National Agency for Food and Drug Administration & Control (NAFDAC)

Vaccines, Biologics and Medical Devices Registration and Regulatory Affairs (VBM-R&RA) Directorate

Guidelines for Compilation of a Product Dossier for Registration of In Vitro Diagnostics - IMDRF ToC

Contents

Acknowledgment

The Agency acknowledges the utilization of some documents and the technical support of the World Health Organization (WHO) as well as the International Medical Device Regulators Forum (IMDRF) in development of these Guidance documents.

Scope

This Guidelines have been developed in pursuance to the NAFDAC Act Cap N1, LFN, 2004 and made to provide guidance to applicant in the organization of information to be provided to the Agency in seeking marketing authorization for in vitro diagnostics for human use. It also provides guidance to the industry on the expectations of NAFDAC as it concerns submission of technical documents.

Introduction

This document provides instructions to manufacturers on the type of information and necessary documents to be submitted in a product dossier for the purposes of regulatory assessment of IVDs (Registration process).

The regulatory assessment process allows for flexibility in a manufacturer's approach to compiling the information required for an application. Alternative approaches to both the principles, and application, of the requirements described in this document may be acceptable provided they are supported by adequate scientific justification.

NAFDAC may request, during the course of the registration process, additional information that is not specifically described in this document. This will be done in order to facilitate a clearer understanding of the quality, safety and performance of a product under assessment. The rationale for any additional requests will be clearly documented in correspondence to the manufacturer.

For the purpose of this document, the verbal forms used follow the usage described below:

- "shall" indicates that the manufacturer is required to comply with the instructions in the document below.
- "should" indicates that the manufacturer is recommended to comply with the instructions, butit is not a requirement.

- "may" indicates that the instructions are a suggested method to compile the documentation request, but it is not a requirement.

Definitions

Accessory - Means an article intended specifically by its manufacturer to be used together with a particular IVD medical device to enable or assist that device to be used in accordance with its intended use (see GHTF SG1 N71:2012).

Full Report - Typically includes a complete, detailed description of the objective of the assessment, the methods and procedures including when applicable why a regional or harmonized/recognized standard/guidance has or has not been complied with, study endpoint(s), pre-defined pass/fail criteria, deviations, results, discussion and conclusions, and may include data. Complete, detailed support of method selection, worst-case justification, study endpoint selection, and pass/fail criteria should be included.

Submission - A regulatory submission can be any type of information related to a medical device regulatory process. This includes but is not limited to a request for approval/authorization to market a device, any communications relating to the original submission, and any request for modification to an existing approval. The submission types that will be accepted will be in the format described in this document.

Summary - A summary should include a brief synopsis of the (1) purpose, (2) methods, (3) acceptance criteria, (4) results and (5) discussion and conclusions. Outliers and deviations should be reported with the results. Results should be stated quantitatively with appropriate statistical context where applicable (e.g. value ± SD, confidence intervals, etc.).

The summary should specifically address;

1. Why the characteristic being evaluated is of interest;
2. Why the particular methods are being used to evaluate the characteristic, if applicable, including why a regional or harmonized/recognized standard/guidance has or has not been complied with.
3. How the stated acceptance criteria and sample size are scientifically supported.
4. What device was tested and how it relates to the devices that will be marketed;
5. Why the tested components are representative of the range of devices that will be marketed.
6. Whether the summary has been previously submitted and reviewed by the regulator, including identification of the device and the reference number for the submission; and

7. The extent to which the duties and functions of a study (e.g. testing, monitoring, etc.) have been conducted by an external organization (e.g. contract research organization or individual contractor)

Language Requirements

Information in the product dossier shall be in English. Any document provided in a language other than English shall be accompanied by a certified translation that is signed and dated by the translator and where the translator has stated that it is a true and accurate translation of the original document.

Intended Audience

This document has been prepared as guidance to manufacturers of IVDs to assist in correctly compiling a product dossier for the registration process.

NOTE: This document should be read in conjunction with all relevant IMDRF guidance documents including the following;

a. **GHTF/SG1/N71:2012 "Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical Device"** GHTF_SG1_Definition_of_the_Terms_'Medical Device' and 'In Vitro Diagnostics' Medical Device's (imdrf.org)

b. **In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC), IMDRF/RPS WG/N13(Edition 2) FINAL:2019** https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech190321-ivd-mdma-toc-n13.docx . **GHTF/SG1/N70:2011"Label and Instructions for Use for Medical Devices"** GHTF SG1 - Label and Instructions for Use for Medical Devices - September 2011 (imdrf.org)

Product Dossier

- About Product Dossier
  There are many terms used internationally to describe a product dossier. These terms include standard technical documentation, technical file, summary technical documentation, product summary file, product master file and others. For the purposes of registration of IVDs, NAFDAC uses the term the product dossier.

NAFDAC expects a manufacturer to prepare and either hold, or provide timely access to, technical documentation that shows how its IVD is designed, developed, validated, and manufactured. This technical documentation, typically controlled in the manufacturer's quality management system (QMS), is often extensive and the documentation is revised over time to reflect any changes made during the life cycle of the IVD through normal application of the manufacturer's QMS.

The product dossier is a selection of records and documents from the entire collection of technical records and documents that a manufacturer holds for a product. Manufacturers compile a product dossier from their existing technical documentation to provide evidence that an IVD conforms to the internationally-recognized set of quality, safety and performance principles as described in the International Medical Device Regulators Forum (IMDRF) document IMDRF/GRRP WG/N47 FINAL:2018Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices (3) (the Essential Principles). Evidence will take the form for example, of results of testing, certifications, standard operating procedures (SOPs), systems and any other documentation necessary to support quality, safety and performance.

NAFDAC requires that a product dossier is submitted in the "Table of Contents" (ToC) format, described in the IMDRF document IMDRF/RPS WG/N13 FINAL:2019 (Edition 3)(4). In this document chapters 1-6 and their subheadings, as well as the corresponding chapters and subheadings of the Product Dossier Checklist are numbered according to IMDRF ToC format. As the IMDRF ToC is comprehensive in nature, not all subheadings are required for the purpose of registration and are therefore excluded.

NAFDAC reviews the product dossier with the purpose of:

- **assessing the product and how it performs**
- **assessing the product manufacture**

Submission of Product Dossier

For the purpose of registration, NAFDAC requires an applicant to submit a product dossier; a product dossier should be submitted using a unique link generated by VBM-R&RA Directorate (For video description, please click on the Link).

Note: All information submitted in the product dossier is **CONFIDENTIAL.** Once an assessment is completed, NAFDAC reserves the right to destroy any dossier materials provided with the application. Dossier materials will not be returned.

Product Dossier Clarity and Completeness

Applicants shall submit all necessary sections of a product dossier, identified both in this document and in the NAFDAC Product Dossier Checklist. All sections listed in

this document are required to be submitted as part of the product dossier unless indicated "if applicable".

Not providing the required information may result in NAFDAC not accepting the dossier, significant delays in the assessment process, or cancellation of the assessment process. Applicants should make every effort to ensure that their product dossier is clear and well organized. Poorly-prepared dossiers are an obstacle to efficient assessment and may be rejected without review.

Do not duplicate files, even if it is possible to include the same evidence under multiple subheadings.

