Ethiopian Food and Drugs Authority

Guideline for Registration Requirements of Medical Devices other than In Vitro Diagnostic Devices

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ACRONYMS

EFDA	Ethiopian Food and Drugs Administration
CAPA	Corrective Action and Preventive Action
CSDT	Common Submission Dossier Template
EU	European Union
GMDN	Global Medical Device Nomenclature
IMDRF	International Medical Device Regulators Forum
MDUFA	Medical Device User Fee Amendments
NB	Notified Body
SUD	Single Use Device
TGA	Therapeutic Goods Administration - Australia
USFDA	United States Food and Drug Administration
IRB	Institutional Review Board

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- Kidanemariam Gebremichael (Senior Pharmacist), JSI Technical Advisor at EFDA
- Keneni Benti (MSc in Biomedical Engineering), Medical Device Registration Dossier Assessor at EFDA
- Daniel Takele (BSc in Biomedical Engineering), Medical Device Registration Dossier Assessor at EFDA
- Solomon Shiferaw (Senior Pharmacist), Mckinsey Technical Advisor at EFDA

1. INTRODUCTION

Ethiopian Food and Drugs Authority is the national regulatory authority responsible to regulate food, medicines, medical devices, cosmetics and other health products mandated by Ethiopian Food and Medicine Administration Proclamation No: 1112/19. The regulated products including medical devices follow various regulatory processes from their premarket assessment to post-market control in order to protect the public health by ensuring the safety, performance and quality of the products. One of the EFDA's premarket assessments is to evaluate the product dossiers of the medical devices. This guideline is therefore intended to provide a comprehensive and well-organized structure for premarket medical device submissions that assists the manufacturers to submit uniform registration dossier when registering their products.

This document provides harmonized, modular, format for use when filing Non-IVD medical device submissions to EFDA for market authorization.

This outline of documentation is to support a smooth documentation process. It remains the applicant's responsibility to ensure all regulatory requirements are met, and that clear and transparent evidence of conformity to these requirements are provided.

Manufacturers of all classes of medical device are expected to demonstrate conformity of the device to the Essential Principles of Safety and Performance (EPSP) through collection and examination of evidence of conformity in technical documentation that shows how each medical device was developed, designed and manufactured together with the descriptions and explanations necessary to understand the manufacturer's determination with respect to such conformity. This technical documentation must be updated as necessary to reflect the current status, specification and configuration of the device.

The evidence of conformity of medical device to the EPSP must be compiled and submitted as per the requirements set in this guideline for the purpose of conformity assessment and submission of application for medical device registration. The compiled documents need to be kept in the premise for audit or inspection purposes.

The EFDA will monitor the use of these structures and work to continually improve the documents at appropriate intervals based on sufficient use and experience.

2. SCOPE

This Guideline is applicable for registration of medical devices other than In-vitro diagnostic devices. This guideline does not apply to medical devices listed under the "*Guideline for Premarket Notification of Low Risk Medical Devices*". The In Vitro diagnostic medical devices are also not in the scope of this guideline as these devices have separate guideline stipulating requirements for their registration.

3. PURPOSE

The purpose of this guideline is to provide guidance on requirements for Non- In Vitro Diagnostic medical devices registration in Ethiopia.

4. DEFINITIONS

Sponsor- Means any individual, company, institution or organization which takes responsibility for the initiation, for the management and setting up of the financing of the clinical investigation;

Single-use device- Means a device that is intended to be used on one individual during a single procedure;

Performance- Means the ability of a device to achieve its intended purpose as stated by the manufacturer;

Compatibility- Means the ability of a device, including software, when used together with one or more other devices in accordance with its intended purpose, to: (a) perform without losing or compromising the ability to perform as intended, and/or (b) integrate and/or operate without the need for modification or adaption of any part of the combined devices, and/or (c) be used together without conflict/interference or adverse reaction.

Interoperability- Means the ability of two or more devices, including software, from the same manufacturer or from different manufacturers, to: (a) exchange information and use the information that has been exchanged for the correct execution of a specified function without changing the content of the data, and/or (b) communicate with each other, and/or (c) work together as intended.

Cyber-security: Means a state where information and systems are protected from unauthorized activities, such as access, use, disclosure, disruption, modification, or destruction to a degree that the related risks to confidentiality, integrity, and availability are maintained at an acceptable level throughout the life cycle.

Reprocessing- Means a process carried out on a used device in order to allow its safe reuse including cleaning, disinfection, sterilization and related procedures, as well as testing and restoring the technical and functional safety of the used device;

Conformity assessment- Means the process demonstrating whether the requirements of this Regulation relating to a device have been fulfilled;

CE marking of conformity or 'CE marking'- Means a marking by which a manufacturer indicates that a device is in conformity with the applicable requirements set out in the European Union Medical Devices Regulation and other applicable Union harmonization legislation providing for its affixing;

Clinical evaluation- Means a systematic and planned process to continuously generate, collect, analyze and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer;

Clinical investigation- Means any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device;

Clinical data- Means information concerning safety or performance that is generated from the use of a device and is sourced from the following:

- clinical investigation(s) of the device concerned,
- clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question can be demonstrated,
- reports published in peer reviewed scientific literature on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated,
- clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up;

Clinical evidence- Means clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer;

Informed consent- Means a subject's free and voluntary expression of his or her willingness to participate in a particular clinical investigation, after having been informed of all aspects of the clinical investigation that are relevant to the subject's decision to participate or, in the case of minors and of incapacitated subjects, an authorization or agreement from their legally designated representative to include them in the clinical investigation;

Adverse event- Means any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational device;

Submission – Means 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.

Medical Devices other than In Vitro Diagnostic Devices: Means all medical devices including Active implantable devices, Anesthetic and respiratory devices, Dental devices, Electro mechanical medical devices, Hospital hardware, Non-active implantable devices, Ophthalmic and optical devices, Reusable devices, Single use devices, Assistive products for persons with disability, Diagnostic and therapeutic radiation devices, Complementary therapy devices, and Biological-derived devices that do not take human samples and perform in vitro analysis for screening, diagnosis or monitoring of diseases.

5. GENERAL GUIDANCE AND PRINCIPLES

The content of this Guideline should be read in conjunction with relevant information described in other existing International Medical Devices Regulators Forum (IMDRF) reference documents and guidelines.

The quality and performance of the intended product to be registered should not be inferior to the available options.

Alternate approaches to the principles and practices described in this Guideline may be acceptable provided they are supported by adequate scientific justification. It is important to note that the Authority may request information or material, or define conditions not specifically described in this guidance, in order to adequately assess the safety, performance, and quality of a medical device prior to and after approval.

