc.
- The collection and transport of the sample shall be described, together with the materials used for this purpose. Critical data such as timing of sample collection, stability in transport, etc., or descriptions of the recommended specifications for this shall be indicated.
- There should be representative performance data for the device with each type of sample.
- The information detailed here should be consistent throughout the technical documentation: IFUs, risk analysis, performance evaluation report, design, etc.

- Performance evaluation of the device

  The following documentation must be attached:

  1. Performance Evaluation Plan (PEP) (Annex XIII, section 1)
     - Must identify the approach and steps necessary to generate clinical evidence regarding the device's characteristics, intended purpose, etc.

- It should clearly specify how the scientific validity, analytical performance and clinical performance of the device will be demonstrated, and detail which parameters are applicable and which are not.
- It should also include a description of the state of the art. In the event that data generated in a device already on the market are used for the evaluation of the device's performance, the adequacy of such data must be justified.

2. Performance Evaluation Report (PER) (Annex XIII- part A, section 1.2.3 and article 56):
   - It shall include the evaluation of scientific validity, analytical performance and clinical performance to confirm the performance characteristics as planned in the PEP.
   - It shall include conclusions derived from post-market performance follow-up (PMPF) reports.
   - The report shall also include the frequency with which the manufacturer plans to update the report.

   The PER shall summarize the information included in the following reports:

   2.1 Scientific Validity Report (Annex XIII section 1.2.1)
   - Report containing the utility of the markers or analytes in the context of the intended use.
   - For a new analyte and/or a new intended use, scientific validity must be demonstrated.
   - To identify and justify scientific validity, the manufacturer may rely on:
     - Information on devices that measure the same analyte/marker (in case of using equivalent products this should be justified).
     - Peer-reviewed scientific literature
     - Consensus opinions of experts (scientific associations)
     - Results of clinical performance studies.

- The result of the analysis must include references, justifications and conclusions that support a valid association between the analyte and the clinical condition/physiological state.
- It is not necessary to establish scientific validity when the association of an analyte with a clinical condition/physiological state is well known. In this case a brief justification should be documented in the report.

2.2 Analytical Performance Report (Annex XIII, section 1.2.2)

- Analytical performance must be demonstrated in accordance with the requirements of Annex I, Section 9.1 and Annex II, Section 6 of the IVDR. The documentation must include the results and critical analyses of all verification and validation studies performed to demonstrate compliance of the device with the requirements of the Regulation under the intended conditions of use of the device.
- The ability of the device to detect or measure an analyte is evaluated based on the following analytical performance parameters:
    - Analytical sensitivity
    - Analytical specificity
    - Veracity (bias)
    - Precision (repeatability and reproducibility)
    - Accuracy (resulting from trueness and precision)
    - Limits of detection and quantification
    - Measurement interval/measurement range
    - Cut-off point of the assay
    - Control of known relevant endogenous and exogenous interferences and cross reactions
    - Metrological traceability and values of calibrators and control material
    - Environment of use
    - Comparison of methods
    - Comparison of instruments

- Where the manufacturer considers that any of the analytical performance characteristics are not applicable to the device, adequate justification shall be provided.
- The evaluation should be performed on all sample types. Consider pre-analytical aspects: sample collection/sample storage/transport conditions, as well as the time from sample collection to analysis.
- In the case of using data from previous versions of the device, a justification that this data complies with IVDR requirements must be included.

2.3 Clinical Performance Report (Annex XIII, sections 1.3.1, 2.3.2 and 2.3.3)

- The manufacturer must demonstrate that the product has been tested for the intended purpose, the target population, within the intended conditions of use, the use environment and with all intended user groups.
- The parameters of clinical performance are highly variable and strongly dependent on the intended purpose and the product claims. Clinical performance of the device should be demonstrated for all parameters described in Annex I, section 9.1 (b), unless an omission can be justified as not applicable.
- Clinical performance parameters (among others):
    - Diagnostic sensitivity and specificity
    - Positive and negative predictive value
    - Likelihood ratio
    - Predicted values in healthy and sick populations
    - Usability/user interface
- The characteristics and performance of the device shall be specifically assesed in case of use by an intended user type:
    - For self-diagnostic products: performance obtained by laypersons;
    - For point-of-care (POC) diagnostic tests: performance data obtained in relevant settings (e.g. health centers, ambulances, etc.).