Provide the evidence under one appropriate subheading and then make specific references (including both section and page numbers) to that material in any subsequent sections that appear relevant. Be specific: references to specific sections or pages of a document should be provided when possible.

Applicability of Supporting Evidence to the Product Under Review

The manufacturer shall carry out relevant investigations to support the intended use, such as analytical and clinical sensitivity and specificity, accuracy, repeatability, reproducibility, linearity, detection limits, and traceability, as appropriate. In addition, NAFDAC requires investigations to assess the potential effects of interfering factors and claims of reagent and product stability. Studies in support of the intended use should consider the intended user and the intended setting of use.

For each performance study submitted in a product dossier, the following shall be provided:

- Study Description: A description of the study that includes information to facilitate record traceability: study identifier, product identifier (for example, lot numbers), IFU version used, the date of initiation and the date of completion. All data shall be clearly labelled, and clearly linked to the study report.
- Study summary: A summary of the study findings including a conclusion that clarifies how the study objectives have been met.
- Full study protocol and report: The study protocol and full report, which incorporates at a minimum, the following information:
- Study objectives, study design, the methodology used and data collected
- The site(s) where the study was performed (for example, manufacturers R&D laboratory, hospital laboratory, health care clinic)
- Operator(s) of the assay
- The reference standard/method, if applicable
- Specimen acceptance/selection criteria, specimen characterization
- Specimen type(s) (e.g., serum, plasma, finger stick whole blood, venous whole blood) and numbers of each type

- Actual test result summaries with their acceptance criteria and not just pass/fail statements
- Results that are reported in sufficient detail to allow the detection of potential differences in performance between the conditions being investigated (e.g. depending on the product this might require the use of either a semi-quantitative scoring system or a calibrated, graduated color chart to record line intensity)
- The numbers of invalid tests observed
- Photographs of all test results, wherever possible
- Details of statistical methods, estimations and calculations applied
- The study conclusion
- When performed by a party other than the manufacturer, details of this third party and the relationship to the manufacturer as well as copy of the contract between the manufacturer and the third-party identifying roles and responsibilities of each party.

Layout

NAFDAC requires the following format for the dossier submission:

- Use the page numbers format page 1 of 2, 2 of 2, and so on.
- Clearly divide the submission into sections and subheadings, as prescribed in the Product Dossier Checklist, and number all pages of each section, including annexes, so that they are easily identified. Documentation for each section (chapter) may be submitted as separate file directories (folders). For example, the device description (Section 2.4.1 Comprehensive device description and principle of operation) may be provided in a file directory (folder) in the electronic submission that is named: “Section 2.4.1”, or similar.
- Use the Product Dossier Checklist as the first page, and cross-reference all sections of the dossier, including associated annexes, to this checklist.
- Ensure that there are appropriately named tab identifiers. The names shall link directly with the sections of the dossier as outlined in this document. For example, the Labelling information shall be separated from the other documents by a tab identifier named “Section 5.2 Product/Package Labels”.
- The page numbers in each section of the dossier and the page numbers summarized in the Product Dossier Checklist should correspond.
- Font sizes for text and tables are of a style and size that are large enough to be easily legible. Fonts smaller than 12 points should be avoided whenever possible, except in tables and footnotes where a font size of 10 points is acceptable.
- Depending on the level of detail, the information requested in each section may either be:

- Provided directly in the corresponding section of the main product dossier file, preceded by an explanatory summary of the information, as appropriate, or
- Provided in summary in the corresponding section of the main product dossier file, with the detailed information (full study validation reports, photographs, other documentation, etc.) included as annexes, duly cross-referenced both in the corresponding section of the report and the Product Dossier Checklist.

Refer to related annexes in the body of the text and list them in the Product Dossier Checklist.

Electronic Copy Requirements

- Portable Document Format (PDF) is the primary file format used for product dossiers. However, do not include any PDF that requires a password to open it. This will result in return of dossiers to manufacturers resulting in delays of the assessment.
- Use file names that are descriptive of a file's content and meaningful to dossier reviewers. The name can be up to 125 characters and can have spaces, dashes (not elongated dashes), underscores, and periods. However, the name of the file shall not contain any of the following special characters as they are not compatible with NAFDAC's storage platform: tilde (~) apostrophe (') colon (:)

vertical bar (|)	greater than sign (>)	various other symbols
asterisk (*)	single quotation mark (‘)	(e.g., →,*,β,α,∞,±,™)
forward slash (/)	less than sign (<)	pound sign (#)
elongated dash (–)	double quotation marks (“)	
backward slash (\)	question mark (?)	

- When creating a PDF from an electronic source document (e.g. Microsoft Word document) avoid using specialist application plug-ins for capture or display data; not all dossier reviewers will necessarily have access to these plug-ins.
- As far as practicable, electronic files shall contain searchable text. Electronic files made by directly scanning paper documents are generally low quality and are difficult to read; moreover, the lack of searchable text can make dossier information difficult to readily locate and may delay assessment of the dossier.
- For any scanned document, optical character recognition (OCR) should be used to allow text to be searchable. This can be verified by: (1) highlighting an area of text and (2) using the software search function to locate a particular word or phrase. If the

word or phrase is not returned in the search, then the OCR did not recognize the text and it is, therefore, not searchable.

Acceptance of Dossiers Previously Prepared for National Regulatory Authorities
Product dossiers should be compiled according to the Agency's requirements described above. However, NAFDAC may consider submissions previously prepared for national regulatory authorities if:

- All the information required by NAFDAC is included
- The information is fully cross-referenced to the requirements of this document using the Product Dossier Checklist
- The information reflects current activities and practices (expired/superseded documentation shall not be used)

Language and Units of Measurement
Information in the product dossier shall be in English. Any document provided in a language other than English shall be accompanied by a certified translation that is signed and dated by the translator and where the translator has stated that it is a true and accurate translation of the original document.
All measurement units used should be expressed in the International System of Units (SI), as appropriate.

Hierarchy Presentation

The following is a hierarchical presentation of the submission structure. The numbering should remain consistent regardless of whether the heading is required or not. For example, if heading 1.02 is not required for the submission type or by NAFDAC, but headings 1.01 and 1.03 are, then the numbering would remain 1.01 followed by 1.03.

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3.05.04.01.01.01	Summary
3.05.04.01.01.02	Full Report
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6.13	Control of monitoring and measuring equipment
6.14	QMS measurement, analysis and improvement
6.15	Device Specific Quality Plan
6.16	Quality management system verification document
6.17	Other Quality System Information

Chapter 1 – Regional Administrative

1.01 Cover Letter

a) The cover letter should state applicant or sponsor name and/or their authorized representative/s, the type of submission, the common name of the device (if applicable), device trade name or proprietary name (both of the base device and a new name if one is given to the new version/model of the device) and include the purpose of the application, including any changes being made to existing approvals.
b) It should include information pertaining to any Master Files referenced by the submission, if applicable.
c) If applicable, acknowledgement that a device sample or alternatives have been submitted to view or access the device.
d) If the submission is requesting approval of a change that is the result of CAPA due to a recall, this should be stated.
e) If the submission is in response to a request for information from the Agency, this should be stated and the date of that letter should be included, as well as any reference number(s).
f) If the submission is unsolicited information (where accepted), this should be stated, and any related reference number(s) provided.

NOTE: The cover letter should not contain any detailed scientific information.