General format and guidance for preparation of dossiers

Well organized and compiled documents will facilitate the evaluation process and decrease the delay in the screening time. In contrast, poorly compiled documents may lead to unnecessary loss of time, both for the applicant and the Authority. Therefore, documents should have unambiguous contents: title, nature, and purpose should be clearly stated. They should be laid out in an orderly fashion and be easy to check.

Formats of all the files to be submitted:

1. Paper size is A4; top, bottom, header, and footer margins are 12.5 mm; left and right margins are 25mm
2. Single-spaced paragraphs
3. Times New Roman font, 12-point; letter space 0%.
4. The weight of the font should be legible when copied.
5. The attached data and documents should appear in the English language.
6. Any abbreviations should be clearly defined.

Applications submitted for registration will be screened chronologically by the date of submission to the Authority, and the applicant will be notified of the evaluation results.

Some products are given assessment priority and they are listed in the “Medical Device Fast-track Directive”.

A request to add supplemental materials must be submitted within six months of being notified of missing elements and/or clarification. If the supplemental submission is not implemented within that time period, urge to be supplemented within 15 days shall follow.

If the supplemental document is not submitted within the urge period, or the contents of the replenishment is inappropriate, the speculation shall be clarified and the document shall be returned and/or rejected. However, if the applicant calls for an extension, the submission period shall be determined based on the speculation.

The agent or the manufacturer should appoint a technical person who is able to understand this and related guidelines of the Authority, who is familiar with the registration process of the products, and who can freely communicate with the assessors should clarification be needed (product-related or administrative) on queries raised by the Authority.

The Authority will not accept applications for registration by different applicants or local agents for the same product manufactured by the same manufacturer and/or subsidiaries of one manufacturer.

If the manufacturer of a medical device has one or more subsidiaries, the applicant is responsible for submitting the technical documents of each specific product under registration from each of the subsidiaries and/or from the site where the file is kept.

If the medical device use accessory and/or consumable (such as reagents, controls, etc.) which is manufactured by a company‘s subsidiary, the free sale certificate should indicate the same and/or a separate free sale certificate should be a part of the document.

If the medical device use accessory and/or consumable (such as reagents, controls, etc.) which is manufactured by an independent manufacturer, information regarding the manufacturer and the technical documents should be submitted. The authority will review on a case-by-case basis.

A medical device that an applicant has registered with the USFDA, Health Canada, European Union, Ministry of Health, Labour and Welfare (Japan), Therapeutic Goods Administration (Australia), or WHO Prequalification Programme is considered to be registered with Stringent Regulatory Authority approved devices registration procedures.

All the required documents should be attached at its respective attachment spaces in PDF format.

The application shall be made online through the Authority’s regulated products registration platform (www.eris.efda.gov.et) after obtaining the username and password from the concerned authorized person of the Registration department of the Authority.

CHAPTER ONE

ADMINISTRATIVE

1.1. Cover Letter

The cover letter should state applicant (Local agent), Manufacturer and License holder and/or their authorized representative name and full address.

It should also state the type of registration (application), the common name of the device, 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.

The cover letter should be stamped and signed by a person authorized by the applicant.

1.2. Agency Agreement

The local agent/representative and the license holder shall have an agreement of distribution as per the requirements set in Medical device Marketing Authorization Directive.

1.3. Evidence for registration application fee

Each application should be accompanied by a relevant service fee for registration.
Applicants are advised to consult the current rates of service fees regulation of the authority for the amount to be paid for application and contact the authority for details of mode of payment.

1.4. Quality Management System, Full Quality System

The Manufacturer shall have valid and genuine certificates confirming the implementation of good quality management system in the device's production process.

One of these certificates to be considered is ISO 13485 certificate in case it is issued by another Notified Body or registrar, CE full quality system certificates (QMS and annex II.3 MDD) covering the scope of products when issued by another Notified Body.

1.5. Good Manufacturing Practice (GMP) Certificates

For applicable high-risk medical devices, the copy of valid Certificate of compliance to Medical device Good Manufacturing Practice shall be provided.

1.6. Free Sale Certificate/Certificate of Marketing Authorization

Certificate issued by the National Regulatory Authority where the medical device is marketable, attesting that the device is marketable, without any restriction at their jurisdiction shall be submitted. This certificate shall indicate the name and full address of the manufacturer, the name(s) of the device(s) (with model if applicable) and explains whether the products are freely sold in the country of origin; if not, the reasons thereof should be clearly stated with appropriate justification. If the manufacturer of the medical device has subsidiaries, a free sale certificate should indicate the name and address of the subsidiaries with the name of the device they manufacture, and/or a separate free sale certificate should be submitted for each subsidiary. The certificate should be original, and valid.

1.7. Risk-free TSE/BSE attestation

The applicant should provide an attestation letter and/or declaration that the materials used for the manufacture of the device are free of any TSE/BSE-risk origin materials.

1.8. Declarations 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) Generic name, trade name and models (if applicable) of the device(s).

d) An appropriate conformity assessment procedure

The declaration must include the following information:

- Date from which the Declaration of Conformity is valid;
- Name and address of the device manufacturer; and,
- The name, position, and signature of the responsible person who has been authorized to complete the Declaration of Conformity on behalf of the manufacturer.

CHAPTER TWO

SUBMISSION CONTEXT

2.1. General Summary of Submission

a) Statement of the device type (e.g. hip implant, infusion pump, standalone software) 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, for example burst testing of a ceramic femoral head; electrical safety evaluation (IEC 60601) testing for an infusion pump).

b) Summary of submission, including

i. The type of submission (e.g. new, amendment, change of existing application, renewal);

ii. 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).

2.2. Device Description

2.2.1. Comprehensive Description and Principles of Operation

a) A general description of the device, including: Device Description

i. A statement of the device name and Principle of operation

ii. What the device does?

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. How it works? Including theory surrounding feature/variants/operating modes that enable the device to be used for indications/intended use (principle of operation/mechanism of action).

vi. If applicable, labelled pictorial representation (diagrams, photos, drawings).

vii. If system, how the components relate?

viii. If applicable, identify if the device incorporates software/firmware and its role

b) Product specification, including:

i. Physical characteristics or relevance to the end user (dimensions, weight)

ii. Features and operating modes

iii. Input specifications (e.g. electrical power requirements, settings and associated allowable ranges/limits)

iv. Output and performance characteristics (e.g. range and type of energy delivered, resolution of images)

v. If applicable, an indication of the variants/models of the devices and a summary of the differences in specifications of the variants (comparison table and/or pictures/diagrams with supporting text).

c) Engineering diagrams/prints/schematics of the device.

d) List of accessories intended to be used in combination with the devices.

e) Indication of any other medical devices or general product intended to be used in combination with the medical device (e.g. infusion sets and infusion pumps, bipolar electrode and RF equipment).

f) Components or accessories that can be sold separately should be identified.

g) If approved by the regulator, provide the approval number and identification for each component or accessory.

h) If the device is to be sterilized, an indication of who is to perform the sterilization and by what method (e.g. EtO, gamma irradiation, dry heat) OR an affirmative statement that the device is non-sterile when used.

