Ethiopian Food and Drug Authority

# Guideline forMedical Devices Good Manufacturing Practice

**Sept, 2021**

**Addis Ababa, Ethiopia**

# Table of Contents

## Acronyms

| | |
|---|---|
| ADE | Adverse Device Event |
| cGMP | Current Good Manufacturing Practice |
| EFDA | Ethiopian Food and Drug Authority |
| ISO | International Organization for Standardization |
| QMS | Quality Management System |

## 1. Introduction

The Ethiopian Food and Drug Authority (EFDA) is mandated by the proclamation No. 1112/2019 to regulate medical devices. Article 25(2) of the proclamation decrees that "It shall be the duty of the manufacturer or importer as appropriate to ensure that every medical device is produced in accordance with the appropriate good manufacturing practice". Hence, manufacturersand importers must ensure that the products intended to be marketed in Ethiopia are manufactured in organizations that establish, implement and maintain quality management systems to ensure that their products consistently meet applicable regulatory requirements and specifications. EFDA recognizes themedical devices quality management systems requirements of the ISO 13485:2016 as the basis for theregulated medical devices current good manufacturing practices (cGMP). However, compliance with ISO 13485: 2016 does not replace the Authority's regulatory requirement of cGMP.

The Authority believes that compliance with medical devicescGMP requirements would be beneficial to the public and the medical device industry for the cGMP regulation to be consistent. Hence, all organizations involved in one or more stages of the life-cycle of a medical device, including design and development, production, storage and distribution, installation, servicing and final decommissioning and disposal of medical devices, or provision of associated activities (e.g. technical support) must meet allnational regulatory requirements and quality management system requirements set out in this guideline. In addition, all suppliers or other external parties providing product (e.g. raw materials, components, subassemblies, medical devices sterilization services, calibration services, distribution services, maintenance services) to such organizations should comply with the same requirements.

The Authority will use the requirements recommended by this guidelineand may request documented information, as applicable, during marketing authorization or conducting cGMP inspections to assess the manufacturers or importers compliance with the quality management system and good practice during manufacturing.

The good manufacturing practice and/or quality management system requirements specified in this guideline are complementary to other national and international general & product specific technical requirements for product that are necessary to meet requirements for safety and performance.The applicability and implementation of the requirements set out in this guideline may be based on the different factors such as organizational environment, product

the organization provides;processes the organization executes; and organization's size and organizational structure etc.

Therefore, it is the responsibility of the manufacturer to use discretion while developing a quality system which suitably applies to their specific products and operations.As there is a wide variety of medical devices, some of the requirements of this guidelinemay only apply to named groups of medical devices.The requirements in this guideline are basically meant to ensure that finished devices will be safe and effective and are following the regulatory requirements of the proclamation 1112/2019.

*All users of this guideline are kindly requested to forward their valuable comments and suggestions to the Food and Drug Control Authority of Ethiopia, via P.O.Box 5681, Tel. 251-11 552 41 22, or email: regulatory@fmhaca.gov.et, Addis Ababa, Ethiopia.*

## 2. Definition

**Clinical evaluation** is assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety andperformance of the device when used as intended by the manufacturer.

**Complaint** is written, electronic or oral communication that alleges deficiencies related to the identity, quality,durability, reliability, usability, safety or performance of a medical device that has been released fromthe organization's control or related to a service that affects the performance of such medical devices.

**Distributor** is natural or legal person in the supply chain who, on his own behalf, furthers the availability of a medical device to the end user.

**Good manufacturing practice (GMP)**is a system for ensuring that products are consistently produced and controlled according to quality standards.

**Implantable medical device** is medical device which can only be removed by medical or surgical intervention and which is intended to:

- be totally or partially introduced into the human body or a natural orifice, or
- replace an epithelial surface or the surface of the eye, and
- remain after the procedure for at least 30 days

**Importer** is natural or legal person in the supply chain who is the first in a supply chain to make a medical device,manufactured in another country or jurisdiction, available in the country or jurisdiction where it is tobe marketed.

**Labelling** is label, instructions for use, and any other information that is related to identification, technicaldescription, intended purpose and proper use of the medical device, but excluding shipping documents.

**Manufacturer** is natural or legal person with responsibility for design and/or manufacture of a medical device with theintention of making the medical device available for use, under his

name; whether or not such a medicaldevice is designed and/or manufactured by that person himself or on his behalf by another person(s).

**Medical device family** is group of medical devices manufactured by or for the same organization and having the same basicdesign and performance characteristics related to safety, intended use and function.

**Organization** is a person involve in design and development, manufacture, storage and distribution of medical devices.

**Performance evaluation** is assessment and analysis of data to establish or verify the ability of an in vitro diagnostic medical deviceto achieve its intended use.

**Post-market surveillance** is systematic process to collect and analyse experience gained from medical devices that have been placedon the market.

**Quality management system (QMS)** is a set of policies, processes and procedures required for planning and execution (production/development/service) in the core business area of an organization (i.e., areas that can impact the organization's ability to meet customer requirements).

**Risk management** is systematic application of management policies, procedures and practices to the tasks of analysing,evaluating, controlling and monitoring risk.

**Sterile barrier system** is minimum package that prevents ingress of microorganisms and allows aseptic presentation of theproduct at the point of use.

**Sterile medical device** is medical device intended to meet the requirements for sterility.

Organization

## 3. Objectives

The objective of this guideline is to provide requirements for current Good Manufacturing Practice (cGMP) during design and development, manufacture, storage,distribution,installation or servicing of medical devices.

## 4. Scope

This guideline is applicable to all medical device manufacturers who are interested to market their products in Ethiopia.

## 5. Requirements Quality management system

### 5.1. General requirements

The quality management system established by the organizationshould comprise all activities by which the organization identifies its objectives and determines the processes and resources required to achieve the desired product safety and performances. This should include all the interacting processes and resources required to provide value and realize desired results as well as the means to identify actions to address intended and unintended consequences in providing products.