1.02 Submission Table of Contents

a) Includes at least level 1 & 2 headings for the entire submission
b) Specifies the page number for each item referred to in the table.

NOTE: Refer to the Pagination Section of this document for information about submission pagination.

1.03 List of Terms/Acronyms

Terms or acronyms used in the submission that require definition, should be defined here.

1.04 Application Form/Administrative Information

1.05 Listing of Device(s)

A table listing each variant/model/configuration/component/accessory that is the subject of the submission and the following information for each:

a) the identifier (e.g. bar code, catalogue, model or part number, UDI)
b) a statement of its name/description (e.g. Trade name, size, intended use)

NOTE:

i. A model/variant/configuration/component/accessory of a device has common specifications, performance and composition, within limits set by the applicant.
ii. Typically each item listed should be available for sale. For example, if everything is sold as part of a kit, then this list would only include the kit. You do not need to list all components that may be sold within a kit/set, unless the component is available for sale independently of the kit.

1.06 Quality Management System, Full Quality System or other Regulatory Certificates

1.07 Free Sale Certificate/Certificate of Market Authorization

a) List of the Regulatory Authorities that have provided current regulatory approval for the supply of this product in their country/region of authority.
b) Details of the type of regulatory approval obtained from each Regulatory Authority.
c) Current evidence of regulatory approval, such as certificates provided by the Regulatory Authority

Copies should be authenticated by the Nigerian Embassy/High Commission in the country of manufacture. The manufacturer may be asked to present the original copy at any time.

1.08 Expedited Review Documentation

1.09 User Fees

1.10 Pre-Submission Correspondence and Previous Interactions with the Agency

a) During the product lifecycle, pre-submission correspondence, including virtual or physical meetings, may be held between the Agency and the applicant. Further, the specific subject device may have been subject to previous regulatory submissions to NAFDAC. The content should be limited to the subject device as similar devices are addressed in other areas of the submission. If applicable, the following elements should be provided:
    i. List prior submissions or pre-submissions where feedback was provided by the Agency.
    ii. For previous regulatory submissions, include the identification of the applicable submission reference number.
    iii. For any pre-submission activities that have not previously been assigned any tracking/reference number, include the information package that is submitted prior to pre-submission meetings, the meeting agenda, any presentation slides, final meeting minutes, responses to any action items arising from the meetings, and any email correspondence related to specific aspects of the application.
    iv. Issues identified by the Agency in prior submissions (i.e., clinical study applications, withdrawn/deleted/denied regulatory submission) for the subject device.
    v. Issues identified and advice provided by the Agency in pre-submission interactions with the applicant.
    vi. Explain how and where the prior advice was addressed within the submission.

OR

b) Affirmatively state there has been no prior submissions and/or pre-submission interactions for the specific device that is the subject of the current submission.

1.11 Acceptance for review Checklist

1.12 Statements/Certifications/Declarations of Conformity

1.12.01 Chapter Retired

1.12.02 Environmental Assessment

1.12.03 Clinical Trial Certifications

1.12.04 Indications for Use Statement with Rx and/or OTC designation Enclosure

1.12.05 Truthful and Accurate Statement

1.12.06 Declaration of Conformity

As part of the conformity assessment procedures, the manufacturer of a medical device is required to make a Declaration of Conformity that declares that the device complies with:

a) The applicable provisions of the Essential Principles/Requirements
b) The classification rules
c) An appropriate conformity assessment procedure

1.13 Letter of Reference

Where applicable, letter from the owner of any separate document referenced in the submission (e.g. Master File or previous regulatory submission), granting access to the information in the referenced document. The letter should include the information of the applicant who cited the separate document (e.g. Master File or previous regulatory submission), the product name, the document number that has been filed, and the page number/chapter information of the separate document authorized to be cited.

1.14 Letter of Authorization

1.15 Other Regional Administrative Information

Heading for other administrative information that may be important to the submission but that does not fit in any of the other headings of this chapter.

NOTE: To ensure all elements of your submission are adequately reviewed, please be sure that any content placed here does not belong under any heading described above.

Chapter 2 – Submission Context

2.01 Chapter Table of Contents

a) Includes all headings and sub-headings for the chapter.
b) Specifies the page number for each item referred to in the table.

2.02 General Summary of Submission

a) Statement of the device type (e.g. Tacrolimus test system, blood specimen collection device, calibrator) and name (e.g. trade name, proprietary name), its general purpose, and a high-level summary of key supporting evidence (i.e. studies that are unique to the risks of this device type).
b) Summary of submission, including;
    i. The type of submission (e.g. new, amendment, change of existing application, renewal);
    ii. if amendment/supplement, the reason of the
    iii. if a change to existing approval, description of the change requested (e.g. changes in design, performance, indications, changes to manufacturing processes, manufacturing facilities, suppliers);
    iv. any high-level background information or unusual details that the manufacturer wishes to highlight in relation to the device, its history or relation to other approved devices or previous submissions (provides context to submission).

2.03 Summary and Certifications for Regulatory Submissions

2.04 Device Description

2.04.01 Comprehensive Device Description and Principle of Operation

a) A general description of the device, including:
    i. The device name.
    ii. What does it do?
    iii. Who uses it and for what? (high level statement)
    iv. Where to use it? (places/environment where the device is intended to be used)

v. General description of the principle of the assay method or instrument principles of operation.
vi. Description of the components (e.g. reagents, assay controls, calibrators, cassette, etc.) and where appropriate, a description of the components (such as antibodies, antigens, nucleic acid primers, probes, etc.).
vii. If applicable, labelled pictorial representation (diagrams, photos, drawings).
viii. If system, how the components relate?
ix. If applicable, identify if the device incorporates software/firmware and its role.
x. If applicable, identify the instrument(s) required to perform the test.

b) Product specifications, including:
   i. Physical characteristics of relevance to the end user (dimensions, weight)
   ii. If applicable, technical features and operating modes
   iii. If applicable, operating specifications and performance characteristics (e.g. electrical power requirements, settings and associated allowable ranges/limits, units of measure, temperature and humidity limits, throughput (number of tests per hour), analytical and clinical sensitivity and specificity)
   iv. If applicable, a complete list of the configurations/models of the devices and a summary of the differences in specifications (comparison table and/or pictures/diagrams with supporting text).
c) Describe the different specimen types that can be used for this device (e.g. serum, plasma, urine, cerebrospinal fluid), including any additives that are required (e.g. anticoagulant).
d) Describe the use of controls. If applicable, a list of compatible control materials or control material specifications.
e) Description of the accessories, other IVD or non-IVD medical devices and other products intended to be used in combination with the IVD medical device.
f) If approved by the Agency, provide the approval number and identification for each of the accessories, other IVD or non-IVD medical devices, and other products, which are intended to be used in combination with the IVD medical device.
g) If applicable, indication of biological material or derivate used in the medical device, including origin (human, animal, recombinant or fermentation products or any other biological material) and source (e.g. blood, bone, heart, any other tissue or cells). Where a significant risk is identified, a brief summary of evaluations performed to minimize biological risks, in particular, with regard to viruses and other transmissible agents.

h) Description of the collection and/or transport container(s) provided with the IVD medical device or a description of specifications or recommended collection and/or transport container(s).
i) If applicable, a listing of assays that are compatible with the instrument.
j) If applicable, a listing of compatible instruments.
k) A list of any software to be used with the IVD medical device and a description of its role in the delivery of the intended purpose.
l) If applicable, engineering diagrams/prints/schematics of the device (should be provided as a separate file within the submission).

