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

Drug Evaluation & Research (DER) Directorate

NAFDAC GOOD MANUFACTURING PRACTICE FOR MEDICAL DEVICES, IVDs, AND RELATED PRODUCTS GUIDELINES 2024

1. INTRODUCTION

1.1 The objective of Good Manufacturing Practice (GMP) Guidelines for Medical Devices and Related Products is to ensure that these products are consistently manufactured in conformance with quality standards.

1.2 The requirements in these guidelines govern the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished medical devices, in vitro diagnostics (IVDs), and related products intended for human use.

1.3 It is necessary to emphasize that, no medical device, IVD, and other related products should be manufactured, exported, advertised, sold, or distributed in Nigeria unless it has been registered in accordance with the provisions of the Food, Drugs and Related Products Act Cap F33 LFN 2004 (formerly decree 19 of 1993) and the accompanying regulations and guidelines.

1.4 These guidelines are established to provide information on the requirements for the manufacture of medical devices, IVDs, and other related products in Nigeria and all countries intending to export these products to Nigeria. The requirements outlined in these guidelines are to ensure that finished medical devices, in vitro diagnostics, and other related products are safe, effective, and compliant with the applicable laws and regulations.

1.5 This document outlines the Quality System Requirements that medical devices, IVDs, and other related products manufacturers must adhere to during device design, manufacturing, contracting, remanufacturing, processing, repackaging, or relabeling for commercial distribution. The guideline provides detailed guidance on Good Manufacturing Practices (GMP) requirements, including:

- Design controls
- Process validation
- Calibration
- Device master records
- Component control

1.6 If a manufacturer only engages in specific operations that are subject to the requirements outlined in these guidelines, and not in others, then that manufacturer is only required to comply with the specific requirements that relate to the operations in which they are involved.

1.7 Premises for the manufacture of medical devices, IVDs, and related products will be inspected in accordance with the requirements of the applicable regulations, these guidelines, the current ISO 13485:2016 and any other applicable international standards.

1.8 The GMP inspection will be conducted using a risk-based approach, taking into account factors such as product and process risk, the manufacturer's compliance history, the risk associated with device usage, and relevant recall actions. The objective of this inspection is to verify that the manufacturer consistently designs, develops, produces, stores, and

distributes medical devices, IVDs, and related products in compliance with applicable regulatory requirements, ensuring customer satisfaction and public health and safety.

1.9 Manufacturers may utilize this guidance when developing and implementing their quality system to ensure compliance with regulatory requirements and industry standards

1.10 Foreign manufacturers should permit the inspection of their facilities by NAFDAC to determine compliance with these guidelines and the applicable regulations to ensure that the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation, or servicing of any devices produced at such facility that are offered for import into Nigeria conform to the requirements of these guidelines and the applicable regulations.

2. QUALITY SYSTEM

2.1 Each manufacturer should establish and maintain a quality system appropriate for the specific medical device(s), IVD, or related product designed or manufactured, and that meets the requirements of these guidelines.

2.2 The Quality System Requirements outline the Quality System that manufacturers of medical devices, IVDs, and related products must consider when designing, manufacturing, contract manufacturing, remanufacturing, processing, repackaging, or relabeling finished medical devices intended for commercial distribution.

2.3 The Quality System should comprise articles that elucidate various good manufacturing practices (GMP) requirements, such as; design controls, process validation, calibration, Device Master Records, component control, labeling, etc.

2.4 The manufacturer should consider quality at the earliest stages in every significant area that impacts the quality, safety, and effectiveness of the medial device, IVD, or related product, including:

I. Product development
II. Design verification and validation
III. Component and/or supplier selection
IV. Documentation
V. Development of labeling
VI. Design Transfer
VII. Process development and validation
VIII. Pilot production
IX. Routine manufacturing
X. Test/inspection
XI. Device History Record evaluation
XII. Distribution
XIII. Service or repair
XIV. Complaints

2.5 **Management Responsibility**

2.5.1 **Quality policy** – The top management of the manufacturing company should establish the organization's quality policy and objectives to ensure commitment to quality. The top management should ensure that the quality policy is understood, implemented, and maintained at all levels of the organization.

2.5.2 **Organization** – The manufacturer should establish and maintain an adequate organizational structure to ensure that medical devices, IVDs, and related products are designed and produced in accordance with the requirements of the applicable regulations and these guidelines.

2.5.3 The manufacturer should establish 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.

2.5.4 Top management of the manufacturing firm should 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 the applicable regulations and these guidelines.