- Performance evaluation studies should be carried out, including, if appropriate, interventional clinical performance studies (Annex XIII section 2), unless justified by the use of other sources of clinical data. If they are carried out, the clinical performance evaluation plan, protocol and corresponding report must be provided.
- If justification is based on data from the scientific literature (peer-reviewed scientific articles), a copy of the scientific articles, the literature search protocol and the corresponding reports must be provided.
- In the case of products previously marketed under IVDD, the data may be based on previous PMS reports. The manufacturer must verify that all IVDR requirements regarding the demonstration of the clinical performance of their product are met and, if not, carry out the relevant studies.

The performance evaluation should include evidence that the product functions properly when used by the intended users (usability engineering). The UNE-EN 62366-1 standard can be used as a reference for the usability evaluation protocol and report.

3.9.2 Device Verification and Validation - Stability (Folder "109_Verif y valid_Estabilidad")

Folder	IVDR	Considerations
Folder 109_ Verif y Valid_Estabilidad	Annex II, point 6.3	Reference: UNE EN ISO 23640 in force This folder shall include a declaration of the device's shelf life as well as the the stability studies that have been carried out

This folder must include the documents presenting the information on the declared shelf life and the stability studies during use and transport, i.e. where necessary: real time stability, accelerated stability, stability in use, and stability during transport. The planning of the studies, with pre-defined acceptance criteria, shall be included.

Declared shelf life

- It shall include a protocol with the acceptance criteria for each test performed and the test methodology used.
- There must be a clear indication of the expected shelf life.
- The tests shall be performed on at least three different product batches manufactured under conditions that are essentially equivalent to normal production conditions. The three batches do not need to be consecutive.
- Accelerated studies or data extrapolated from real-time data are acceptable for initial shelf life claims, but must be followed by data generated from real-time stability studies.
- Where accelerated studies have been conducted in anticipation of real-time studies, the method used for such studies should be described.
- The report should state all conclusions and the stated shelf life.

Stability in use

- Data should be generated using at least one batch of reagents that reflects the routine use of the product. Data can be generated using real or simulated conditions. This may include open vial stability and/or, for automated instruments, on-board stability (time that the reagent remains valid once opened and placed inside the analyzer).
- Protocols and reports must be submitted that establish all conclusions and the declared in-use stability.

Shipping and transportation stability

- Data should be generated using at least one batch of the device to assess tolerance to anticipated shipping conditions.
- These may be real or simulated studies and should include extreme temperature variations.
- Manufacturers must submit:
    - The study report (including the protocol and acceptance criteria).
    - The method used for simulated conditions.
    - Conclusion and recommended shipping conditions.

3.9.3 Device verification and validation - Verification and validation of software (Folder "110_PSDIV_Verif y valid_programas informaticos")

Folder	IVDR	Considerations
Folder "110_ Verif y valid_programas informáticos"	Annex II, point 6.4	Reference: EN 62304 in force This folder shall include a summary of results of all verifications, validations and tests performed internally and applicable to the actual environment in which the device will be used. It shall take into account all configurations and operating systems.

This folder must include documentation demonstrating that the software has been validated as used in the final product.

The documentation must demonstrate that the product has been developed in accordance with the state of the art, taking into account the principles of software life cycle, risk management, information security, verification and validation.

In particular, the following must be provided:

- Validation and testing procedures used, including information on the data used for validation and the established acceptance/rejection criteria.
- Test records and test reports, dated and signed, which shall unambiguously identify the version tested. Validations and tests shall address all the different hardware configurations and, where applicable, the operating systems identified in the labeling.

3.9.4 Verification and Validation - Other Cases (Folder "111_PSDIV_Otros casos especificos")

Folder	IVDR	Considerations
Folder "111 Otros casos específicos"	Annex II, point 6.5	This folder shall include additional information on: - Sterile devices - Containing tissues of animal, human or microbial origin - Measuring function - Connection to other equipment

This folder shall contain information relating to sterile devices, devices containing tissues of animal, human or microbial origin, measuring function and connection to other equipment, where applicable, organised in separate sub-folders.