2.04.02 Material Specifications

Details of relevant material identifications and specifications, including critical raw materials and components, should be provided. Information should include complete chemical and physical characterization of all component materials.

NOTE: If applicable, chemicals should be identified using either the IUPAC (International Union of Pure and Applied Chemistry) or the CAS (Chemical Abstract Service) Registry number. Reference to applicable material standards may also be useful in this description.

2.04.03 Description of Device Packaging

a) A brief description of the packaging of the devices, including the packaging configuration and materials involved. This is not intended to include shipping/transport packaging.
b) Specific packaging of accessories marketed together with the IVD medical devices shall also be described.

2.04.04 History of Development

For any device versions/prototypes referenced in the evidence presented in the submission, a table describing the version/name, with 4 columns (Device Name and/or Version; Description of changes from previous row; motivation for the change; list of verification/validation activities, including clinical studies, conducted using this version).

For any design verification or validation activities presented in this submission (including clinical studies) performed on any earlier versions of the subject device, include a justification for why the changes do not impact the validity of the data collected under those activities in supporting the safety and performance of the final IVD medical device design.

2.04.05 Reference and Comparison to Similar and/or Previous Generations of the Device

a) A list of the similar devices (available on the local and international market) and/or previous generation of the devices (if existent) relevant to the submission. This should include any similar/previous generation devices that were previously reviewed and refused by the Agency.
b) Description of why they were selected.
c) A key specification comparison, preferably in a table, between the references (similar and/or previous generation) considered and the device.

2.04.06 Substantial Equivalence Discussion

2.05 Indications for Use and/or Intended Use

2.05.01 Intended Use; Intended Purpose; Intended User; Indications for Use

This section should include, as appropriate:

a) Intended Use: The statement of intended use should specify what specific disorder, condition, or risk factor of interest (i.e. the analyte to be measured) is detected and the purpose provided by the device (e.g. screening, monitoring, diagnosis or aid to diagnosis). It should identify:
    i. Instruments on which the device can be used,
    ii. if the assay is automated or not,
    iii. is the IVD medical device qualitative or quantitative,
    iv. and the specimen types (e.g. serum, plasma, urine, cerebrospinal fluid), including any additives that are required (e.g. anticoagulant)
b) Intended user: Lay person or professional?
c) Identify if the device is intended for single or multiple use
d) Indications for Use:
    i. Disease or medical condition that the device will diagnose, treat, prevent, mitigate, or cure, parameters to be monitored and other considerations related to indication for use.
    ii. If applicable, information about patient selection criteria.
    iii. If applicable, when/where the use of the IVD medical device should be avoided.

iv. If applicable, information about the intended patient population (e.g. adults, pediatrics or newborn) or a statement that no subpopulations exist for the disease or condition for which the device is intended.

e) For amendments/supplements or changes to existing approvals, identify any changes to the previously approved intended use/intended purpose/intended user/indications. If there are no changes, this should be stated.

NOTES:

i. The statements of intended use and indications for use must be as presented in the labelling.
ii. If more than one device is included, the information should be provided for each device.

2.05.02 Intended Environment/Setting for use

a) The setting where the device is intended to be used (e.g. home use, domestic use, self-testing, near-patient, point of care). Multiple options can be indicated.
b) If applicable, environmental conditions that can affect the device's safety and/or performance (e.g. temperature, humidity, power, pressure, movement).

2.05.03 Pediatric Use

2.05.04 Limitations/Contraindications for Use

If applicable, specify the disease or medical conditions that would make use of the device inadvisable due to unfavorable risk/benefit profile.

NOTE: The statement of limitations/contraindications for the device must be as presented in the labelling.

2.06 Global Market History

2.06.01 Global Market History

a) Up to date indication of the markets (all countries or jurisdictions) where the device is already marketed, including any marketing under compassionate use regulations.

b) Should include history of the marketing of the device by any other entity in as much detail as possible, acknowledging that detailed information may not be available in all cases.
c) Include a list of all countries in which the device has been removed from marketing for any reason related to the safety or effectiveness of the device.

2.06.02 Incident Reports and Recalls

a) List adverse events/incidents associated with the device and a statement of the period associated with this data.
b) If the number of events is voluminous, provide a summary by event type that state the number of reported events for each event type.
c) List of the IVD medical device recalls and/or advisory notice, and a discussion of the handling and solution given by the manufacturer in each case.
d) A description of any analysis and/or corrective actions undertaken in response to items listed above.
e) If there have been no adverse events/incidents, recalls and/or advisory notice to date, provide an attestation from device owner on company letterhead, that there have been no adverse events/incidents, recalls and/or advisory notice since commercial introduction of the device.

2.06.03 Sales, Incident and Recall Rates

a) A summary of the number of units sold in each country/region and a statement of the period associated with this data.
b) Provide the rates calculated as follows for each country/region:
    i. Incident rate = # adverse events/incidents divided by # units sold expressed as a percentage
    ii. Recall rate = # recalls divided by # units sold expressed as a percentage

Rates may be presented in other appropriate units such as per patient year of use or per use. In this case, methods for determining these rates should be presented and any assumptions supported.

c) Critical analyses of the rates calculated (e.g. Why are they acceptable? How do they break down in terms of incidents? Is there some outlier data that has driven the rates up? Are there any trends associated with any sub-groups of the devices that are subject of submission (e.g. size, version)?

NOTE:

Sales in this context should be reported as the number of units sold.

2.06.04 Evaluation/Inspection Reports

2.07 Post-Market Study Plans

Post-Market Study Plans may include clinical or non-clinical study plans. The documentation provided here will not include final reports and analysis and instead includes study plan information only. This may include:

a) Study Objectives
b) Study Design
c) Subjects and Sites information
d) Endpoints (primary and secondary)
e) Summary of Data Analysis plan
f) Length and frequency of follow-up

Note: Post-Market Non-Clinical or Clinical Data from a region provided during the pre-market phase would be considered non-clinical or clinical data and would reside in Chapter 3 or Chapter 4, respectively.

2.08 Risk Management

a) A summary of the risks identified during the risk analysis process and how these risks have been controlled to an acceptable level. Plans can be considered part of the risk management documentation.
b) The results of the risk analysis should provide a conclusion with evidence that remaining risks are acceptable when compared to the benefits.
c) Where a standard is followed, identify the standard.

2.09 Essential Principles (EP) of Safety and Performance Checklist

a) An EP checklist established for the medical devices, information about method(s) used to demonstrate conformity with each EP that applies, references for the method

adopted and identification of the controlled document with evidence of conformity with each method used.

b) For the controlled documents indicated which are required for inclusion in the submission: a cross-reference of the location of such evidence within the submission.
c) If any EP indicated in the checklist does not apply to the device: a documented rationale of the non-application of each EP that does not apply.

NOTE: Methods used to demonstrate conformity may include one or more of the following:

a) conformity with recognized or other standards;
b) conformity with a commonly accepted industry test method(s);
c) conformity with an in-house test method(s);
d) the evaluation of pre-clinical and clinical evidence;

comparison to a similar device already available on the market.