NOTE: The validation report is not expected be presented at this point, only the device sterility condition shall be indicated here. If appropriate, for the validation report, see Chapter 3 – Non-Clinical Studies.

i) Summary of the composition of the device including, at minimum, the material specification and/or chemical composition of the materials that have direct or indirect contact with the user and/or patient. When required, full details to support how these specifications are met are to be provided in chapter 3 of this guideline required under “Chemical/Material Characterization”.

NOTE: If applicable, chemicals may 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.

j) 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), source (e.g. blood, bone, heart, any other tissue or cells), and the intended reason for its presence and, if applicable, its primary mode of action.

k) If the device contains an active pharmaceutical ingredient (API) or drug, an indication of the substance, should be provided. This should include its identity and source, and the intended reason for its presence and its primary mode of action.

2.2.2. Description of Device Packaging

a) Information regarding the packaging of the devices, including, when applicable, primary packaging, secondary and any other packaging associated;

b) Specific packaging of accessories marketed together with the medical devices shall also be described;

c) If the user needs to package the medical device or its accessories before they perform sterilization, information about the correct packaging (e.g. material, composition, dimension) should be provided.

2.2.3. 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 effectiveness of the final device design.

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

a) A list of similar devices (available on 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 Authority.

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.

2.2.5. Substantial Equivalence Discussion

a) Identify the predicate device(s), and optionally reference devices

i. trade name and model number

ii. Ensure the identified predicate device(s) is consistent throughout the submission

b) Include a comparison of indications for use and the technology (including features materials and principles of operation) between the predicate device(s) and subject device(s).

c) Include an analysis of why any differences between the subject device(s) and the predicate device(s) do not render the subject device(s) Not Substantially Equivalent, affect safety or effectiveness or raise different questions of safety and effectiveness.

2.3. Indications for Use and/or Intended Use and Contraindications

2.3.1. 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 the therapeutic or diagnostic function provided by the device and may describe the medical procedure in which the device is to be used (e.g. Diagnosis in vivo or in vitro, treatment monitoring rehabilitation, contraception, disinfection).

b) Intended Purpose: What is expected with the use of this medical device? Which results are expected?

c) Intended user and skills/knowledge/training that the user should have to operate or use the device.

d) Identify if the device is intended for single or multiple use

e) 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, information about 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.

NOTES:

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

2.3.2. Intended Environment/Setting for use

a) The setting where the device is intended to be used (e.g. domestic use, hospitals, medical/clinical laboratories, ambulances, medical/dental offices). 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).

2.3.3. Pediatric Use

a) Description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose or cure,
b) The number of affected pediatric patients, as a whole and within each pediatric subpopulation.

OR

c) Statement that no pediatric subpopulation exists for the disease or condition for which the device is intended.

2.3.4. 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 if contraindications for the device must be as presented in the labeling.

2.4. Global Market History

2.4.1. Global Market History

a) Up to date indication of the markets (all countries or jurisdictions) where the device is approved for marketing, including any marketing under compassionate use regulations. As an evidence, the list shall be supported by copies of Marketing Authorization, free sale certificates or any other supporting certificates issued by the National Regulatory Authorities of the listed Countries.

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) If the subject device is different in any way (e.g. design, labeling, specifications) from those approved or marketed in other jurisdiction, the differences should be described.

d) The month and year of market approval in each country or jurisdiction where the device is marketed. If the device has been marketed for greater than 10 years, a statement of greater than 10 years can be made.

e) For each of the markets listed in (a) above, and statement of the commercial names used in those markets OR a clear statement that the commercial names are the same in all jurisdictions.

f) State the date of data capture for the market history data.

g) If the subject device has been the subject of any previous compassionate use and/or clinical trials this should be identified and, if applicable, relevant reference numbers provided.

2.4.2. Global 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 adverse events is voluminous, provide a summary by event type that state the number of reported events for each event type.

c) List of the 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.

2.4.3. 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 for each country/region, for example:

i. Incident rate = # adverse events/incidents divided by # units sold x 100

ii. Recall rate = # recalls divided by # units sold x 100

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 analysis 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 the submission (e.g. size, version)?).

NOTES

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

ii. The summary of sales should be broken down by components when appropriate.

2.4.4. Evaluation/Inspection Reports

Copies of Evaluation/Inspection Reports from other parties (e.g. Notified Body inspection reports).

CHAPTER THREE

NON-CLINICAL EVIDENCES

3.1. 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.
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.

3.2. Essential Principles (EP) Checklist

a) An EP checklist (As per the Annex-I of this guideline) must be appropriately filled and submitted.
b) 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.
c) 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.
d) 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;
e) Comparison to a similar device already available on the market.

3.3. Standards

a) List the standards that have been complied with in full or in part in the design and manufacture of the device.

b) At a minimum should include the standard organization, standard number, standard title, year/version, and if full or partial compliance.

c) If partial compliance, a list the sections of standard that

i. Are not applicable to the device, and/or

ii. Have been adapted, and/or

iii. Were deviated from for other reasons – discussion to accompany

3.4. Non-clinical Studies

3.4.1. Physical and Mechanical Characterization

Evidence that support the physical or mechanical properties of the subject device is to be included in this section. This should include:

a) A summary of the non-clinical evidence that falls within this category

b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

c) Discussion to support why the evidence presented is sufficient to support the application.

OR

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

A summary of the specific study and the test report for the study described in the physical and mechanical characterization must be provided.

3.4.2. Chemical/Material Characterization

Tests that describe the chemical or structural composition of the device and its components are to be included in this section. This should include:

a) A summary of the non-clinical evidence that falls within this category

b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

c) Discussion to support why the evidence presented is sufficient to support the application.

OR

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

A summary of the specific study and the test report for the study described in the chemical/material characterization must be provided.

3.4.3. Electrical Systems: Safety, Mechanical and Environmental Protection, and Electromagnetic Compatibility

Evidence supporting electrical safety, mechanical and environmental protection, and electromagnetic compatibility are to be included in this section. This should include:

a) A summary of the non-clinical evidence that falls within this category

b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

c) Discussion 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.

A summary of the specific study and the test report for the study described in the electrical systems must be provided.

3.4.4. Radiation Safety

Studies supporting radiation safety, where the device emits radiation or where the device is exposed to radiation are to be included in this section. This should include:

a) A summary of the non-clinical evidence that falls within this category

b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

c) Discussion to support why the evidence presented is sufficient to support the application.

OR

d) A statement of why this category of non-clinical laboratory study is not applicable to this case. A summary of the specific study and the test report for the study described in the radiation safety must be provided.