**5.1.1** Any organization interested to manufacturemedical devices and placethem on Ethiopia marketshouldestablish, implement, document a quality management system and maintain its effectiveness in accordance with the requirements of Authority`s up to date regulations& directives and this guideline. The manufacturer or importer should establish and maintain a quality system that is appropriate for the specific medical device(s) designed or manufactured.

The organization should be able to provide documented information thatspecifies the role(s) it undertakesregarding the medical devices marketing.

**5.1.2** The organization should determine the processes needed for the quality management system and the application ofthese processes throughout the organization taking into account the roles it undertakes; apply a risk-based approach to the control of the appropriate processes needed for the qualitymanagement system; determine the sequence and interaction of these processes.

**5.1.3** For each QMS process, the organization should:

a) determine criteria and methods needed to ensure that both the operation and control of theseprocesses are effective.

b) ensure the availability of resources and information necessary to support the operation andmonitoring of these processes.

c) Implement actions necessary to achieve planned results and maintain the effectiveness of theseprocesses.

d) Monitor, measure as appropriate, and analyse these processes.

e) Establish and maintain records needed to demonstrate conformance to this guidelineand compliance with applicable regulatory requirements.

**5.1.4** The organization should manage the quality management system processes in accordance withthe requirements of this guideline andother applicable EFDA regulation & directives. Changes to bemade to these processes should be:

a) evaluated for their impact on the quality management system.

b) evaluated for their impact on the medical devices produced under this quality management system;

c) controlled in accordance with the requirements of this guideline and applicableregulatory requirements.

**5.1.5** When the organization chooses to outsource any process that affects product conformity torequirements, it should monitor and ensure control over such processes. The organization should retainresponsibility of conformity to the requirements of this guideline and to customer and other applicable regulatoryrequirements for outsourced processes. The controls should be proportionate to the risk involved and theability of the external party to meet the requirements. The controls should includewritten quality agreements.

**5.1.6** The organization should document procedures for the validation of the application of computersoftware. Such software applications should be validated prior toinitial use and, as appropriate, after changes to such software or its application.

The specific approach and activities associated with software validation and revalidation should beproportionate to the risk associated with the use of the software.Records of such activities should be maintained.

### 5.2. Documentation requirements

5.2.1 General

The management with executive responsibility should establish its policy and objectives for, and commitment to, quality. Itshould ensure that the quality policy is communicated, understood, implemented, and maintained at all levels of the organization. Thequality management system documentation should include:

a) documented statements of a quality policy and quality objectives;

b) a quality manual;

c) documented procedures and records

d) documents, including records, determined by the organization to be necessary to ensure theeffective planning, operation, and control of its processes; and

e) other necessary documentation

5.2.2 Quality manual

The organization should document a quality manual or maintain an equivalent documented information, that can vary in detail and format to suit the size and complexity of the organization's role. The quality manual should include:

a) the scope of the quality management system, including details of and justification for any exclusion or non-application;

b) the documented procedures for the quality management system, or reference to them;

c) a description of the interaction between the processes of the quality management system.

The quality manualshould outline the structure of the documentation used in the quality management system.

5.2.3 Medical device file

For each medical device type or medical device family, medical device manufacturers and others involved in the supply chainshould establish and maintain one or more files either containing or referencing documents generated to demonstrate conformity to the requirement of this guideline and compliance with relevant authority`s regulation & directive requirements. Theorganizationshould standardize their design and development processes, production processes, medical products record, inspection protocols and compliance controls for each product family.The content of the file(s) should include, but is not limited to:

a) general description of the medical device, along with its designed application, intended use/purpose, and labelling, including any instructions for use

b) Medical device specifications. All products within a medical device family, where applicable should have their own separated specifications documents and unique drawings.

c) Established procedures manufacturing, packaging, storage, handling and distribution.All manufacturing process flows, covering the quality inspection points, for every medical device family must be documented clearly.

d) Procedures for measuring and monitoringinclude or state reference to documents containing specifications (such as; product critical dimensions, approved raw material grades, production specifications, and surface finishing specifications) for each unique product type.

e) specifications & procedures for measurement of products should also state the procedure for quality control of devices in a family, the points of inspection in the processes, the critical factors of the products, and type of instruments which will be allocated to check critical points of the product.

f) As appropriate, installation requirements for installation and procedures for servicing

g) Organization`s reference documents proving conformity should be retained either as a the certificate of conformity, or it should mention any document that shows that all processes in the design, production, packing, storage, and handling suffice the requirements of this guideline.

h) documentation for servicing & installation should state the steps, guidelines or installation troubleshooting and recordsfor devices that need servicing or installation procedures. The organization should provide, as appropriate, the schedule of routine maintenance, qualification of the device, checklists for servicing and the flow charts for preventive maintenance and repairs

i) Documented evidence showing the stability of medical devices

5.2.4 Control of documents

The organizationshould establish & maintain a procedure to control documents required by the quality management system.Such a documented procedure shouldensure that:

a) review for adequacy and approvalare under taken prior to issuance of all documents for use

b) the approval, including the date and signature of the individual(s) approving the document, is documented

c) documents established to meet the requirements of this guideline are available at all locations for which they are designated, used, or otherwise necessary,

d) suitable identificationsare applied to all obsolete documents, and they are promptly removed from all points of use or otherwise prevented from unintended use

e) changes to documents are reviewed and approved by an individual(s) in the same function or organization that performed the original review and approval, unless specifically designated otherwiseto an individual(s) who has access to pertinent background information

f) approved changes are communicated to the appropriate personnel in a timely manner

g) records of changes to documents are maintained

h) change records include a description of the change, identification of the affected documents, the signature of the approving individual(s), the approval date, and when the change becomes effective.

i) the current revision status of and changes to documents are identified

j) relevant versions of applicable documents are available at points of use

k) documents remain legible and readily identifiable

l) documents of external origin, determined by the organization to be necessary for theplanning and operation of the quality management system, are identified and theirdistributioncontrolled

m) mechanisms are in place to prevent deterioration or loss of documents

n) the period for which at least one copy of obsolete documents should beretained is defined.

o) documents to which medical devices have been manufacturedand tested are available for at least the lifetime of the medical device as defined by the organization,but not less than the retention period of any resulting record.