2.5.5 Top management should ensure a clear definition of responsibilities and authority to ensure that quality system requirements are effectively established and maintained, and performance of the quality system is reported to management

2.5.6 **Management Review** – Top management should review 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 applicable regulations and these guidelines and the dates and outcomes of quality system reviews are documented.

2.5.7 **Quality Planning** – The manufacturer should establish a quality plan that defines the quality practices, resources, and activities relevant to medical devices, IVDs, and related products that are designed and manufactured and how the requirements for quality will be met.

2.5.8 **Quality System Procedures** – The manufacturer should establish the quality system procedures and instructions and provide an outline of the structure of the documentation used in the quality system where appropriate.

2.6 Quality Risk Management

2.6.1 Top management must integrate risk management into the organization's quality management system (QMS), by establishing policies and principles for effective implementation.

2.6.2 The manufacturer must establish a risk management system, implement risk management principles and activities throughout the QMS, and regularly update the risk management system

2.6.3 The risk management system should apply throughout the lifecycle of the medical device, IVD, or related product and must cover:

a. Identification of potential risks
b. Assessment of risks during intended use and foreseeable misuse
c. Controlling risks through design, manufacture, and protection
d. Continuous monitoring and updating of risk management plans

2.6.4 The risk management system can be characterized by phases of activities, including:
a. Determination of acceptable risk levels (risk acceptability criteria)
b. Risk analysis (identifying hazards and estimating risks)
c. Risk evaluation (comparing estimated risks to acceptability criteria)
d. Risk control and monitoring activities (eliminating or reducing risks)

2.6.5 Medical devices, IVD, and related product manufacturers should incorporate safety considerations into every phase of the QMS by identifying and mitigating potential risks to ensure the safety and effectiveness of their products.

2.6.6 Manufacturers must ensure that the degree of safety considerations is commensurate with the degree of risk associated with, and the nature of the medical device, IVD, and related product.

2.6.7 The manufacturer should incorporate risk control measures throughout the product life cycle, from design input to servicing.

2.6.8 Documents and records resulting from risk management activities such as risk management procedures, reports, etc. should be maintained and should be referenced in either a risk management file or other appropriate files (e.g., Design History File, Technical Documentation, Design Dossier, Device Master Record, Device History Record, or Process Validation files).

2.7 Quality Audit

2.7.1 The manufacturer should establish procedures for quality audits and conduct such audits to assure that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system.

2.7.2 Quality audits should be conducted by individuals who do not have direct responsibility for the matters being audited.

2.7.3 A report of the results of each quality audit, and reaudit(s) where taken, including the dates of the audits, should be provided by the Auditors and such reports should be reviewed by individuals having responsibility for the matters audited as well as the top management.

2.7.4 Individuals with responsibility for ensuring the effectiveness of the QMS should make sure that corrective action(s) are taken on any deficiencies observed during the audits.

3. PERSONNEL

3.1 Each manufacturer of medical devices, IVDs, and related products should have sufficient personnel with the necessary education, background, training, and experience to ensure that all activities required by the applicable Regulations and these Guidelines are correctly performed.

3.2 The manufacturer should establish procedures for identifying training needs and ensuring that all personnel are trained to adequately perform their assigned responsibilities.

3.3 Training activities should be properly documented and the effectiveness of training programs should be evaluated.

3.4 The methodology used to check effectiveness of training programs should be proportionate to the risk associated with the work for which the training is being provided.

3.5 Training of personnel should include awareness of device defects that may occur from the improper performance of their specific jobs.

3.6 Personnel who perform verification and validation activities should also be made aware of defects and errors that may be encountered as part of their job functions.

4. DESIGN CONTROLS

4.1 Each manufacturer should establish and maintain procedures to control the design of the medical device, IVD, and related product, ensuring that specified design requirements are met.

4.2 **Design and development planning -** The manufacturer should establish and maintain plans that describe or reference the design and development activities and define responsibility for implementation.

4.3 The plans should identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process.

4.4 The design and development plans should be reviewed, updated, and approved as the design and development of the medical devices, IVDs, and related products evolves.

4.5 **Design input -** The manufacturer should establish and maintain procedures to ensure that the design requirements relating to a medical device, IVD, and related product are appropriate and address the intended use of the product, including the needs of the user and patient.

4.6 The design input requirements should be documented, reviewed, and approved by a designated individual(s), including the signature of the individual(s) and the date of approval of the requirements.