3.4.5. Software/Firmware

3.4.5.1. Software/Firmware Description

a) Specify the name of the software

b) Specify 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) Provide a description of the software including the identification of the 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.

d) Provide a statement about software version naming rules, specify all fields and their meanings of software version, and determine the complete version of software and its identification version used for release.

3.4.5.2. Hazard Analysis

The Hazard Analysis should take into account all device hazards associated with the device's intended use, including both hardware and software hazards.

NOTE:

i. This document can be in the form of an extract of the software-related items from comprehensive risk management documentation, described in ISO 14971.

ii. Hazard analysis, should address all foreseeable hazards, including those resulting from intentional or inadvertent misuse of the device.

3.4.5.3. Software Requirement Specification

The Software Requirements Specification (SRS) documents the requirements for the software. This typically includes functional, performance, interface, design, developmental, and other requirements for the software. In effect, this document describes what the Software Device is supposed to do. For example, hardware requirements, programming language requirement, interface requirements, performance and functional requirements.

3.4.5.4. Architecture Design Chart

Detailed depiction of functional units and software modules. May include state diagrams as well as flow charts.

3.4.5.5. Software Design Specification

The Software Design Specification (SDS) describes the implementation of the requirements for the Software Device. The SDS describes how the requirements in the SRS are implemented.

3.4.5.6. 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.

3.4.5.7. Software Life Cycle Process Description

A summary describing the software development life cycle and the processes that are in place to manage the various life cycle activities.

3.4.5.8. Software Verification and Validation

This should include:
a) An overview of all verification, validation and testing performed both in-house and in a simulated or actual user environment prior to final release.
b) Discussion to support why the evidence presented is sufficient to support the application.
OR
c) A statement of why this category of non-clinical laboratory study is not applicable to this case.

NOTE

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

A summary of the specific study and the test report for the study described in the Software Verification and Validation must be provided.

3.4.5.9. Revision Level History

Revision history log, including release version number and date.

3.4.5.10. Unresolved Anomalies (Bugs or Defects)

All unresolved anomalies in the release version of the software should be summarized, along with a justification for acceptability (i.e. the problem, impact on safety and effectiveness, and any plans for correction of the problems).

3.4.5.11. Cyber-security

Evidence to support the cyber-security should be provided here. For example, but not limited to:

a) Cyber-security vulnerabilities and risks analysis

b) Cyber-security controls measures

c) Traceability matrix linking cyber-security controls to the cyber-security vulnerabilities and risks.

3.4.5.12. Interoperability

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

3.4.6. Biocompatibility and Toxicology Evaluation

Studies supporting biocompatibility and assessing toxicology are to be included in this section. Studies to assess the immunological response to animal or human tissues, tissue components or derivatives are to be included in this section. This should include:

a) A list of all materials in direct or indirect contact with the patient or user.

b) State conducted tests, applied standards, test protocols, the analysis of data and the summary of results

c) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

d) Discussion to support why the evidence presented is sufficient to support the application.

OR

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

NOTES:

i. The sponsor/applicant should explicitly address all existing EFDA's regulatory guidance related to the non-clinical study results provided in this section regarding the subject device

ii. Tests should be conducted on samples from the finished, sterilized (when supplied sterile) device.

A summary of the specific study and the test report for the study described in the Biocompatibility and Toxicology Evaluation must be provided.

3.4.7. Non-Material-Mediated Pyrogenicity

Studies to support pyrogenicity evaluation of final release are to be included in this section. This should include:

a) A summary of the non-clinical evidence that falls within this category

b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

c) Discussion to support why the evidence presented is sufficient to support the application.

OR

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

NOTE: The sponsor/applicant should explicitly address any existing regional regulatory guidance related to the non-clinical study results provided in this section regarding the subject device.

A summary of the specific study and the test report for the study described in the Non-Material-Mediated Pyrogenicity must be provided.

3.4.8. Safety of Materials of Biological Origin (human/animal)

Evaluations performed to demonstrate the safety of materials of biological origin (e.g. animal sourced, human sourced material) are to be included in this section. This should include:

a) A description of biological material or derivate

b) State the harvesting, processing, preservation, testing and handling of tissues, cells and substances

c) If applicable, discussion of infectious agents/transmissible agents known to infect the source animal

d) Clarify the origin (including details of donor screening and source country), and describe the tests on validation of removal or inactivation methods of viruses and other pathogens in the manufacturing process.

e) A brief summary of process validation should be included to substantiate that manufacturing and screening procedures are in place to minimize biological risks, in particular, with regard to viruses and other transmissible agents.

f) The system for recordkeeping to allow traceability from sources to the finished device should be fully described

g) Discussion to support why the evidence presented is sufficient to support the application.

OR

h) A statement of why this category of non-clinical laboratory study is not applicable to this case.

3.4.8.1. Certificates

Certificates that support the safety of materials of biological origin.

A summary of the specific study and the test report for the study described in the Safety of Materials of Biological Origin (human/animal) must be provided.

3.4.9. Sterilization Validation

3.4.9.1. End-User Sterilization

Information and validation of end-user sterilization where it is necessary for the end-user to sterilize the device. This should include:

a) A description of the sterilization process (method, parameters)

b) A summary of the non-clinical evidence that falls within this category

c) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

d) If applicable, state the rationale on the durability of the product against two or more sterilization.

e) Discussion to support why the evidence presented is sufficient to support the application.

OR

f) A statement of why this category of non-clinical laboratory study is not applicable to this case.

3.4.9.2. Manufacturer Sterilization

Information and validation of manufacturer sterilization where the device is provided sterile. This should include:

a) A description of the sterilization process (method, parameters) and Sterility Assurance Level (SAL)

b) State if parametric release is used

c) A summary of the non-clinical evidence that falls within this category

d) Information on the ongoing revalidation of the process. Typically, this would consist of arrangements for, or evidence of, revalidation of the packaging and sterilization processes.

e) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)

f) Discussion to support why the evidence presented is sufficient to support the application.

OR

g) A statement of why this category of non-clinical laboratory study is not applicable to this case.

3.4.9.3. Residual Toxicity

Contain the information on the testing for sterilant residues, where the device is supplied sterile and sterilized using a method susceptible to residues. This should include:

a) A summary of the non-clinical evidence that falls within this category

b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)
c) Discussion to support why the evidence presented is sufficient to support the application.
OR
d) A statement of why this category of non-clinical laboratory study is not applicable to this case.
A summary of the specific study and the test report for the study described in the Residual Toxicity must be provided.

3.4.9.4. Cleaning and Disinfection Validation

Contains information on the validation of cleaning and disinfection instructions for reusable devices. This should include:
a) A summary of the non-clinical evidence that falls within this category
b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)
c) Discussion to support why the evidence presented is sufficient to support the application.
OR
d) A statement of why this category of non-clinical laboratory study is not applicable to this case.