5.2.5 Control of records

The organizationshould maintain records to provide evidence of conformity to requirements and of the effectiveoperation of the quality management system.

The organization should document procedures to define the controls needed for the identification, storage, security and integrity, retrieval, retention time and disposition of records.Records should remain legible, readily identifiable and retrievable. Changes to a recordshould remain identifiable. The organizationshould give due attention to:

a) Accessibility: the organizationshould ensure that records are maintained at the manufacturing establishment or other location that is reasonably accessible to responsible officials of the manufacturer and to inspectors of EFDA designated to perform inspections. Those records that are not stored at the inspected establishment, at least copies should be made readily available for review during inspection.The organizationshould also provide objective evidence that records stored in automated data processing systems are backed up.

b) Confidentiality: the organizationshould define and implement methods for protecting confidential health information contained in records.

c) Retention period: all records required by this guidelineshould be retained for at least a period of time equivalent to the design and expected lifetime of the medical device, but not less than 2 years from the date of release for commercial distribution by the manufacturer.

d) Device history record: organizations should maintain device history records andshouldestablish and maintain procedures to ensure that device history record for each batch, lot,or unit are maintained to demonstrate that the device is manufactured in accordance with the medicaldevice file. This manufacturing related recordsshouldat least include:

    - The dates of manufacture;
    - The quantity manufactured;
    - The quantity released for distribution;
    - The acceptance criteria;
    - The primary identification label and labeling used for each production unit; and
    - Any unique device identifier (UDI) or universal product code (UPC), and any other device identification(s) and control number(s) used

e) Quality system record: the organizationshould maintain a quality system record that include, or refer to the location of, procedures and the documentation of activities required by this guideline.

## 6. Management responsibility

### 6.1. Management commitment

Organization`s top managementshould provide evidence of its commitment to the development andimplementation ofthe quality management system and maintenance of its effectiveness by:

a) communicating to the organization the importance of meeting customers' needs as well as applicableregulatory requirements.

b) establishing its policy and objectives for, and commitment to quality.

c) ensuring that the quality policy is understood, implemented, and maintained at all levels of the organization.

d) ensuring that quality objectives are established;

e) conducting management reviews to ensure the suitability and effectiveness of the quality system at defined intervals and with sufficient frequency according to established procedures to ensure that the quality system satisfies the requirements of the quality management system and the manufacturer's established quality policy and objectives.

f) Documenting the dates and results of quality system reviews

g) ensuring the availability of resources and providing adequate resources, including the assignment of trained personnel, for management, performance of work, and assessment activities, including internal quality audits.

h) establishing and maintaining an adequate organizational structure

i) establishing the appropriate responsibility, authority, and interrelation of all personnel who manage, perform, and assess work affecting quality, and provide the independence and authority necessary to perform these tasks.

j) Ensuring that quality system requirements are effectively established and effectively maintained

k) Reporting on the performance of the quality system to management with executive responsibility for review.

l) establishing a quality plan which defines the quality practices, resources, and activities relevant to devices that are designed and manufactured.

m) establishing quality system procedures and instructions.

### 6.2. Customer focus

Organizations top management should ensure that customer requirements and applicable regulatoryrequirements are determined and met. This may be demonstrated by documented information on:

a) recognizing direct and indirect customers as those who receive value from the organization;

b) understanding customers' current and future needs and expectations;

c) linking the organization's objectives to customer needs and expectations;

d) communicating customer needs and expectations throughout the organization;

e) planning, designing, developing, producing, delivering and supporting products and services to meet customer needs and expectations;

f) measuring and monitoring customer satisfaction and take appropriate actions;

g) determining and taking action on relevant interested parties' needs and appropriate expectations that can affect customer satisfaction;

h) managing relationships with customers to achieve sustained success.

### 6.3. Quality policy

organizations top management should ensure that the quality policy:

a) is applicable to the purpose of the organization;

b) includes organization's top management's commitment to comply with requirements and to maintain the effectiveness of thequality management system;

c) provides a framework for establishing and reviewing quality objectives;

d) is communicated and understood within the organization;

e) is reviewed on regular basis for continuing suitability

## 6.4. Planning

6.4.1 Quality objectives

Top management should ensure that quality objectives, including those needed to meet applicableregulatory requirements and requirements for product, are established at relevant functions and levelswithin the organization. The quality objectives should be measurable and consistent withthe organization`s quality policy.

6.4.2 Quality management system planning

During planning, the top management should ensure that the planning:

a) is carried out in order to meet the requirementsof the QMS

b) is carried out in order to meet its quality objectives;

c) considers the integrity of the quality management system when changes to the qualitymanagement system is planned and implemented.