2.10 Standards

2.10.01 List of Standards and Guidance Documents

This section should include:

a) If applicable, a list of the standards that have been complied with in full or in part in the design and/or manufacture of the device.
    i. At a minimum should include the standard organization, standard number, standard title, year/version, and if full or partial compliance.
    ii. If partial compliance, a list the sections of standard that
        - Are not applicable to the device, and/or
        - have been adapted, and/or
        - were deviated from for other reasons – discussion to accompany
b) If applicable, a list of relevant guidance documents published by regulators and referenced in the design and/or manufacture of the device with the jurisdiction of publication, publication date and title identified.

If applicable, a list of relevant clinical guidelines referenced in the design and/or manufacture of the device, the publisher, publication date and title identified.

2.10.02 Declaration and/or Certification of Conformity

2.11 Other Submission Context Information

Heading for other submission context information that may be important to the submission but that does not fit in any of the other headings of this chapter.

NOTE: To ensure all elements of your submission are adequately reviewed, please be sure that any content placed here does not belong under any heading described above.

Chapter 3 – Analytical performance and other evidence

3.01 Chapter Table of Contents

a) Includes major headings for the chapter, to the level of the custom headings.
b) Specifies the page number for each item referred to in the table.

3.02 Chapter Retired

3.03 Chapter Retired

3.04 Chapter Retired

3.04.01 Chapter Retired

3.04.02 Chapter retired

3.05 Analytical Performance

3.05.01 Stability of Specimen(s)

Information regarding and studies to support stability, storage and where appropriate transport, of all of the specimen type(s) identified in the labelling, including any and all recommended additives (e.g. anticoagulants) is to be provided in this section. This should include:

a) For each specimen type identified in the labelling, a description of the recommended storage parameters and when applicable, transport conditions (e.g. duration, temperatures and freeze/thaw cycles).
b) A justification on the selection of the studies performed.
c) Provide a summary of the evidence that falls within this category.
d) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.
   OR
e) A discussion of why this category of study is not applicable to this case.

3.05.01.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone. For example, the structure will look something like this

Level 3: Storage of serum samples for 7 days at 2-8ºC or 4 days at -20ºC. Level 4: Summary Level 4: Full Report Level 3: Validation of 3 freeze/thaw cycles for serum samples Level 4: Summary Level 4: Full Report

3.05.01.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.01.01.02 Full Report

The test report for the test is described in the custom heading above.

3.05.01.01.03 Statistical Data

3.05.02 Validation of Specimens

Studies to support the validity of specimen type(s) used in the analytical and clinical studies as representative of all of the sample type(s) identified in the labelling, including any and all

recommended additives (e.g. anticoagulants), as well as contrived specimens used in certain analytical studies are to be included in this section. This should include:

a) A list of the specimen type(s) used, including any additives (e.g. anticoagulants), in each of the analytical performance studies. If the same specimens are used for all analytical studies this can be stated and the specimen type identified.
b) For any or all of the analytical and clinical studies, if a particular specimen type(s) including additives (e.g. anticoagulants), has been chosen as representative of other specimen types identified in the labelling, this should be described and supported.
c) If the preparation of the specimen has not followed the protocol described in the current labelling, this should be identified and validated.
d) Justification of the selection of the studies performed.
e) Provide a summary of the evidence that falls within this category.
f) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.
OR
g) A statement of why this category of study is not applicable to this case.

3.05.02.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.05.02.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.02.01.02 Full Report

The test report for the test is described in the custom heading above.

3.05.02.01.03 Statistical Data

3.05.03 Metrological traceability of calibrator and control material values

Evidence that supports the metrological traceability of values assigned to calibrators and trueness control materials. This should include:

a) A description of all calibrators and trueness control materials associated with the system.
b) Justification of the selection of the studies performed.
c) Provide a summary of the evidence that falls within this category, including for example, methods and acceptance criteria for the metrological traceability to reference materials and/or reference measurement procedures and a description of value assignment and validation.
d) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.
   OR
e) A statement of why this category of study is not applicable to this case.

NOTE:

Precision control materials used during analytical studies to establish the reproducibility of a measurement procedure do not require the assessment of metrological traceability to a reference material or a reference method.

3.05.03.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.05.03.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.03.01.02 Full Report

The test report for the test is described in the custom heading above.

3.05.03.01.03 Statistical Data

3.05.04 Accuracy of Measurement

NOTE: The general term measurement accuracy is currently used to cover both trueness and precision, whereas this term was used in the past to cover only the one component now named trueness. While measurement trueness, affected by systematic error, is normally expressed in terms of bias, measurement precision, affected by random error, is naturally expressed in terms of standard deviation. Accuracy is affected by a combination of systematic and random effects that contribute as individual components of the total error of measurement.

3.05.04.01 Trueness

This section should provide a summary of information and evidence relating to the trueness of the measurement procedure. Trueness measures apply to both quantitative and qualitative assays only when a reference standard or method is available. This should include:

a) A rationale for the reference standard or method(s) used
b) A summary of the evidence that falls within this category
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.
   OR
d) A statement of why this category of study is not applicable to this case.

3.05.04.01.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.05.04.01.01.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.04.01.01.02 Full Report

The test report for the test is described in the custom heading above.

3.05.04.01.01.03 Statistical Data

3.05.04.02 Precision (Repeatability and Reproducibility)

A summary of evidence that supports the precision characteristics of the measurement of the subject IVD medical device is to be included in this section. This should include:

a) Justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category, including:
    i. Repeatability estimates and a brief summary about the studies used to estimate, as appropriate, within-run variability.
    ii. Reproducibility estimates and a brief summary of the studies used to estimate, as appropriate, variability between days, runs, sites, lots, operators (intended users) and instruments. Such variability is also known as "Intermediate Precision".
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of study is not applicable to this case.

NOTE: Studies should include the use of specimens that represent the full range of expected analyte (measured) concentrations that can be measured by the product, as claimed by the manufacturer.

3.05.04.02.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.05.04.02.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.04.02. 01.02 Full Report

The test report for the test is described in the custom heading above.

3.05.04.02.01.03 Statistical Data

3.05.05 Analytical Sensitivity

Evidence that supports the analytical sensitivity of the subject IVD medical device is to be included in this section. This may include studies to establish the limit of blank (LoB), limit of detection (LoD), and/or limit of quantitation (LoQ). This should include:

a) A justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of study is not applicable to this case.

3.05.05.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.05.05.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.05.01.02 Full Report

The test report for the test described in the custom heading above.

3.05.05.01.03 Statistical Data

3.05.06 Analytic Specificity

Evidence that supports the analytical specificity (interference, including as appropriate, selectivity, and cross reactivity) of the subject IVD medical device is to be included in this section. This should include:

a) A justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of study is not applicable to this case.

3.05.06.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.05.06.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.06.01.02 Full Report

The test report for the test described in the custom heading above.

3.05.06.01.03 Statistical Data

3.05.07 High Dose Hook Effect

Evidence that supports the absence of a high dose hook effect or prozone effect. This should include:

a) A justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category

c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of study is not applicable to this case.

3.05.07.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.05.07.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.07.01.02 Full Report

The test report for the test described in the custom heading above.

3.05.07.01.03 Statistical Data

3.05.08 Measuring Range of the Assay

Evidence that supports the measuring range (linear and non-linear measuring systems). This measuring range should include the lower limit of quantification. This should include:

a) A justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of study is not applicable to this case.

3.05.08.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.05.08.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.08.01.02 Full Report

The test report for the test described in the custom heading above.