The manufacturer must provide documentation that justifies the demonstration of compliance with the applicable GSPR according to the provided "IVDR_DEX_14_IVDR Safety and Performance Requirements Table" form.

3.9.4.1 Sterile devices or with a defined microbiological condition

For this kind of devices, the following must be provided:

- Description of the sterilisation method used and the environmental conditions at the relevant stages of manufacture, with reference to the applicable harmonised standards.
- Validation reports for packaging, sterilisation and maintenance of sterility. The validation report should cover tests for bioburden, absence of pyrogens and, where appropriate, sterilisation residues.
- Sterile barrier system validation reports.

3.9.5.2 Devices containing tissues, cells and substances of animal, human or microbial origin

For devices containing tissues, cells and substances of animal, human or microbial origin, information on the origin of said material and the conditions under which it was collected (i.e. inactivation of attenuated viruses) must be provided.

This section should include a description of the specific risk control measures, in particular, to ensure the absence of viruses and other transmissible agents. The affected component should be defined, as well as the specific control measures applied.

3.9.5.3 Devices with measuring function

For devices with a measuring function, the documentation should include a description of the methods used to guarantee the accuracy indicated in the specifications. The units of measurement should be in accordance with the provisions of Directive 80/181/EEC.

The information may be included by means of a cross-reference to specific sections of the documents related to the evaluation of the analytical performance included in the Performance Evaluation folder.

3.9.5.4 Devices that need to be connected to other equipment in order to function according to their intended purpose

If the device needs to be connected to other equipment in order to work as intended, a description of the resulting combination and a demonstration that the general safety and performance requirements are met must be included.

This information must be consistent with that contained in other sections of the technical documentation (design, instructions for use, performance evaluation, etc.).

3.10. EU Declaration of Conformity (Folder "112_Declar. UE de Conf")

Folder	IVDR	Considerations
Folder "112_Declar. EU de Conf"	Art. 17 and Annex IV	A draft of the UE Declaration of Conformity shall be included.

The application must include a copy of the Declaration of Conformity (unsigned). The EU Declaration of Conformity must include all the information contained in Annex IV of the IVDR.

3.11. Post-Market Surveillance (PMS-PMPF) (Folder "113_Sgto Poscomer (PMS_PMPF)")

Folder	IVDR	Considerations
Folder "113_ Sgto Poscomer (PMS_PMPF)"	Annex III Articles 78 to 80	This folder shall include: - Post-marketing surveillance plan (PMS plan). - Post-marketing performance surveillance plan (PMPF plan).

		For non-initial assessments (already IVDR certified): - Post-marketing performance surveillance report (PMPF report). - For class B devices: Post-marketing surveillance report (PMS).

This folder shall contain the following documents:

- The Post-Market Surveillance Plan (PMS plan) that is drawn up as indicated in Article 79 and point 1 of Annex III of the IVDR. The plan is part of a proactive and systematic process with defined methods for collection and analysis of appropriate data. The plan should include indicators and limit values that will be used in the continuous reassessment of the benefit-risk analysis and risk management, as well as in post-marketing surveillance activities. The post-marketing surveillance plan should be maintained throughout the life of the device.
- The Post-Market Performance Follow-Up Plan (PMPF plan) as indicated in Annex XIII (B). Where applicable, manufacturers must also include a post-market performance follow-up plan (PMPF) or a justification as to why it is not applicable. The PMPF plan must contain the specific objectives and methods that will be applied to address the provisions of Annex XIII, Part B, Section 5.1.

Only in the case of devices with an IVDR certificate, in the context of a periodic sample review at the request of the CNCps, this folder must also include:

- For class B devices, the Post-Market Surveillance (PMS) Report shall be included in accordance with Article 80 of the IVDR.
- For all devices, the Post-Market Performance Follow-Up (PMPF) Report shall be included, in which the findings obtained based on the PMPF plan must be analyzed and the results of such evaluation must be documented.