## 6.5. Responsibility, authority and communication

6.5.1 Responsibility and authority

Top management should ensure that:

a) responsibilities and authorities are defined, documented and

b) communicated within the organization

c) the interrelation of all personnel who manage, perform and verify work affectingquality are documented and the independence and authority necessary to perform these tasks are defined

6.5.2 Management representative

Management with executive responsibility should appoint, and document such appointment of, a member of management who, irrespective of other responsibilities, should have established authority over and responsibility for ensuring:

a. that quality system requirements are effectively established and effectively maintained

b. that processes needed for the quality management system are documented;

c. promotion of awareness of applicable regulatory requirements and qualitymanagement system requirements throughout the organization; and

d. reporting on the performance of the quality system and any need for improvement to management with executive responsibility for review

## 6.6. Management review

6.6.1 General

The organizationshould document procedures for management review and maintain documented evidence that proves the top managementhas reviewed the suitability and effectiveness of the quality system at defined intervals and with sufficient frequency(preferably at least once a year) to ensure that the quality system satisfies the requirements of this guideline and the manufacturer's established quality policy and objectives. The dates and results of quality system reviews should be documented. The top management should determineitsQMS continuing suitability, adequacy and effectiveness by:

a. evaluating whether it is serving its purpose and satisfying the needs of the organization
b. whether the QMS conform to the standard's requirements
c. evaluating whether the activities are performed according to procedures
d. assessing accomplishments of the planned results

6.6.2 management review input and out puts

The documented quality review should reflect on the management decisions at least on the following

a) feedback
b) complaint handling;
c) audits (internal & external);
d) monitoring and measurement of processes;
e) monitoring and measurement of product;
f) corrective action;
g) preventive action;
h) follow-up actions from previous management reviews;
i) changes that could affect the quality management system; including changes needed to respond to applicable new or revised regulatory requirements
j) improvement needed &recommendations to maintain the suitability, adequacy, and effectiveness of the quality management system and its processes;

k) improvement of product related to customer requirements; and

l) resource needs

## 7. Resource management

### 7.1. Provision of resources

The organizationshould provide adequate resources, including the assignment of trained personnel, for management, performance of work, and assessment activities, including internal quality audits, to meet the requirements of quality system for medical devices.It should determine and provide the resources needed to:

a) implement the quality management system and to maintain its effectiveness;

b) meet applicable regulatory and customer requirements.

### 7.2. Human resources

The organizationshould ensure that personnel performing work affecting product quality are competent based on appropriateeducation, training, skills and experience. It shoulddocument the process(es) for establishing competence, providing neededtraining, and ensuring awareness of personnel.

The organizationshould provide documented information to the designated EFDA inspectors, during audit, regarding:

a) How itdetermines the necessary competence for personnel;

b) Trainings provided or other actions taken to achieve or maintain the necessary competence;

c) How to evaluate the effectiveness of the actions taken;

d) How to ensure that its personnel are aware of the relevance and importance of their activities

e) how to ensureits personnel contribute to the achievement of the quality objectives;

f) maintain appropriate records of education, training, skills and experience.

### 7.3. Infrastructure

The organization should document the requirements for the infrastructure needed to achieve

conformity to product requirements, prevent product mix-up and ensure orderly handling of product. The organizationshould ensure:

a) buildings, workspace and associated utilitiesare of suitable design, environmental condition (temperature, humidity etc.), cleanliness;

b) that it hasenough space to perform necessary operations, prevent mix-ups, and assure orderly handling;

c) process equipment (both hardware and software) meet manufacturers recommended requirements and are appropriately designed, constructed, placed, and installed to facilitate maintenance, adjustment, cleaning, and use;

d) computers or automated data processing systems that are used as part of production or the quality systemare validated to serve the intended use according to an established protocol;

e) all software changes are validated before approval and issuance ;

f) supporting services (such as transport, communication, or information systems) are suitable and adequate;

g) document requirements are maintained for the maintenance activities, including the intervalof performing the maintenance activities, when such maintenance activities, or lack thereof, can affectproduct quality;

h) as appropriate, documented requirements are applied to equipment used in production, thecontrol of the work environment and monitoring and measurement

i) that schedules for the adjustment, cleaning, and other maintenance of equipment to ensure that manufacturing specifications are met are established & maintained;

j) records of equipment maintenance, including the date and individual(s) performing the maintenance activities,aremaintained;

k) periodic self-inspections are conducted in accordance with established procedures, documented and reviewed to verify that the system, including necessary equipment, is adequate, maintained as per applicable equipment maintenance schedules, and functioning properly;

l) that the under taken inspections, including the date and individual(s) conducting the inspections, are documented; and

m) that any inherent limitations or allowable tolerances are visibly posted on or near equipment requiring periodic adjustments or are readily available to personnel performing these adjustments.

### 7.4. Work environment and contamination control

#### 7.4.1. Work environment

The organization should document the requirements for the work environment needed to achieve conformity to product requirements. Where environmental conditions could reasonably be expected to have an adverse effect on product quality, the manufacturer shoulddocument the requirements, establish and maintain procedures to adequately monitor and/or control these environmental conditions.

The organization should guarantee suitability of environment and should document:

a) requirements for health, cleanliness and clothing of personnel when entering work environment especially where the contact between suchpersonnel and the product or work environment could affect medical device safety or performance;

b) record of all maintenance and other personnel (who worked temporarily) under special environmentalconditions

c) competency of personnel and/or supervisors working in area that requires special environmental conditions

#### 7.4.2. Contamination control

The organizationshouldplanand document arrangements (maintain procedures)for the control of contaminatedor potentially contaminated product in order to prevent contamination of the work environment,personnel, or product.

For sterile medical devices, the organization should document requirements for control of contaminationwith microorganisms or particulate matter and maintain the required cleanliness during assembly orpackaging processes.The documented information should include acceptable limits, alarm limits and action limits for microbial and particulate matter monitoring results based on the cleanliness of the work environment.

## 8. Product realization

### 8.1. Planning of product realization

The organizationshould appropriately plan and develop the processes needed for product realization which is consistent with the requirements of the other processes of the qualitymanagement system.

The organization should document one or more processes for risk management in product realization.Records of risk management activities should be maintained.

In planning product realization, the organization should determine the following, as appropriate:

a) quality objectives and requirements for the product;

b) the need to establish processes and documents andto provide resources specific to theproduct, including infrastructure and work environment;

c) required verification, validation, monitoring, measurement, inspection and test, handling, storage,distribution and traceability activities specific to the product together with the criteria for productacceptance;

d) records needed to provide evidence that the realization processes and resulting product meetrequirements.