3.4.9.5. Reprocessing of Single Use Devices, Validation Data

The required validation data including cleaning and sterilization data, and functional performance data demonstrating that each single use device (SUD) will continue to meet specifications after the maximum number of times the device is reprocessed as intended by the person submitting the premarket application.

3.4.10. Animal Testing

Contains information about any animal studies conducted to support the submission. This should include:
a) A summary of the non-clinical evidence that falls within this category

b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)
c) Discussion to support why the evidence presented is sufficient to support the application.
OR
d) A statement of why this category of non-clinical laboratory study is not applicable to this case.
A summary of the specific study and the test report for the study described in the Animal Testing must be provided.

3.4.11. Usability/Human Factors

Studies specifically assessing the instructions and/or device design in terms of impact of human behaviour, abilities, limitations, and other characteristics on the ability of the device to perform as intended should be included here. This should include:
a) A summary of the non-clinical evidence that falls within this category
b) A statement of the test environment and relation to the intended use environment
c) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)
d) If a clinical study has been conducted that includes human factors/usability endpoints, reference to the studies and endpoints should be made, but full results do not need to be repeated.
e) Discussion to support why the evidence presented is sufficient to support the application.
OR
f) A statement of why this category of non-clinical laboratory study is not applicable to this case.
NOTES:
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.

3.5. Non-clinical Bibliography

This section should include:

a) A listing of published non-clinical studies involving this specific device (e.g. cadaveric evaluations, biomechanical assessments)
b) A legible copy of key articles, including translation where applicable to meet the regulators language requirements
c) Discussion to support why the evidence presented is sufficient to support the application.
OR
d) A statement that no literature related to the device was found.

3.6. Expiration Period and Package Validation

This section should include:
a) An indication of environmental conditions for correct storage of the device (e.g. temperature, pressure, humidity, luminosity).
b) A statement of the expiration period considering the materials and sterilization (when applicable), indicated as a period of time or any other means of appropriate quantification.
OR
c) A rationale that storage conditions could not affect device safety or effectiveness.

3.6.1. Product Stability

Contains details relating to product stability under specified storage conditions and in final packaging or simulated conditions. This should include:
a) A summary of the non-clinical evidence that falls within this category
b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)
c) Discussion to support why the evidence presented is sufficient to support the application.
OR
d) A statement of why this category of non-clinical laboratory study is not applicable to this case.

This section should provide information on stability testing studies to support the claimed shelf life. Testing should be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these do not need to be

consecutive lots). Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but need to be followed up with real time stability studies.

If applicable, product stability shall also include:

a) **In use stability**, containing details and evidence supporting the stability during actual routine use of the device (real or simulated);

b) **Shipping stability** containing details and evidence supporting the tolerance of device components to the anticipated shipping conditions.

A summary of the specific study and the test report for the study described in the Product Stability Testing must be provided.

c) **Use by date**: A use by date is required where a safety-related characteristic or claimed performance is likely to deteriorate over time. It is not a lifetime determination, as described above.

In deciding whether there is such a safety-related deterioration, the manufacturer must provide proper risk analysis and measures taken to manage risk:

 The risk analysis will identify those performances and characteristics necessary for the safe use of the particular device. For example, the risk analysis may indicate that sterility is necessary for safe use. Equally, the risk analysis would not cover the color of the device if this is purely aesthetic, but it might cover the color of the device if that color has a purpose related to safe use of the device (e. g., the color signifies the size of the device).

 The risk analysis and measures taken to manage risk will also identify the level or extent of performance or characteristic but only in so far as they are relevant to safe use of the device. For example, the level of resistance to gas flow or rate of leakage from a breathing system, or the probability of non-sterility.

 The risk analysis and measures taken to manage risk will also identify the period over which the relevant performance or characteristic would be expected to be maintained for safe use, including the shelf life and intended period of use. For example, the period over which a pacemaker battery maintains sufficient energy to function after implantation as long as intended by the manufacturer.

3.6.2. Package Validation

Contains details relating to package integrity over the claimed shelf-life and in the packaging and distribution environment (transport and packaging validation) and when applicable, following exposure to the sterilization process. This should include:

a) A summary of the non-clinical evidence that falls within this category
b) A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)
c) Discussion to support why the evidence presented is sufficient to support the application.
OR
d) A statement of why this category of non-clinical laboratory study is not applicable to this case.

CHAPTER FOUR

CLINICAL EVIDENCES

4.1. 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 (RCT, case study, literature review) 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 devices differ from the devices to be marketed, including competitors devices, a description of these differences and their impact on the validity of the evidence in terms of support for the application.
c) A discussion of the clinical evidence considered for the 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.

4.1.1. Clinical Evaluation Report

a) A clinical 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 device.
b) A complete curriculum vitae, or similar documentation, to justify the manufacturer's choice of the clinical expert.

4.1.2. Device Specific Clinical Trials

Clinical trial information under this heading should be grouped by trial.

4.1.2.1. [Trial description, protocol #, date of initiation]

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

4.1.2.1.1. Clinical Trial Synopsis

a) A summary of the specific study described in the custom heading above.
b) 2-3 page summary document that presents a summary of:

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, # patients, inclusion/exclusion criteria) and
ii. Summary of the results of the analysis
iii. Summary of conclusions related to the endpoints

4.1.2.1.2. Clinical Trial Report

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

NOTES:
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.

4.1.2.1.3. Clinical Trial Data

The sponsor/applicant should explicitly address EFDA's applicable guidance or any recognized standard related to the clinical study and data provided in this section regarding the subject device.

4.2.3. 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 effectiveness of the device.
b) A legible copy of key articles, including translation where applicable to meet the regulators language requirements.

OR

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

4.3. IRB Approved Informed Consent Forms

Copies of IRB approved informed consent forms are to be provided here (if any).

4.4. Investigators Sites and IRB Contact Information

Investigators and study administrative structure information should be provided, including (as appropriate):

a) Investigators (who signed the Investigator agreement)-name, address, telephone # (contact info), CV

b) Sites- Site number as reflected in the study report in reference to the investigator, address if different from the above

c) Sponsor- address and regulatory contact information

d) Contract Research Organization (CRO), if applicable-name, address, and contact information and Laboratory facilities (central lab and/or local lab that participated in the study)-name, address, contact information.

CHAPTER FIVE

LABELLING AND PROMOTIONAL MATERIAL

5.1. Product/Package Labels

Samples of the primary and secondary packaging labels but exclusive of labels for shipping.