3.05.08.01.03 Statistical Data

3.05.09 Validation of Assay Cut-off

Evidence that supports the determining assay cut-off is to be included here. This should include:

a) A justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of study is not applicable to this case.

3.05.09.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.05.09.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.09.01.02 Full Report

The test report for the test described in the custom heading above.

3.05.09.01.03 Statistical Data

3.05.10 Validation of the Assay Procedure

This section should provide a summary of information and evidence supporting the validity of the assay procedure in terms of important reaction conditions (e.g. reaction time, reaction temperature, reagent volume, reading time). This should include:

a) A justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category.
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of study is not applicable to this case.

3.05.10.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.05.10.01.01 Summary

A summary of the specific study described in the custom heading above.

3.05.10.01.02 Full Report

The test report for the test described in the custom heading above.

3.05.10.01.03 Statistical Data

3.06 Other Studies

3.06.01 Electrical Systems: Safety, Mechanical and Environmental Protection, and Electromagnetic Compatibility mechanical and environmental protection, and electromagnetic compatibility are to be included in this section. This should include:

a) A justification of the selection of the studies performed.
b) A summary of the evidence that falls within this category.
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of laboratory study is not applicable to this case.

3.06.01.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.06.01.01.01 Summary

A summary of the specific study described in the custom heading above.

3.06.01.01.02 Full Report

The test report for the test described in the custom heading above.

3.06.01.01.03 Statistical Data

3.06.02 Software/Firmware/Programmed or programmable medical

LEVEL Studies and supporting information on the software design, development process and evidence of the validation of the software, as used in the finished IVD medical device, are to be included in this section and the associated sub-sections. It should also address all the different hardware configurations and, where applicable, operating systems identified in the labelling. Documentation should be organized according to software or hardware systems.

3.06.02.01 Software/Firmware Description

The software description should include:

a) A comprehensive overview of significant software features and functions, which may include images, flow charts, and state diagrams as needed to adequately explain the software functionality,
b) The version of the software - The version tested must be clearly identified and should match the release version of the software, otherwise justification must be provided,
c) Identification of the IVD medical device features that are controlled by the software, the programming language, hardware platform, operating system (if applicable), use of Off-the-shelf software (if applicable), a description of the realization process.

If the product is a machine learning-enabled medical device (such as adaptive models, natural language processing, neural networks, and related approaches), please provide, as applicable:

i. a detailed description of each algorithm/model, including its inputs, outputs, data selection and management for training, testing, and validation
ii. model selection and evaluation;
iii. risk management activities;
iv. materials/approaches used to provide transparency; and
v. post-market performance monitoring activities.

3.06.02.02 Risk Management File (including Hazard Analysis)

The risk management file should be provided and include the risk management plan, risk assessment (e.g. hazard analysis), and risk management report. The risk assessment (e.g. hazard analysis) should take into account all device hazards associated with the IVD medical device's intended use.

For Software that is part of a system, a risk assessment should be performed on the system comprising the software and its whole hardware environment and noted in the software documentation with reference to the particular section of the premarket submission.

3.06.02.03 Software Requirement Specifications (SRS)

The Software Requirements Specifications (SRS) documentation should describe the needs or expectations for a system or software, presented in an organized format, at the software system level or subsystem level, as appropriate, and with sufficient information to understand the traceability of the information with respect to the other software documentation elements (e.g. risk management file, software design specification, system and software architecture design chart, software testing).

The SRS documents the requirements for the software which typically specifies inputs and outputs, functions that the software will perform, hardware, performance, interfaces, user interaction, error definition and handling, intended operating environment, safety and security related requirements derived from a risk assessment (hazard analysis) and all ranges, limits, defaults, and specific values that the software will accept.

3.06.02.04 System and Software Architecture Design (SAD) Chart

The System and Software Architecture Design (SAD) Chart should consist of detailed diagrams of the modules, layers, and interfaces that comprise the device, their relationships, the data inputs/outputs and flow of data, and how users or external products (including information technology (IT) infrastructure and peripherals) interact with the system and software. If the System and Software Architecture Design Chart is included in another document, such as the SRS, a reference to the location of the System and Software Architecture Design Chart in the submission should be included.

3.06.02.05 Software Design Specification (SDS)

Software Design Specification (SDS) documentation should be provided, including sufficient information to understand the technical design details of how the software functions, how the software design completely and correctly implements all the requirements of the SRS, and how the software design traces to the SRS in terms of intended use, functionality, safety, and effectiveness.

In terms of the relationship between the SRS and the SDS, the SRS describes what the software function will do and the SDS describes how the requirements in the SRS are implemented. The information presented in the SDS should be sufficient to ensure that the work performed by the software engineers who created the device software function was clear and unambiguous, with minimal ad hoc design decisions.

3.06.02.06 Traceability Analysis

A Traceability Analysis links together your product design requirements, design specifications, and testing requirements. It also provides a means of tying together identified hazards with the implementation and testing of the mitigations.

3.06.02.07 Software Life Cycle Process Description/Software Development, Configuration Management, and Maintenance Practices

The Software Life Cycle Process Description/Software Development, Configuration Management, and Maintenance Practices description should describe the software development life cycle and the processes that are in place to manage the various life cycle activities.

3.06.02.08 Software Testing as Part of Verification and Validation

You should provide an overall description of the verification and validation activities performed for the final software version. You should provide the applicable test protocols and reports including the expected results, observed results and pass/fail determination.

NOTE: Discussion should address all of the different hardware configurations and, where applicable, operating systems identified in the labelling.

3.06.02.09 Software Version / Revision Level History

The Software Version / Revision Level History documentation should include the history of software versions that were tested and documented as part of verification and validation activities. This typically takes the form of a line-item tabulation including the date, version number that was tested and a brief description of all changes in the version relative to the previously tested version.

The last entry in a line-item tabulation should be the final version to be incorporated in the released device. This entry should also include any differences between the tested version of software and the released version.

3.06.02.10 Unresolved Software Anomalies

Documentation should include a list of unresolved anomalies present in the software with the following items (e.g. in tabular format) for each unresolved anomaly:

i. A description of what the anomaly is and what root cause(s) of the anomaly could be;
ii. Identification of how the anomaly was discovered and, where possible, identification of the root cause(s) of the anomaly;
iii. Evaluation of the impact of the anomaly on the device's safety and effectiveness, including operator usage and human factors considerations;
iv. Outcome of the evaluation; and
v. Risk-based rationale for not correcting or fixing the anomaly in alignment with the risk management plan or procedure(s).

3.06.02.11 Cybersecurity

For a description of the Cybersecurity Common Content, please refer to IMDRF/CYBER WG/N60 FINAL:2020 "Principles and Practices for Medical Device Cybersecurity"

3.06.02.12 Interoperability

If the IVD medical device can communicate with other devices. Evidence to support interoperability should be provided.

3.06.03 Cleaning and Disinfection Validation

Contains information on the validation of cleaning and disinfection instructions for reusable devices, including evidence to support maintenance of performance when subject to this procedure over a number of cycles that is representative of the IVD medical device's expected useful life. Information to be included in this section includes:

a) If applicable, a discussion of how the number of cycles that is representative of the IVD medical device's expected useful life has been determined.
b) A justification of the selection of the studies performed.
c) A summary of the evidence that falls within this category
d) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

e) A statement of why this category of laboratory study is not applicable to this case.