**8.2. Customer-related processes**

8.2.1. Determination of requirements related to product

The organizationshouldmaintain procedure (document) and how to determine:

a) requirements specified by the customer

b) other necessary requirements for specified or intended use

c) any user training and after sale services

d) any additional (including optional) requirements

8.2.2. Review of requirements related to product

The organizationshould maintain procedure for reviewing the requirements related to product. This review results and actions arising from the review shouldbe documented and it should include but not limited to:

a) The reviewer and time the review was conducted on tenders,contracts or orders, changes to contracts or orders etc.

b) Defined product requirements and capability of the organization to meet the requirements.

c) Any resolved differences from those previously expressed contract or order requirements

d) Identified must met regulatory requirements; and

e) any user training identified or planned to be available and after sale services required

#### 8.2.3. Communication

The organization shouldmaintain procedure for communicating with customers inrelation toproduct information; enquiries, contracts or order handling, including amendments;customer feedback, complaints; advisory notices etc.

The organizationshould alsocommunicate the authorityat least on the following issues:

a) Notify the authority of any variation affecting safety, quality or effectiveness of a registered medical device

b) furnish adverse event(incident) reports and other relevant information to EFDA based on post marketing surveillance outcomes

c) Provide reports on any ADE observed during clinical trial

The organizationshould, asappropriate, maintain records of such communications.

### 8.3. Design and development

#### 8.3.1. General

The organization should document procedures for design and development.

#### 8.3.2. Design and development planning

The plans should describe or reference the design and development activities and define responsibility for implementation as well as identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process. The plans should be reviewed, updated, and approved as design and development evolves.Theorganization should maintain document on plan and control of the design and development of product as well as updates as the design and development progresses. The document should contain:

a) the design and development stages;

b) the review(s) made at each design and development stage;

c) the verification, validation, and design transfer activities that are appropriate at each design and development stages

d) the responsibilities and authorities for design and development;

e) the methods to ensure traceability of design and development outputs to design anddevelopment inputs;

f) The resource needed, including necessary competence of personnel.

8.3.3. Design and development inputs

The organizationshould maintain a procedure(s) used for the identification and control of design input for the device. The procedure shoulddescribe at least the process or mechanism for addressing incomplete, ambiguous, or conflicting requirements and explain how design inputs are documented, reviewed, and approved.

The following should be considered, but not limited to, as examples of potentially relevant aspects for design input:

a) intended use

b) user / patient / clinical (interfaces or needs)

c) performance characteristics

d) safety requirements

e) safety and performance parameters

f) toxicity

g) biocompatibility

h) electromagnetic interference

i) compatibility with accessories or auxiliary devices

j) compatibility with the environment of intended use

k) human factors

l) clinical reports

m) physical or chemical characteristics

n) labelling and packaging

o) statutory and regulatory requirements

p) past design history files

q) manufacturing capability

r) Emerging risks including changes made to design

8.3.4. Design and development outputs

The organization should maintain the procedure(s) used to define and document design output in terms that allow an adequate and measurable evaluation of conformance to design input requirements and approval prior to release. Records of the design and development outputs should be maintained. Design and development outputs should:-

a) meet the input requirements for design and development;

b) provide appropriate information for purchasing, production and service provision;

c) contain or reference product acceptance criteria;

d) specify the characteristics of the product that are essential for its safe and proper use.

The outputs of design and development should be in a form suitable for verification against the designand development inputs.

8.3.5. Design and development review

The organization should maintain procedure(s) that define and control the design reviews for medicaldevices. The procedure(s) should explain/describe:-

a) how formal systematic design reviews are planned

b) how the organization ensure that formal design reviews are conducted at appropriate stages of the design and development process

c) how the organization ensures comprehensiveness of thedesign reviews

d) representatives of functions and people involved with the stage under design review

e) independent individual (other specialist personnel) who participates in all formal design reviews and, identified & proposed necessary actions

f) method of recording design reviews for the design history file

Records of the results of the reviews and any necessary actions should be maintained and include theidentification of the design under review, the participants involved and the date of the review.

### 8.3.6. Design and development verification

The organization shall document verification plans that include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size.

The organization should maintain a procedure(s) used to verify the device design for medical devices in a planned arrangement. Such procedure(s) should describe the process that conorganizations the design outputs meet the design input requirements and the mechanism for resolving any discrepancies. The procedure should also define the method of recording design verification activities for the design history file and should include:

a) Verification plan (that includes methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size)

b) Identification of the design

c) Verification methods

d) Date(s) of verifications

e) Individual(s) performing the verifications

f) Verification results, conclusions and necessary actions

If the intended use requires that the medical device be connected to, or have an interface with, othermedical device(s), verification recordsshouldinclude conorganizationation that the design outputs meet design inputswhen so connected or interfaced.

### 8.3.7. Design and development validation

The organization should maintain procedure(s) used to validate the device design to ensure that the resulting product can meet the requirements for the specified application or intended use. It should also define the method of recording design validation for the design history file.

The organization shall document validation plans that include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size.

When validation activities are performed on devices that are not made using production methods or equipment expected to be used during full scale manufacturing, summary of the process or scientific method used to prove equivalence should be documented.

The organization should conduct design validation on representative product; which includes initial production units, batches or their equivalents, and the rationale for the choice of product used for validation should be recorded.

If the intended use requires that the medical device be connected to, or have an interface with, other medical device(s), validation should include conorganizationation that the requirements for the specified application or intended use have been met when so connected or interfaced.

As part of design and development validation, the organization should perform clinical evaluations or performance evaluations of the medical devices as per article 27 of proclamation 1112/2019 and guideline on GCP requirements of medical device clinical investigation or submit results of clinical trial conducted when requested by authority.A medical device used for clinical evaluation or performance evaluation shallnot be released for use to the customer.