4.7 **Design output –** The manufacturer should establish and maintain procedures for defining and documenting design output in a way that allows an adequate evaluation of conformance to design input requirements.

4.8 Design output procedures should contain or make reference to acceptance criteria and identify those design outputs that are essential for the proper functioning of the device.

4.9 Design output should be documented, reviewed, and approved before release with the approval documentation showing the signature of the individual(s) approving the output and the date of the approval.

4.10 **Design review -** The manufacturer should establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the device's design development.

4.11 The procedures should ensure that participants at each design review include representatives of all functions concerned with the design stage being reviewed and an

individual(s) who does not have direct responsibility for the design stage being reviewed, as well as any specialists needed.

4.12 The results of a design review, including identification of the design, the date, and the individual(s) performing the review, should be documented in the Design History File (DHF).

4.13 **Design Verification** - Manufacturers should establish and maintain procedures for verifying the device design, confirming that design output meets design input requirements.

4.14 The results of the design verification, including identification of the design, method(s), the date, and the individual(s) performing the verification, should be documented in the DHF.

4.15 **Design Validation** - Manufacturers should establish and maintain procedures for validating the device design under defined operating conditions on initial production units, lots, batches, or their equivalents.

4.16 Manufacturers should ensure that design validation demonstrates that devices conform to defined user needs and intended uses through testing of production units under actual or simulated use conditions.

4.17 Design validation should include software validation and risk analysis, where appropriate.

4.18 The results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, should be documented in the DHF.

4.19 Clinical evaluations or performance evaluations should be conducted in line with applicable regulatory requirements.

4.20 **Design Transfer** - Manufacturers should establish and maintain procedures to ensure that the device design is correctly translated into production specifications.

4.21 **Design Changes** - Manufacturers should establish and maintain procedures for identifying, documenting, validating or verifying, reviewing, and approving design changes before implementation.

4.22 **Design History File (DHF) -** Manufacturers should establish and maintain a DHF for each product (medical device, IVD, and related product) type, containing or referencing records necessary to demonstrate that the design was developed following the approved design plan and the requirements of the applicable Regulations and this guideline.

5. INFRASTRUCTURE

5.1 Buildings

5.1.1 Buildings to be used to manufacture medical devices, IVDS, and related products must be suitably designed and maintained to ensure conformity to product requirements.

5.1.2 The buildings must have sufficient workspace to prevent mix-ups and ensure orderly handling of products.

5.2 Equipment

5.2.1 Equipment to be used for the manufacture and processing of medical devices, IVDs, and related products must be suitable, appropriately designed, constructed, placed, and installed for maintenance, adjustment, cleaning, and use.

5.2.2 The equipment must be designed and constructed to suit the production of the product.

5.2.3 Equipment surfaces in contact with in-process materials must not react with or adsorb the materials.

5.2.4 Equipment used in manufacturing must be easily cleaned and not adversely affect the product.

5.2.5 Equipment used for flammable substances must be explosion-proof.

5.2.6 **Equipment Installation and Location**

a. Equipment should be located to avoid congestion and properly identified to prevent product mix-ups.
b. Installation and inspection instructions and test procedures should be established and maintained.

5.2.7 **Equipment Maintenance**

a. The manufacturer should establish procedures for maintenance, including schedules for adjustment, cleaning, and preventive maintenance activities.
b. The manufacturer should ensure that weighing, measuring, testing, and recording equipment are serviced and calibrated regularly.

5.2.8 **Equipment Calibration**

a. The manufacturer should establish procedures and records for calibration of all instruments and equipment requiring calibration.
b. Accuracy and precision limits for calibrated instruments and equipment must be met, and remedial action taken where necessary.
c. Standards used for calibration of instruments and equipment must be traceable to national or international standards with documentary evidence provided.
d. Equipment identification, calibration dates, and individuals performing the calibration must be documented.

5.2.9 **Work Environment**

a. The manufacturer should document the requirements for the work environment necessary to achieve conformity to product requirements.
b. Where the conditions of the work environment have the potential to adversely impact product quality, procedures should be established to monitor and control the work environment as follows:
    i. The manufacturer should define the physical and environmental conditions necessary for product quality, such as temperature, humidity, and lighting.
    ii. The manufacturer should establish procedures to monitor and control these conditions, ensuring that the work environment is maintained in a state that supports product quality.
    iii. The requirements and procedures for the work environment should be documented and records of monitoring should be kept.
    iv. The manufacturer should ensure that the work environment is regularly reviewed and updated as necessary.