NOTE: This applies most typically to devices intended for Point of care and/or home use (near patient testing) involving whole blood.

3.06.03.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.06.03.01.01 Summary

A summary of the specific study described in the custom heading above.

3.06.03.01.02 Full Report

The test report for the test is described in the custom heading above.

3.06.03.01.03 Statistical Data

3.06.04 Usability/Human Factors

Studies specifically assessing the instructions and/or IVD medical device design in terms of impact of human behavior, abilities, limitations, and other characteristics on the ability of the IVD medical device to perform as intended should be included here. This should include:

a) State the test environment and relation to the intended use environment
b) A justification of the selection of the studies performed.
c) A summary of the evidence that falls within this category
d) A discussion and conclusion to support why the evidence presented is sufficient to support the application.

OR

e) A statement of why this category of laboratory study is not applicable to this case.

NOTE: If a clinical study has been conducted that includes usability/human factors endpoints, **reference to the studies and endpoints should be made, but full results do not need to be repeated and should be included in Chapter 4 – Clinical Evidence**.

3.06.04.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.06.04.01.01 Summary

A summary of the specific study described in the custom heading above.

3.06.04.01.02 Full Report

The test report for the test is described in the custom heading above.

3.06.04.01.03 Statistical Data

3.06.05 Stability of the IVD

3.06.05.01 Claimed Shelf life

Contains details and evidence supporting the claimed shelf-life of the IVD medical device components (e.g. reagents, calibrators/reference materials, control material, any other components susceptible to degradation). Information provided in this section should include:

a) A description of recommended environmental conditions for storage of the IVD medical IVD medical device (e.g. temperature, pressure, humidity, light conditions).
b) A statement of the claimed shelf-life indicated as a period of time or any other means of appropriate quantification.

c) An indication of the packaging used in any studies conducted in support of the shelf life. If the packaging used in the studies differs from the final device packaging, a discussion of why the evidence can be consider valid in support of the claimed shelf-life.
d) A description of the simulated transport conditions that the IVD was exposed to before the start of shelf-life studies.
e) A justification of the selection of the studies performed.
f) A summary of the evidence that falls within this category
g) A discussion and a conclusion to support why the evidence presented is sufficient to support the claimed shelf-life.

OR

h) A rationale that, for an indefinite period, the storage conditions could not affect IVD medical device safety or performance.

3.06.05.01.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The sub headings below would be for this study alone.

3.06.05.01.01.01 Summary

A summary of the specific study described in the custom heading above.

3.06.05.01.01.02 Full Report

The test report for the test is described in the custom heading above.

3.06.05.01.01.03 Statistical Data

3.06.05.02 In Use Stability

Contains details and evidence supporting the stability during actual routine use of the IVD medical device (real or simulated), including all applicable components (e.g. reagents,

reaction cartridges). This may include open vial stability and/or, for automated instruments, onboard stability. Information provided in this section should include:

a) A description of recommended environmental conditions for use of the IVD medical device (e.g. temperature, pressure, humidity, light conditions).
b) A justification of the selection of the studies performed.
c) A summary of the evidence, covering shelf-life period when stored at the proposed storage condition, that falls within this category.
d) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

e) A rationale that, for an indefinite period, the storage conditions could not affect IVD medical device safety or performance.

3.06.05.02.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.06.05.02.01.01 Summary

A summary of the specific study described in the custom heading above.

3.06.05.02.01.02 Full Report

The test report for the test is described in the custom heading above.

3.06.05.02.01.03 Statistical Data

3.06.05.03 Shipping Stability

Contains details and evidence supporting the tolerance of IVD medical device, or if provided separately, the components (e.g. reagents, calibrators/reference materials) to the specified or expected shipping conditions. Information provided in this section should include:

a) An indication of environmental conditions for correct shipment of the IVD medical device (temperature, pressure, humidity, light conditions, mechanical protection etc.).
b) A justification of the selection of the studies performed.
c) A summary of the evidence, covering shelf life period, that falls within this category
d) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

e) A rationale that, for an indefinite period, the storage conditions could not affect IVD medical device safety or performance.

3.06.05.03.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.06.05.03.01.01 Summary

A summary of the specific study described in the custom heading above.

3.06.05.03.01.02 Full Report

The test report for the test is described in the custom heading above.

3.06.05.03.01.03 Statistical Data

3.07 Analytical Performance and Other Evidence Bibliography

a) A listing of published studies relevant to the context of this Chapter that involve this specific IVD medical device (e.g. analytical specificity, analytical sensitivity)
b) A legible copy of key articles, including translation where applicable.
c) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

OR

d) A statement that no literature related to the IVD medical device was found.

3.08 Other Evidence

Heading for other information that may be important to the submission but that does not fit in any of the other headings of this chapter. For example, for tests performed to ensure the safety and/or performance of the IVD medical device that are not delineated in the rest of Chapter 3. In addition

a) Describe the purpose of the test, the risk/safety issue the test is addressing; the test methods and results of the test
b) A justification of the selection of the studies performed.
c) A summary of the evidence that is being submitted under this heading
d) A discussion and a conclusion to support why the evidence presented is sufficient to support the application.

3.08.01 [Study description, study identifier, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone.

3.08.01.01 Summary

A summary of the specific study described in the custom heading above.

3.08.01.02 Full Report

The test report for the test is described in the custom heading above.

3.08.01.03 Statistical Data

Chapter 4 – Clinical Evidence

4.01 Chapter Table of Contents

a) Includes all headings for the chapter.
b) Specifies the page number for each item referred to in the table.

4.02 Overall Clinical Evidence Summary

a) This should be a brief (1-2 page) summary of the available clinical evidence being presented in support of the submission. The document should list the evidence presented, its characteristics (e.g. well controlled studies, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, literature review, post market data from another jurisdiction or from a marketed device)) and provide a discussion of how this is considered sufficient to support request for marketing for the requested indications. A tabular listing of clinical studies may be included in this section.
b) If any of the study IVD medical devices differ from the IVD medical devices to be marketed, including competitors' IVD medical devices, a description of these differences and their impact on the validity of the evidence in terms of support for the application for any device referenced in the application. This may include a detailed comparison of the clinical, technical and biological characteristics of the two devices, with a detailed critical analysis demonstrating the devices to be similar to such an extent that there would be no clinically significant difference in safety or performance.
c) A discussion of the clinical evidence considered for the IVD medical device and support for their selection (i.e. what type of evidence was considered and why they were or were not used)
d) Discussion to support why the evidence presented is sufficient to support the application.

NOTE: Human factors testing that include patients should be included here.

4.02.01 Expected Values/Reference Ranges

This section should include information on what values to expect in healthy normal patients versus affected patients.

4.02.02 Clinical Evidence Evaluation Report

a) A clinical evidence evaluation report reviewed and signed by an expert in the relevant field that contains an objective critical evaluation of all of the clinical data submitted in relation to the IVD medical device.
b) A complete curriculum vitae, or similar documentation, to justify the manufacturer's choice of the clinical expert.