The organization should maintain summarized data to support that the clinical evaluations of the device ensure that the device meets user needs and the intended uses.

For automated devices with computer software, the organization`s procedure should explain how it will complete the software validation and include any system integration testing.

All risk management issues should be addressed throughout the design control process. The organizationshould describe how and when risk analysis will be performed as well as how the organizationwill document, use, and update its risk management program.

All validationsshould be completed prior to release for use of the product to the customer and records of validation should be maintainedand should include:

a) Validation plans /Validation methods
b) Validation results
c) Identification of the design
d) Date(s) of validation
e) Individual(s) performing the validation
f) Result, conclusion & necessary actions

### 8.3.8. Design and development transfer

The organization should document all procedures used to transfer the design and development outputs tomanufacturing. The procedure(s) should explain how the organizationconducts the final review and approval of design and development activities in order to transfer the design to manufacturing. These procedures should ensure that design and development outputs are verified

as suitable for manufacturing before becoming final production specifications and that production capability can meet product requirements.

It should also describe what design documents comprise the device master record.The organization should retain records of all results and conclusions of the transfer.

8.3.9. Control of design and development changes

The organization should maintain a procedure(s) for controlling design and development changes.

The procedure(s) should describe when and how theorganizationuses change control within the original design process and after the original design has been transferred to manufacturing. The change control procedures should ensure that change control is implemented after the organizationinitially approve any design inputs. It should also describe when verification is used for certain design changes instead of using validation and the reason for choosing verification. The organizationshould determine the significance of the change to function, performance, usability, safety and applicable regulatory requirements for the medical device and its intended use. Records should bemaintained for:

a) Outcome of review of the effect of the changes on:

   -constituent parts and product in process or already delivered,

   - inputs or outputs of risk management and

   - product realization processes

b) verification or validation report

The review of design and development changes should include evaluation of the effect of the changes onconstituent parts and product in process or already delivered, inputs or outputs of risk managementand product realization processes.

Records of changes, their review and any necessary actions should be maintained.

8.3.10. Design and development files

The organization should maintain a design and development file for each medical device type or medical device family. Furthermore, The organization should have a procedure(s) for maintaining the contents of the design and development file.If more than one device shares a common design & development file, there should be explanation on how the organization identifies each device within the group having common design elements. The file

shouldinclude, or reference records generated to demonstrate conformity to therequirements for design and development and records for design and development changes.

## 8.4. Purchasing

### 8.4.1. Purchasing process

The organization should maintain procedure(s) for purchasing controls to ensure that purchased product conforms to specified purchasing information. The procedure should:

a) Explain if theorganization uses a contract design service or contract manufacturer(s)

b) Specify controls applicable to these suppliers

c) describe suppliers evaluation process

d) describe how the organization will determine the type of and extent of control it will exercise over suppliers

e) define how to maintain records of acceptable suppliers and how to address the purchasing data approval process

f) explain how the organization will balance purchasing assessment and receiving acceptance to ensure that products and plan the monitoring and re-evaluation of suppliersservices are acceptable for their intended use

The organization should establish criteria for the evaluation and selection of suppliers based on:

a) supplier`s ability to provide product that meets requirements;

b) supplier`s performance;

c) the effect of the purchased product on the quality of the medical device;

d) the risk associated with the medical device.

The organization should maintain records of plan for the monitoring and re-evaluation of suppliers, the results of evaluation, selection, monitoring and re-evaluation of supplier capability orperformance and any necessary actions arising from these activities.

### 8.4.2. Purchasing information

The organization should retain purchasing information that ispertaining to, but not limited to:

a) product specifications;

b) requirements for product acceptance, procedures, processes and equipment;

c) requirements for qualification of supplier personnel;

d) quality management system requirements;

e) a written agreement with the supplier; and

f) notification from supplier to the organization on any changes

The organization should ensure the adequacy of specified purchasing requirements prior to their communication to the supplier.

#### 8.4.3. Verification of purchased product

The organization should establish and implement the inspection or other activities necessary for ensuring that purchased product meets specified purchasing requirements. The extent of verification activities should be based on the supplier evaluation results and proportionate to the risks associated with the purchased product.

When the organization becomes aware of any changes to the purchased product, the organization should determine whether these changes affect the product realization process or the medical device.

When the organization or its customer intends to perform verification at the supplier's premises,

the organization should state the intended verification activities and method of product release in the purchasing information. Records of the verification shall be maintained

The organization should maintain records of verification. These should include:

a) results of inspection or other activities undertaken to ensure that purchased product meets specified purchasing requirements;

b) determinations made by the organization on any change to the purchased product that affects the product realization process or the medical device; and

c) verifications activities performed at the supplier's premises

### 8.5. Production and service provision

#### 8.5.1. Control of production and service provision

The organization should plan, monitor, and control the conditions in which the production and service provision are executed to ensure that product conforms to specification.

The production controls should include but not limited to:

a) documentation of procedures and methods for the control of production;

b) qualification of infrastructure.

c) implementation of monitoring and measurement of process parameters and product characteristics;

d) availability and use of monitoring and measuring equipment;

e) implementation of defined operations for labelling and packaging;

f) implementation of product release, delivery and post-delivery activities.

The organizationshould also maintain a verified and approved record for each medical device or batch ofmedical devices that provides traceability and identifies the amountmanufactured and amount approved for distribution.

### 8.5.2. Cleanliness of product

The organization should document requirements for cleanliness of the product or contamination control if:

a) product is cleaned by the organization prior to sterilization or its use;

b) product is supplied non-sterile and is to be subjected to a cleaning process prior to sterilization or its use;

c) product cannot be cleaned prior to sterilization or its use, and its cleanliness is of significance in use;

d) product is supplied to be used non-sterile, and its cleanliness is of significance in use;

e) process agents are to be removed from product during manufacture.