6.0 DOCUMENTATION

Documentation is essential for ensuring product quality and compliance with regulatory standards. It involves creating detailed records of manufacturing processes, procedures, and controls to ensure consistency and traceability. GMP documentation should be accurate, clear, and comprehensive, covering all aspects of production, quality control,

and distribution. This includes batch records, standard operating procedures (SOPs), and validation protocols.

6.1 The manufacturer should establish procedures and maintain records of all processes that have impacts on the quality, safety, and effectiveness of the medial device, IVD, or related product, including:

6.1.1 Product development
6.1.2 Design verification and validation
6.1.3 Device labelling
6.1.4 Design Transfer
6.1.5 Component and/or supplier selection
6.1.6 Conformity Assessment Report
6.1.7 Process development and validation
6.1.8 Production
6.1.9 Internal Audit
6.1.10 Quality Control and Testing
6.1.11 Device History
6.1.12 Distribution
6.1.13 Service or repair
6.1.14 Complaints and/or Recall

6.2 Quality Management System

a) The manufacturer should document all the requirements for Quality management system such as Quality Manual, Quality Policy and Objective defining the organization's commitment to quality and specific quality goals.
b) Roles, responsibilities, and authorities within the organization must be clearly documented

6.3 Safety, Performance

a) The Manufacturer should provide documented comprehensive information supporting the safety, effectiveness, and quality of [Device/IVD Name], in compliance with relevant global regulations and standards.
b) Manufacturers should document and maintain the record of all Medical Devices, IVDs and related product's Design and development plan, Design inputs, Design outputs, Design verification and validation record.
c) The manufacturer should document all processes to identify, evaluate, and mitigate risks associated with the medical device.

6.4 Document Control

a) The manufacturer should establish and maintain procedures to control all documents, ensuring that documents are reviewed and approved for adequacy prior to issue.
b) Document should be reviewed, updated, and re-approved as necessary. It is important to identify the current revision status and changes to documents, and to ensure that relevant document versions are available at points of use.

c) Documents must be legible and identifiable. Additionally, the control of documents of external origin, necessary for the planning and operation of the quality management system, must be maintained.
d) Measures should be taken to prevent document deterioration or loss, and to prevent the unintended use of obsolete documents, with suitable identification applied.

6.5 Medical Device File

a) Manufacturers should establish and maintain a medical device file. The content of the file should include, but is not limited to, a general description of the medical device, its intended use or purpose, and labelling, including any instructions for use.
b) The medical device file should contain specifications for the product, specifications or procedures for manufacturing, packaging, storage, handling, and distribution of products.
c) The medical device file should include procedures for measuring and monitoring, and, where appropriate, requirements for installation and servicing.

7.0 VALIDATION

7.1 The key elements of qualification and validation programme of manufacturing facilities should be clearly defined and documented in a validation master plan.
7.2 The Manufacturers should establish, maintain, and provide documentary evidence that they perform process validation, cleaning validation, water validation, and analytical validation where necessary.
7.3 Manufacturers must determine the need for revalidation based on risk management activities and utilize risk management tools, such as FTA, FMEA, HAZOP, HACCP, PAT, or others, when performing process validation.
7.4 Manufacturers should identify the need for additional risk control measures based on validation results and establish validation protocols that describe the qualification and validation to be performed.
7.5 Validation protocols should include, unique document number and version number, objective and scope, site and responsible personnel, reference to applicable standard operating procedures, equipment or instruments to be used, reference to standards as appropriate, stage of validation, processes and/or parameters, sampling, testing, and monitoring requirements, stress testing where appropriate, calibration requirements, predetermined acceptance criteria for drawing conclusions, change control, deviations, attachments, and reference to attachments, including source data where relevant, and archiving and retention.
7.6 Manufacturers must ensure that all validation activities, results, and approvals (including name, dates, and signatures details) are properly documented.
7.7 Manufacturers must establish procedures for monitoring and controlling process parameters to ensure continued compliance with specifications. Validated processes

must be performed by qualified individuals, and all monitoring and control data, including dates and personnel/equipment details, must be documented.

7.8 Manufacturers are required to review and evaluate their processes whenever changes or deviations occur. Revalidation must be conducted as necessary, with thorough documentation of these activities.

7.9 Manufacturers must ensure that all equipment is qualified before use, including Design Qualification (DQ), Installation Qualification (IQ), Performance Qualification (PQ), and Operational Qualification (OQ). Additionally, utilities, systems, and equipment must be maintained in a qualified state.