5.2. Contents of medical devices labeling

Irrespective of the class of the device, the labeling of any medical device should bear the following information:

a) Name or trade name of the device;

b) Name and complete address of the actual manufacturer of the device (street name, number, telephone, fax, e-mail, website);

c) Date of issue or latest revision of the instructions for use and, where appropriate, an identification number;

d) Sufficient details for the user to identify the device and, where these are not obvious, its intended purpose, user, and patient population of the device, and, where relevant, the contents of any packaging;

e) An indication of either the batch code/lot number (e.g., on single-use disposable devices or reagents) or model, or the serial number (e.g., on electrically-powered medical devices), where relevant, to allow appropriate actions to trace and recall the devices.

f) An unambiguous indication of the date until when the device may be used safely, expressed at least as the year and month (e.g., on devices supplied sterile, single-use disposable devices or reagents), where this is relevant. Where relevant, the storage conditions and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions.

g) For devices other than those covered by (f) above, and as appropriate to the type of device, an indication of the dates of manufacture and expiration. This indication may be included in the batch code/lot number or serial number;

h) The information needed to verify whether the device is properly installed and can operate correctly and safely, plus details of the nature and frequency of preventative and regular maintenance and, where relevant, any quality control, replacement of consumable components, and calibration needed to ensure that the device operates properly and safely during its intended life;

i) Any warnings, precautions, limitations, or contra-indications;

j) The performance intended by the manufacturer and, where relevant, any undesirable side effects;

k) An indication on the external packaging of any special storage and /or handling conditions that apply;
l) Details of any further treatment or handling needed before the device can be used (e.g., sterilization, final assembly, calibration, preparation of reagents and/or control materials, etc.) where relevant;
m) If the device is sterile, an indication of that condition and necessary instructions in the event of damage to the sterile packaging and, where appropriate, description of methods for re-sterilization;
n) If the device has been specified by the manufacturer as intended for single-use only, an indication of that state;
o) If the device is intended for premarket clinical investigation, or for in vitro diagnostic medical devices, or for performance evaluation only, an indication of that situation;
p) If the device is intended for presentation or demonstration purposes only, an indication of that situation;
q) If the device is to be installed with or connected to other medical devices or equipment, or with dedicated software in order to operate as required for its intended use, sufficient details of its characteristics to identify the correct devices or equipment to use in order to obtain a safe combination;
r) If the device is implantable, information regarding any particular risks in connection with its implantation;
s) Information regarding the risks of reciprocal interference posed by the reasonably foreseeable presence of the device during specific investigations, evaluations, treatment, or use (e.g., electromagnetic interference from other equipment);
t) If the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging, and, where appropriate, the method of re-sterilization, and any restriction on the number of reuses. Where a device is supplied with the intention that it is sterilized before use, the instructions for cleaning and sterilization should be such that, if correctly followed, the device will still perform as intended by the manufacturer and comply with the Essential Principles of Safety and Performance of Medical Devices;
u) If the device emits radiation for medical purposes, details of the nature, type, and where appropriate, the intensity and distribution of this radiation,
v) Precautions and/or measures to be taken in the event of changes in the performance, or malfunction, of the device including a contact telephone number, if appropriate;
w) Precautions and/or measures to be taken as regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, temperature, humidity, acceleration, thermal ignition sources, proximity to other devices, etc.;
x) If the device administers medicinal products, adequate information regarding any medicinal product(s) that the device in question is designed to administer, including any limitations in the choice of substances to be delivered;

y) Any medicinal substances or biological material incorporated into the device as an integral part of the device;
z) Any requirement for special facilities, or special training, or particular qualifications of the device user and/or third parties;
aa) Any precautions to be taken related to the disposal of the device and/or its accessories (e.g., lancets), to any consumables used with it (e.g., batteries or reagents), or to any potentially infectious substances of human or animal origin;
bb) Where relevant, for devices intended for lay persons, a statement clearly directing the user not to make any decision of medical relevance without first consulting his or her health care provider.

5.3. e-labeling

a) For eligible medical devices and stand-alone software, the applicant needs to identify which form of e-labeling is being used in case of e-labeling (e.g. electronic storage system or built-in system, website).
b) Provide details of risk management in relation to e-labeling. If this is part of the overall risk management, refer to it here.
c) A description of the procedure and operations on providing IFU's when requested.
d) Provide written information for user Information on webpage where IFU and further information can be found in relevant languages.
e) Description on how the requirements detailed for the website have been met.

CHAPTER 6A

QUALITY MANAGEMENT SYSTEM PROCEDURES

6A.1. Administrative

Administrative information needed to evaluate the premarket submission related to the QMS.

6A.1.1. Product Descriptive Information

Abbreviated description of the device, operating principles and overall manufacturing methods

6A.1.2. General Manufacturing Information

a) Address and contact information for all sites where the device or its components are manufactured.
b) 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.

6A.2. Quality management system procedures

High level quality management system procedures for establishing and maintaining the quality management system such as the quality manual, quality policy, quality objectives, and control of documents and records ISO 13485 Elements– SOPs to satisfy clause 4.

6A.3. Management responsibilities procedures

Procedures that document the management commitment to the establishment and maintenance of the QMS by addressing quality policy, planning, responsibilities/authority/communication and management review.
ISO 13485 Elements – SOPs implementing clause 5.

6A.4. Resource management procedures

Procedures that document the adequate provision of resources to implement and maintain the QMS including human resources, infrastructure and work environment. ISO 13485 Elements – SOPs implementing clause 6.

6A.5. Product realization procedures

High level product realization procedures such as those addressing planning and customer related processes

ISO 13485 Elements – SOPs implementing sub clause 7.1 and 7.2.

6A.5.1. Design and Development Procedures

Procedures that document the systematic and controlled development of the device design from initiation of the project to transfer to production. ISO 13485 Elements – SOPs for implementing sub clause 7.3.
This section should include the following information:

a) Design Control Procedure(s) b) Design & Development Planning Procedure(s) c) Design Input Procedure(s) d) Design Output - Procedure(s) e) Design Review Procedure(s) f) Design Verification Procedure(s) g) Design Validation Procedure(s) h) Risk Analysis Procedure(s) i) Design Transfer Procedure(s) j) Design Changes Procedure(s) k) Design History File Procedure(s).

6A.5.2. Purchasing Procedures

Procedures that document that purchased products/services conform to established quality and/or product specifications.
ISO 13485 Elements – SOPs to implement sub clause 7.4.

6A.5.3. Production and service controls procedures

Procedures that document the production and service activities are carried out under controlled conditions. These SOPS address issues such as cleanliness of product and contamination control; installation and servicing activities; process validation; identification and traceability; etc. ISO 13485 Elements – SOPs implementing sub clause 7.5.

6A.5.4. Control of monitoring and measuring devices procedures

Procedure that document that monitoring and measuring equipment used in the QMS is controlled and continuously performing per the established requirements.
ISO 13485 Element- SOPs for implementing sub clause 7.6.