### 8.5.3. Installation activities

The organization should document requirements for installation activities and acceptance criteria for verification of the installation.

In cases when the installation activities are performed by an external party that is not a supplier of the organization, documented requirements for medical device installation must be provided by the organization. The organization should retain records of medical device installation and verification of installation performed by the organization orits supplier should be maintained.

### 8.5.4. Servicing activities

In cases when servicing of a medical device is an explicit requirement, the organization must document the procedures and records; as well as materials and measurements used for performing and verifying servicing activities.

The records of servicing activities should also be analysed to determine whether the information should be handled as a complaint, or as an input for the improvement of process.

### 8.5.5. Particular requirements for sterile medical devices

For medical devices that require sterilization, theorganization should keep records of the sterilization process parameters for each sterilization batch. These records must be traceable to each production batch of medical devices.

### 8.5.6. Validation of processes for production and service provision

The organization should validate any processes for production and service provision where the resultingoutput cannot be or is not verified by subsequent monitoring or measurement and, as a consequence,deficiencies become apparent only after the product is in use or the service has been delivered.

The organization should document procedure for validation of processes. Validation should be performed before or during process execution when process outputs can’t be verified with later monitoring and measurement, and when product defects are identifiable only after using the product or service provision. The validation should demonstrate the capability of the process to deliver the intended results consistently. The procedure for validation should include:

a) defined criteria for review and approval of the processes;

b) equipment qualification and qualification of personnel;

c) use of specific methods, procedures and acceptance criteria;

d) as appropriate, statistical techniques with rationale for sample sizes;

e) requirements for records

f) revalidation and criteria for revalidation;

g) approval of changes to the processes.

The organization should document procedures for the validation of the application of computer software used in production and service provision. Such software applications should be validated prior to initial use and, as appropriate, after changes to such software or its application

The organization should also maintain records of all verification activities, results and conclusion of validation and necessary actions from the validation.

8.5.7. Particular requirements for validation of processes for sterilization and sterilebarrier systems

The organization should document procedure for validation of the sterilization process and sterile barrier systems. The sterilization process must be validated before the implementation, and results of the validation and necessary subsequent actions must also be documented.

The organization should retain records of the results and, conclusion of validation and necessary subsequent actions from the validation.

8.5.8. Identification

The organization should document a procedure(s) for product identification and for identifying the product status with respect to monitoring and measurement requirements throughout the manufacturing process. It should retain records of such identification throughout the entire lifecycle of the product, from production and storage to installation and servicing, in order to ensure its compliance with requirements for the product or release under an authorized concession. The organization should provide, when requested, evidence to ensure that all products pass required inspections and tests before reaching the end user.

The organization should document a system to assignunique device identification to the medical device.

8.5.9. Traceability

The organization should document procedures for traceability, at least referring to the origin of the product, material and parts, history of processing (in which process phase is the product, material, or part), distribution, and product location after delivery. The procedure should define the extent of traceability and the records to be maintained. Where traceability is

needed, the organization must establish a unique identification system for the product and maintain recordsof traceability.The records should include records of components, materials, and conditions for the work environment used, if these could cause the medical device not to satisfy its specified safety and performance requirements. The organization should require that suppliers of distribution services or distributors maintain records of the distribution of medical devices to allow traceability and that these records are available for inspection. The stablished traceability system should enable ease product withdrawal from the market.

The records required for traceability of implantable medical devices should include records of components, materials, and conditions for the work environment used, if these could cause the medical device not to satisfy its specified safety and performance requirements. The organization should require that suppliers of distribution services or distributors maintain records of the distribution of medical devices to allow traceability and that these records are available for inspection. Records of the name and address of the shipping package consignee should be maintained.

#### 8.5.10. Customer Property

The organization should identify, verify, protect, and safeguard customer property provided for useor incorporation into the product while it is under the organization's control or being used by theorganization. If any customer property is lost, damaged or otherwise found to be unsuitable for use, theorganization shall report this to the customer and maintain records.

#### 8.5.11. Preservation of product

The organization should establish a documented procedure to ensure that the product maintains its conformity to requirements during processing, warehousing, handling, and distribution. The conformity of a product and its components must be kept throughout the whole process of realization and delivery to the planned destination, for example, temperature, sterile conditions, etc. The procedure should ensure protection of the medical device from any alteration, contamination, or damage. It should also define the storage conditions andensure suitability of the design and construction of packaging and shipping containers to protect the product. The organization should maintain records of any special conditions controlled.

### 8.6. Control of monitoring and measuring equipment

The organization should document procedures to carry out monitoring and measurement in a manner that is consistent with the monitoring and measurement requirements.

As necessary to ensure valid results, measuring equipment should:

a) be calibrated or verified, or both, at specified intervals, or prior to use, against measurementstandards traceable to international or national measurement standards: when no such standardsexist, the basis used for calibration or verification should be recorded;

b) be adjusted or re-adjusted as necessary: such adjustments or re-adjustments shall be recorded;

c) have identification in order to determine its calibration status.

d) be safeguarded from adjustments that would invalidate the measurement result.

e) be protected from damage and deterioration during handling, maintenance and storage.

The organization shall perform calibration or verification in accordance with documented procedures.

In addition, the organization should assess and record the validity of the previous measuring resultswhen the equipment is found not to conform to requirements. The organization should take appropriateaction in regard to the equipment and any product affected.Records of the results of calibration and verification shall be maintained.

The organization should identify the monitoring and measuring activities necessary to maintain compliance of the medical device with its requirements as well as the monitoring and measurement equipment necessary to perform these monitoring and measurement activities. Monitoring equipment must be calibrated or verified on regular schedule. The organization should maintain records of:

- Monitoring and measurement activities
- calibration or verification activities including traceability of standards to international or national measurement standards,
- adjustments and readjustments,
- the results and conclusion of validations and
- necessary actions from any of the above

## 9. Measurement, analysis, and improvement

### 9.1. General

The organizationshould plan and implement monitoring, measurement, analysis and improvementprocesses needed to demonstrate conformity of the medical device to the QMS and to maintain its effectiveness. Results of these monitoring, measurement, and analysis should be embodied as an input in the process of improvement and management review.