4.02.03 IVD medical Device Specific Clinical Studies

LEVEL Clinical study information under this heading should be grouped by study

4.02.03.01 [Study description, protocol, date of initiation, date of completion]

This heading should be CUSTOM AND BASED ON STUDY DETAILS and created for each study under the parent heading. The subheadings below would be for this study alone. For example, the structure will look something like this Level 3: EU Pilot Study, CT4203, 2010-10-10 Level 4: Clinical Study Synopsis Level 4: Clinical Study Report Level 3: NA Controlled Study, CT4584, 2011 01-23 Level 4: Clinical Study Summary Level 4: Clinical Study Report

4.02.03.01.01 Clinical Study Summary

a) A summary of the specific study described in the custom heading above that includes:
    i. The key characteristics of the study (e.g. title of study, investigators, sites, study period (date of enrollment/date of last completed), objectives, methods, statistical design, interpretation of design, patients, inclusion/exclusion criteria) and
    ii. Summary of the results of the analysis
    iii. Summary of conclusions related to the endpoints

NOTE: The applicant should explicitly state whether the data are disaggregated by sex, gender, age, race, and ethnicity. If the data are not disaggregated, the sponsor/applicant should provide a rationale why.

4.02.03.01.02 Clinical Study Report

a) A clinical study report of the specific study described in the custom heading above.

NOTE: The clinical study report should include elements such as the investigational plan/study protocol, protocol changes and deviations, description of patients, data quality assurance, analysis/results.

4.02.04 Clinical Literature Review and Other Reasonable Known Information

a) Clinical literature review that critically reviews available information that is published, available, or reasonably known to the applicant/sponsor that describes safety and/or performance of the IVD medical device
b) A legible copy of key articles, including translation where applicable.

OR

c) A statement that no literature related to the IVD medical device was found.

NOTE: Please see Chapter 2.07 for Post-Market Study Plans

4.03 Informed Consent Information

4.04 Investigators Sites and IRB contact information

4.05 Real World Data (RWD)

Where applicable, other clinical experience data/real world data (including device registries, post-market studies conducted in other jurisdictions)

4.06 Post-Market Surveillance Data

4.07 Other Clinical Evidence

Heading for other information that may be important to the submission but that does not fit in any of the other headings of this chapter.

Chapter 5 – Labelling and Promotional Material

5.01 Chapter Table of Contents

a) Includes all headings for the chapter.
b) Specifies the page number for each item referred to in the table.

5.02 Product/Package Labels

Samples of the primary and secondary packaging labels.

NOTE: Do not include shipping labels.

5.03 Package Insert/Instructions for Use

Package Insert/Instructions for Use included in the package, when required or provide support for why this element is not applicable.

5.04 e-labelling

In addition to the e-labelling itself, the following should be provided:

a) For eligible IVD medical devices and Software as a Medical Device, the applicant needs to identify which form of e-labelling is being used (e.g. electronic storage system or built-in system, website).
b) Provide details of risk management in relation to e-labelling. If this is part of the overall risk management, refer to it here
c) When IFUs are requested, a description of the procedure and operations on providing these IFUs.
d) Provide written information for users on the webpage identifying where the IFU and further information can be found in relevant languages.
e) A description on how the e-labelling requirements for the website have been met.
f) If a video/App is available to demonstrate how the test is intended to perform and be interpreted, provide a link as well as details about how it is maintained and updated throughout the life cycle of the device.

5.05 Patient Labelling

Labelling directed at the patient other than the package insert, such as informational material written to be comprehended by the patient or lay caregiver

5.06 Technical and/or Operators Manuals

Labelling directed to the technical users and operators of IVD medical devices focusing on the proper use and maintenance of the IVD medical device

5.07 Product Brochures

5.08 Other Labelling and Promotional Material

Heading for other information that may be important to the submission but that does not fit in any of the other headings of this chapter.

Chapter 6 – Quality Management System

6.01 Cover Letter

A Cover Letter is only required under this chapter when the submission only includes quality system information.

6.02 Chapter Table of Contents

a) Includes all headings for the chapter.
b) Specifies the page number for each item referred to in the table.

6.03 Product Descriptive Information

Abbreviated description of the device, operating principles and overall manufacturing methods. This section includes general information such as:

a) A description of the device, including pictures, and where possible, the proprietary name, common name, model number(s), product code, and intended use; and
b) A description of how the device works

Product Descriptive Information is only provided under this chapter when the submission includes quality system information, and Chapter 2.04 "Device Description" is not provided as part of the submission.

6.04 General Manufacturing Information

a) Name, address, scope/role, and contact information for all sites where the device or its components are manufactured.
b) Description of any relationship between the facilities and the applicant when there is more than one involved in the manufacturing process for the applicable device.
c) Where applicable, addresses for all critical subcontractors, such as outsourced production, critical component, or raw material production (e.g., animal tissue, drugs), and sterilization, will need to be provided.

6.05 Required Forms

6.06 Quality Management System

High level quality management system documents, including procedures for establishing and maintaining the quality management system such as the quality manual, quality policy, quality objectives, and control of documents and records, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

- ISO 13485 Elements– SOPs and device specific documentation to satisfy clause 4

6.07 Management Responsibilities

Documents, including procedures that provide evidence of the management commitment to the establishment and maintenance of the QMS by addressing quality policy, planning, responsibilities/authority/communication and management review, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

- ISO 13485 Elements – SOPs and device-specific documentation to satisfy clause 5

6.08 Resource Management

Documents, including procedures that provide evidence of the adequate provision of resources to implement and maintain the QMS, as referenced in the Agency's regulation, including human resources, infrastructure, and work environment, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

- ISO 13485 Elements – SOPs and device specific documentation to satisfy clause 6

6.09 Planning of Product Realization and Customer Related Processes

High level product realization documents, including procedures such as those addressing planning and customer related processes, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

Records demonstrating conformance to requirements are only provided under this chapter when the submission includes quality system information, and these records were not provided within the submission as part of a previous subchapter.

- ISO 13485 Elements – SOPs and device specific documentation implementing sub clause 7.1 and 7.2

6.10 Design and Development

Documents, including procedures that provide evidence of the systematic and controlled development of the device design from initiation of the project to transfer to production, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

Records demonstrating conformance to requirements are only provided under this chapter when the submission includes quality system information, and these records were not provided within the submission as part of a previous subchapter.

- ISO 13485 Elements – SOPs and device specific documentation implementing sub clause 7.3

6.11 Purchasing

Documents, including procedures that provide evidence that purchased products/services conform to established relevant quality and/or product specifications, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

- ISO 13485 Elements – SOPs and device specific documentation implementing sub clause 7.4

6.12 Production and Service Controls

- ISO 13485 Elements – SOPs and device specific documentation implementing sub clause 7.5

6.13 Control of Monitoring and Measuring Equipment

Documents, including procedures that provide evidence of monitoring and measuring equipment used in the QMS is controlled and continuously performing per the established requirements, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

- ISO 13485 Element- SOPs and device specific documentation for implementing sub clause 7.6

6.14 QMS Measurement, Analysis and Improvement

Documents, including procedures that provide evidence of how monitoring, measurement, analysis and improvement to ensure the conformity of the product and QMS, and to maintain the effectiveness of the QMS, as well as records providing evidence of conformance to requirements, and of the effective operation of the quality management system (when applicable).

- ISO 13485 Element – SOPs and device specific documentation for implementing clause 8.

6.15 Device Specific Quality Plan

6.16 Quality management system verification document

6.17 Other Quality System Information

Heading for other information that may be important to the submission but that does not fit in any of the other headings.