3.12. Periodic Safety Updated Report (PSUR) Folder "114_Inf. Periodico Seguridad (PSUR)")

Folder	IVDR	Considerations
Folder "114_Inf. Periódico Seguridad (PSUR)"	Article 81	Only applicable for Class C and D already IVDR certified devices

In case of non initial applications (devices already IVDR certified) of class C and D devices, the Periodic Safety Update Report (PSUR) shall be included in accordance with Article 81.

At the time of the initial conformity assessment, it is not necessary to submit the post-marketing (PMS) or post-marketing performance (PMPF) follow-up reports. These reports will be evaluated during the post-certification follow-up of the device.

Folder	IVDR (Annex II)	Considerations
Folder "100_Indice doc" (Table of contents and cover letter)	-	This folder should include: - Cover letter - Table of contents - Identification of documents in each folder
Folder "101_Descrip y Espec" (Description and specifications)	Annex II, point 1	In addition to classification according to Annex VIII, describe the IVR, IVD, IVP, IVS and IVT codes applicable to the device, as well as the generic group according to the European Nomenclature (EMDN).
Folder "102_Etiquetas" (Labels)	Annex II, point 20.1, 20.2, 20.3 Annex II, point 2 a)	- If applicable, include the translation procedure - If there are different trademarks for the same device, include the labels for each trademark
Folder "103_Inst. de uso" (Instructions for use)Inst. for use	Annex II, point 20.1, 20.2, 20.3 Annex II, point 2 b)	- If applicable, it shall include the translation procedure. - Inform if there are electronic IFUs (eIFUs). - If applicable, include promotional material.
Folder "104_PSDIV_Resumen Segur. Y Func (SSP)" (Summary of Safety and Performance)	Article 29	Only applicable for Class C and Class D devices
Folder "105_Diseño y fabricacion" (Design and manufacture)	Annex II, point 3	- If the devices were IVDD certified, history of design modifications. - The design procedure must be included
Folder "106_Req, segyrudad y func" (General Safety and Performance Requirements)	Annex II, point 4	- The "IVDR_DEX_14_Tabla de requisitos de seguridad y funcionamiento IVDR" form must be provided - For instruments, justification of conformity with the provisions of Directive 2006/42/EC shall also be included.
Folder "107_Analisis benef_riesgo" (Benefit-risk analysis)	Annex II, point 5	Reference to EN ISO 14971 in force This folder shall include: - Risk management procedure - Risk management plan - Risk management report
Folder "108_Verif y valid_Eval funcionamiento" (Verification and validation. Performance Evaluation)	Annex II, points 6.1 and 6.2	This folder shall include: - Information on the types of simples - Performance Evaluation Plan (PEP) - Performance Evaluation Report (PER) - Scientific validity report - Analytical performance report

		- Clinical Performance Report
Folder "109_ Verif and valid_Estabilidad" (Verification and Validation - Stability)	Annex II, point 6.3	Reference: UNE EN ISO 23640 in force This folder shall include a declaration of the device's shelf life as well as the the stability studies that have been carried out
Folder "110_ Verif and valid_Valid prog informaticos" (Verification and validation - software)	Annex II, point 6.4	Reference: EN 62304 in force This folder shall include a summary of results of all verifications, validations and tests performed internally and applicable to the actual environment in which the device will be used. It shall take into account all configurations and operating systems.
Folder "111_PSDIV_Otros casos" (Verification and Validation - Other Cases)	Annex II, point 6.5	This folder shall include any additional information on: - Sterile devices - Containing tissues of animal, human or microbial origin - Measuring function - Connection to other equipment
Folder "112_Declar. UE de Conf" (EU Declaration of Conformity).	Art. 17 and Annex IV	A draft of the UE Declaration of Conformity shall be included.
Folder "113_ _Sgto Poscomer (PMS_PMPF)" (Post-Marketing Monitoring (PMS-PMPF)	Annex III Articles 78 to 80	- This folder shall include: - Post-marketing surveillance plan (PMS plan). - Post-marketing performance surveillance plan (PMPF plan). For non-initial assessments (already IVDR certified): - Post-marketing performance surveillance report (PMPF report). - For class B devices: Post-marketing surveillance report (PMS).
Folder "114_Inf. Periódico Seguridad (PSUR)" (Periodic Safety Updated Report (PSUR))	Article 81	Only applicable for Class C and D already IVDR certified devices

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