### 9.2. Monitoring and measurement

#### 9.2.1. Feedback

The organization should document procedure for feedback process, which should include the methodology for obtaining and using this information. Records of customer feed backs and those used as inputs into risk management should be retained.

#### 9.2.2. Complaint handling

The organization should document a procedure to define the process of complaint handling, from receiving and recording the information to investigating the complaint-related product and determining the need to initiate corrective action.These procedures should include at a minimum requirements and responsibilities for:

a) receiving and recording information;
b) evaluating information to determine if the feedback constitutes a complaint;
c) investigating complaints;
d) determining the need to report the information to the appropriate regulatory authorities;
e) handling of complaint-related product;
f) determining the need to initiate corrections or corrective actions.

The organization should retain records of complaint handling, which should include at a minimum

a) complaints received
b) investigation reports
c) actions resulting from /taken as a result of/ the complaint handling
d) justification for not investigating complaints (if any satisfactory reasons)

### 9.2.3. Reporting to the authority

The organization should document procedure for notifying appropriate regulatory authorities regarding complaints, adverse events or issuance of advisory noticesand keep records of reports/notifications addressed to regulatory authorities. It should provide adverse event information and other required information to EFDA as per the proclamation 1112/2019, article 38(2).

### 9.2.4. Internal audit

The organization should document procedure to describe the responsibilities and requirements for planning and conducting audits and recording and reporting audit results. The internal audit should determine whether QMS conforms to the organization's documentation, implemented standards, and applicable legalrequirements as well as whether the QMS is effectively implemented and maintained.

The organization should retain records of audits and their results including but not limited to:

a) audit plan, audit criteria, scope, interval and methods used
b) area audited
c) audit findings
d) actions taken following audit results
e) verification of actions taken

### 9.2.5. Monitoring and measurement of processes

The organization shoulddocument methods applied for monitoring and, as appropriate, measuring whether thequality management system processes are delivering the expected/planned results or not. The organization should retain records of actions taken when the planned results are not achieved.

### 9.2.6. Monitoring and measurement of product

Theorganiztion should maintain plan and documented arrangements formonitoring and measuring the characteristics of the product to verify that productrequirements have been met. This should be carried out at applicable stages of the product realizationprocess. It should retain records of:

a) evidence of conformity to the acceptance criteria
b) the personauthorizing release of product

c) thetest equipment used to perform measurement activities
d) personnel performing any inspection or testing (for implantable medical devices)

### 9.3. Control of nonconforming product

The organization should document a procedure that defines the controls and roles, responsibilities and authorities in the process of control of nonconforming products, from identification to disposition of the nonconforming product in order to prevent its unintended use or delivery. It should also retain records of the nature of the nonconformities and any subsequent action taken, including the evaluation, any investigation and the rationale for decisions. Such records should comprise response of the organization to non-conforming products detected both before delivery and after delivery. It should include:

a) investigations
b) notificationssent to any responsible external party.
c) actions taken to eliminate the detected nonconformity;
d) action taken to preclude nonconforming products original intended use or application;
e) if the product is accepted by concession:
    - the person authorizing its use, or release
    - justifications provided
    - approval for meeting applicable regulatory requirements

The organization should maintain procedure for any rework to be performed on a medical device. The procedure(s) must takes into account the potential adverse effects of the rework on the device. Record of the rework should be retained as a prove that the medical device has been verified to demonstrate its compliance with applicable acceptance criteria.

### 9.4. Analysis of data

The organization should maintain procedure to determine, collect and analyse appropriate data to demonstrate the suitability, adequacy and effectiveness of the QMS; how the organization uses the results of analysis as input for improvement and it should retain records for results of the analysis. The procedures should include determination of appropriate methods, including statistical techniques and the extent of their use. It should also mention possible data sources, such as:

a) feedback;
b) conformity to product requirements;
c) trends of processes and product,

d) suppliers;
e) audits; and
f) service reports, as appropriate.

## 9.5. Improvement

### 9.5.1. General

The organizationshould provide evidence (documented information) for the effectiveness of identified and implemented changes in order to ensure and maintain the continued suitability, adequacy and effectiveness of the quality management system as well as medicaldevice safety and performance. This may be achieved using the quality policy, quality objectives, audit results, post-marketsurveillance, analysis of data, corrective actions, preventive actions and management review.

### 9.5.2. Corrective action

The organization should maintain procedure for identifying /reviewing nonconformities, determining the cause, evaluating the need for corrective action, verifyingand executing corrective action as well as evaluating the effectiveness of the corrective actions. It shall also maintain records of any investigation and of action taken to certify that the corrective action process is performed in the way it hasbeen defined & effective indeed.The record should contain but not limited to:

a) The review inputs & identified nonconformities (including complaints)
b) Causes of nonconformities
c) Determined, planned and implemented actions to ensure nonconformities do not recur
d) verifications to make sure that the corrective actions do not adversely affect the ability to meet applicable regulatory requirements or the safety and performance of the medical device.
e) reviews undertaken to evaluate the effectiveness of the corrective action taken

### 9.5.3. Preventive action

The organization should maintain procedure for identifying potential nonconformities, determining actions to eliminate their causes and prevent their occurrences. The determined preventive actions should be proportionate to the effects of the potentialproblems. It should maintain records for:

a) The identified potential nonconformities and their causes;
b) Determined,planned and implemented actions to prevent occurrence of nonconformities;
c) verifications to make sure that actions donot adversely affect the ability to meet applicable regulatory requirements or the safety and performance of the medical device;
d) reviews undertaken to evaluate the effectiveness of the preventive action taken