6A.6. QMS measurement, analysis and improvement procedures

Procedures that document how monitoring, measurement, analysis and improvement to ensure the conformity of the product and QMS, and to maintain the effectiveness of the QMS. ISO 13485 Element – SOPS for implementing clause 8.

This section should:

a) Explain how complaint handling ties to MDR procedures b) Explain how risk management is tied to the CAPA activities c) CAPA Subsystem Procedures d) Nonconforming Product Procedure(s) e) Complaint Handling Procedures f) Quality Audit Procedures.

CHAPTER 6B

QUALITY MANAGEMENT SYSTEM DEVICE SPECIFIC INFORMATION

6B.1. Quality management system information

Documentation and records specific to the subject device that results from the high level quality management system procedures for establishing and maintaining the quality management system such as the quality manual, quality policy, quality objectives, and control of documents, noted in Chapter 6A.
ISO 13485 Elements – documentation specific to the subject device for the implementation of clause 4.

6B.2. Management responsibilities information

Documentation and records specific to the subject device that result from the implementation the management responsibilities procedures noted in Chapter 6A. ISO 13485 Elements – documentation specific to the subject device for the implementation of clause 5.

6B.3. Resource management information

Documentation and records specific to the subject device that result from the implementation the resource management procedures noted in Chapter 6A.
ISO 13485 Elements – documentation specific to the subject device for the implementation of clause 6.

6B.4. Product realization information

Documentation and records specific to the subject device that results from the implementation of the high level product realization procedures noted in Chapter 6A. ISO 13485 Elements – documentation specific to the subject device for the implementation of sub clause 7.1 and 7.2.

6B.4.1. Design and development information

Documentation and records specific to the subject device that results from the implementation of the design and development procedures noted in Chapter 6A. NOTE: The source of this information is the Design and

Development Records (e.g. DHF - Design History File). ISO 13485 Elements – documentation specific to the subject device for the implementation of sub clause 7.3.

6B.4.2. Purchasing information

Documentation and records specific to the subject device that results from the implementation of purchasing procedures noted in Chapter 6A ISO 13485 Elements – documentation specific to the subject device for the implementation of sub clause 7.4.
List of suppliers of goods or services that affect product conformity with requirements (critical suppliers) and a description of how purchasing requirements are fulfilled for these suppliers.

6B.4.3. Production and service controls information

a) Detailed Manufacturing Flow Diagram
b) Summary of in-process acceptance activities for subject device
c) Process Validation Master Plan
d) List of processes that have not be validated
e) For each process validation considered critical to the safety and effectiveness of the device:
    i. Protocols/Procedures for the validated process
    ii. Process validation report
    iii. The procedures for monitoring and controlling the process parameters of a validated process should be fully described.
    iv. State the frequency of re-validation.

6B.4.4. Control of monitoring and measuring devices information

Documentation and records specific to the subject device that results from the implementation of the control of monitoring and measuring device procedures noted in Chapter 6A.
ISO 13485 Elements – documentation specific to the subject device for the implementation of sub clause 7.6.

6B.5. QMS measurement, analysis and improvement information

Documentation and records specific to the subject device that results from the implementation of the QMS measurement, analysis and improvement procedures noted in Chapter 6A. ISO 13485 Elements – documentation specific to the subject device for the implementation of clause 8.

ANNEX-I

Essential Principles of Safety and Performance Requirements Checklist

Ethiopian Food and Drug Authority, Medical Device Registration Requirements- Checklist for Essential Principles of Safety and Performance Requirements

Manufacturer's Name: **Manufacturer's full Address:**	**Date:**
Device Name and features:	

Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
General Requirements			
5.1 Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.			
5.2 The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer should control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed: ▪ identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse, ▪ eliminate risks as far as reasonably practicable through inherently safe design and manufacture, ▪ reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms, ▪ inform users of any residual risks.			

Ethiopian Food and Drug Authority, Medical Device Registration Requirements- Checklist for Essential Principles of Safety and Performance Requirements

Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.3 Devices should achieve the performance intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions within the scope of the definition of a medical device.			
5.4 The characteristics and performances referred to in Clauses 5.1, 5.2 and 5.3 should not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.			
5.5 The devices should be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected under transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.			
5.6 The benefits must be determined to outweigh any undesirable side effects for the performances intended.			
Design and Manufacturing Requirements			
5.7 Chemical, physical and biological properties			
5.7.1 The devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Clauses 5.1 to 5.6 of the 'General Requirements'. Particular attention should be paid to: ▪ the choice of materials used, particularly as regards toxicity and, where appropriate, flammability, ▪ the compatibility between the materials used and biological tissues, cells, body fluids, and specimens, taking account of the intended purpose of the device, ▪ the choice of materials used should reflect, where appropriate, matters such as hardness, wear and fatigue strength.			

Ethiopian Food and Drug Authority, Medical Device Registration Requirements- Checklist for Essential Principles of Safety and Performance Requirements

Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.7.2 The devices should be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product. Particular attention should be paid to tissues exposed and to the duration and frequency of exposure.			
5.7.3 The devices should be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they should be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.			
5.7.4 Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product/drug as defined in the relevant legislation and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and usefulness of the substance should be verified, taking account of the intended purpose of the device.			
5.7.5 The devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that may leach or leak from the device.			
5.7.6 Devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by the unintentional ingress or egress of substances into or from the device taking into account the device and the nature of the environment in which it is intended to be used.			
5.8 Infection and microbial contamination			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.8.1 The devices and manufacturing processes should be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate the risk of infection to patients, users and, where applicable, other persons. The design should: ▪ allow easy handling, and, where necessary: ▪ reduce as far as reasonably practicable and appropriate any microbial leakage from the device and/or microbial exposure during use, ▪ prevent microbial contamination of the device, or specimen where applicable, by the patient, user or other person.			
5.8.2 Where a device incorporates substances of biological origin, the risk of infection must be reduced as far as reasonably practicable and appropriate by selecting appropriate sources, donors and substances and by using, as appropriate, validated inactivation, conservation, test and control procedures.			
5.8.3 Products incorporating tissues, cells and substances of non-human origin may be considered medical devices. In this case, such tissues, cells and substances should originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. National regulations may require that the manufacturer and/or the Regulatory Authority retain information on the geographical origin of the animals. Processing, preservation, testing and handling of tissues, cells and substances of animal origin should be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.			
• Products incorporating human tissues, cells and substances may be considered medical devices. In this case, the selection of sources, donors and/or substances of human origin, the processing, preservation, testing and handling of tissues, cells and substances of such origin should be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
• Devices labelled as having a special microbiological state should be designed, manufactured and packed to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.			
• Devices delivered in a sterile state should be designed, manufactured and packed in a non-reusable pack, and/or according to appropriate procedures, to ensure that they are sterile when placed on the market and remain sterile, under the transport and storage conditions indicated by the manufacturer, until the protective packaging is damaged or opened.			
5.8.4 Devices labelled either as sterile or as having a special microbiological state should have been processed, manufactured and, if applicable, sterilized by appropriate, validated methods.			
5.8.5 Devices intended to be sterilized should be manufactured in appropriately controlled (e.g. environmental) conditions.			
5.8.6 Packaging systems for non-sterile devices should keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system should be suitable taking account of the method of sterilization indicated by the manufacturer.			
5.8.7 The packaging and/or label of the device should distinguish between identical or similar products placed on the market in both sterile and non-sterile condition.			
5.9 Manufacturing and environmental properties			
5.9.1 If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system should be safe and should not impair the specified performance of the devices. Any restrictions on use applying to such combinations should be indicated on the label and/or in the instructions for use.			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.9.2 Devices should be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate: ▪ the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features; ▪ risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, pressure, humidity, temperature or variations in pressure and acceleration; ▪ the risks connected to their use in conjunction with materials, substances and gases with which they may come into contact during normal conditions of use; ▪ the risks of accidental penetration of substances into the device; ▪ the risk of incorrect identification of specimens; ▪ the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given; ▪ risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.			
5.9.3 Devices should be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.			
5.9.4 Devices must be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.			
5.10 Devices with a diagnostic or measuring function			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.10.1 Devices with a measuring function, where inaccuracy could have a significant adverse effect on the patient, should be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose of the device. The limits of accuracy should be indicated by the manufacturer.			
5.10.2 Diagnostic devices should be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended use, based on appropriate scientific and technical methods. In particular the design should address sensitivity, specificity, trueness, repeatability, reproducibility, control of known relevant interference and limits of detection, as appropriate.			
5.10.3 Where the performance of devices depends on the use of calibrators and/or control materials, the traceability of values assigned to such calibrators and/or control materials should be assured through a quality management system.			
5.10.4 Any measurement, monitoring or display scale should be designed in line with ergonomic principles, taking account of the intended purpose of the device.			
5.10.5 Wherever possible values expressed numerically should be in commonly accepted, standardised units, and understood by the users of the device. **Note:** While SG1 generally supports convergence on the global use of internationally standardised measurement units, considerations of safety, user familiarity, and established clinical practice may justify the use of other recognised measurement units.			
5.11 Protection against radiation			
5.11.1 General			
5.11.1.1 Devices should be designed and manufactured and packaged in such a way that exposure of patients, users and other persons to any emitted radiation should be reduced as far as practicable and appropriate, compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.			
5.11.2 Intended radiation			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.11.2.1 Where devices are designed to emit hazardous, or potentially hazardous, levels of visible and/or invisible radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it should be possible for the user to control the emissions. Such devices should be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.			
5.11.2.2 Where devices are intended to emit potentially hazardous, visible and/or invisible radiation, they should be fitted, where practicable, with visual displays and/or audible warnings of such emissions.			
5.11.3 Unintended radiation			
5.11.3.1 Devices should be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as practicable and appropriate.			
5.11.4 Instructions for use			
5.11.4.1 The operating instructions for devices emitting radiation should give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user and on ways of avoiding misuse and of eliminating the risks inherent in installation.			
5.11.5 Ionizing radiation			
5.11.5.1 Devices intended to emit ionizing radiation should be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry and energy distribution (or quality) of radiation emitted can be varied and controlled taking into account the intended use.			
5.11.5.2 Devices emitting ionizing radiation intended for diagnostic radiology should be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimising radiation exposure of the patient and user.			
5.11.5.3 Devices emitting ionizing radiation, intended for therapeutic radiology should be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the energy distribution of the radiation beam.			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.12 Requirements for medical devices connected to or equipped with an energy source			
5.12.1 Devices incorporating electronic programmable systems, including software, should be designed to ensure the repeatability, reliability and performance of these systems according to the intended use. In the event of a single fault condition in the system, appropriate means should be adopted to eliminate or reduce as far as practicable and appropriate consequent risks.			
5.12.2 Devices where the safety of the patients depends on an internal power supply should be equipped with a means of determining the state of the power supply.			
5.12.3 Devices where the safety of the patients depends on an external power supply should include an alarm system to signal any power failure.			
5.12.4 Devices intended to monitor one or more clinical parameters of a patient should be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health			
5.12.5 Devices should be designed and manufactured in such a way as to reduce as far as practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.			
5.12.6 Devices should be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.			
5.12.7 Protection against electrical risks Devices should be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal use and in single fault condition, provided the devices are installed and maintained as indicated by the manufacturer.			
5.13 Protection against mechanical risks			
5.13.1 Devices should be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance to movement, instability and moving parts.			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.13.2 Devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.			
5.13.3 Devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.			
5.13.4 Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle should be designed and constructed in such a way as to minimize all possible risks.			
5.13.5 Accessible parts of the devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings should not attain potentially dangerous temperatures under normal use.			
5.14 Protection against the risks posed to the patient by supplied energy or substances			
5.14.1 Devices for supplying the patient with energy or substances should be designed and constructed in such a way that the delivered amount can be set and maintained accurately enough to guarantee the safety of the patient and of the user.			
5.14.2 Devices should be fitted with the means of preventing and/or indicating any inadequacies in the delivered amount which could pose a danger. Devices should incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy from an energy and/or substance source.			
5.14.3 The function of the controls and indicators should be clearly specified on the devices. Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information should be understandable to the user and, as appropriate, the patient.			
5.15 Protection against the risks posed to the patient for devices for self-testing or self-administration			

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Essential Principles	Applicable to the device?	Method of Conformity	Identity of Specific Documents
5.15.1 Such devices should be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to users and the influence resulting from variation that can reasonably be anticipated in user's technique and environment. The information and instructions provided by the manufacturer should be easy for the user to understand and apply.			
5.15.2 Such devices should be designed and manufactured in such a way as to reduce as far as practicable the risk of use error in the handling of the device and, if applicable, the specimen, and also in the interpretation of results.			
5.15.3 Such devices should, where reasonably possible, include a procedure by which the user can verify that, at the time of use, that the product will perform as intended by the manufacturer.			
5.16 Information supplied by the manufacturer			
5.16.1 Users should be provided with the information needed to identify the manufacturer, to use the device safely and to ensure the intended performance, taking account of their training and knowledge. This information should be easily understood. **Note:** Further information is provided in *SG1/N009 Labelling for Medical Devices* and in SG1/N043 *Labelling for Medical Devices (revised).*			
5.17 Performance evaluation including, where appropriate, clinical evaluation			
5.17.1 All data generated in support of performance evaluation should be obtained in accordance with the relevant requirements.			
5.17.2 Clinical investigations on human subjects should be carried out in accordance with the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the results. In addition, some countries may have specific regulatory requirements for pre-study protocol review or informed consent.			