7.10 Any changes made to equipment must be managed through the change control procedure. Requalification should be performed based on identified needs and risk management principles. Factors such as frequency of use, breakdowns, operational results, criticality, preventive maintenance, repairs, calibration, and verification should be considered.

8.0 **PURCHASING CONTROLS**:

8.1 There should be written procedures describing in detail the receipt, identification/internal labelling, storage, handling, sampling, testing, and approval or rejection of raw materials and packaging materials.

8.2 The Manufacture should establish and maintain procedures to ensure purchased materials and services conform to specified requirements

8.3 Manufacturers should evaluate and select suppliers, contractors, and consultants based on their ability to meet quality requirements

8.4 The Manufacturer must define and document the type and extent of control to be exercised over suppliers, contractors, and consultants

8.5 Manufacturers should establish and maintain records of acceptable suppliers, contractors, and consultants

8.6 The person responsible for quality assurance should have responsibility together with other relevant departments for approving suppliers who can reliably supply starting and packaging materials that meet established specifications

8.7 The purchase of starting materials is an important operation that should involve staff who have particular and thorough knowledge of the products and suppliers.

a. Manufacturers should ensure starting materials are purchased only from approved suppliers and, where possible, directly from the producer, against an agreed specification. It is also recommended that the specifications established by the manufacturer for the starting materials be discussed with the suppliers. It is beneficial for all critical aspects of the production and control of the starting material in question, including handling, labelling and packaging requirements as well as complaints and rejection procedures, to be contractually agreed between the manufacturer and the supplier.

b. Where the supplier of a critical material is not the manufacturer of that material, the name and address of the latter should be known by the finished product manufacturer.

c. Changes in materials or the source of supply of raw materials should be handled through the formal change control system of the manufacturer to evaluate the effect of the change on the product quality.
d. There should be written procedures and records for the receipt of and delivery of each starting material checked for the integrity of package and seal.

9.0 PRODUCTION AND PROCESS CONTROL

Manufacturers must ensure that designated personnel perform and supervise production activities. All material and product handling, including receipt, quarantine, sampling, storage, labeling, dispensing, processing, packaging, releasing, and distribution, should follow written procedures and be recorded.

9.1 Manufacturers must ensure that designated personnel perform and supervise production activities. All material and product handling, including receipt, quarantine, sampling, storage, labeling, dispensing, processing, packaging, releasing, and distribution, should follow written procedures and be recorded.

9.2 Manufacturers must ensure that their production processes consistently yield devices that meet specifications by developing, implementing, and monitor production processes that guarantee conformity to specifications.

9.3 Manufacturers must identify potential deviations from specifications while establishing process control procedures to mitigate them. The process control must include clear, documented instructions and standard operating procedures (SOPs) that govern production.

9.4 Incoming materials and finished products should be physically or administratively quarantined immediately after receipt or processing, until they have been released for use or distribution. Administrative quarantine refers to the use of automated warehouse management systems where there may be no need for physical segregation of quarantine material provided the system is validated. The Manufacturer must provide evidence of computer systems validation (CSV), otherwise physical segregation remains a desirable option Intermediate and bulk products purchased as such should be handled on receipt as though they were starting materials.

9.5 At every stage of processing, products and materials should be protected from microbial and other forms of contamination.

9.6 At all times during processing, all materials, bulk containers, major items of equipment, the rooms and packaging lines being used should be labelled or otherwise identified with an indication of the product being manufactured.

9.7 Labels applied to containers, equipment or premises should be clear, unambiguous and in the company's agreed format.

9.8 Manufacturers must establish and maintain procedures for change control, which involve verifying and validating changes to specifications, methods, processes, or procedures before implementation.

9.9 They must also control environmental conditions that could impact product quality through periodic inspections and documentation.

9.10 Personnel requirements must ensure the health, cleanliness, and training of staff to prevent adverse effects on product quality.

9.11 Contamination control procedures must be in place to prevent equipment and product contamination.

9.12 Facilities and equipment must be designed and maintained to support operations, prevent mix-ups, and ensure orderly handling.

9.13 Equipment must meet specifications, be properly designed, constructed, and installed, with maintenance schedules established and documented.

9.14 Periodic inspections must be conducted to ensure adherence to maintenance schedules, and inherent limitations or tolerances for equipment requiring adjustments must be posted.

9.15 Access to production premises should be restricted to authorized personnel.

9.16 Manufacturers should establish and maintain acceptance procedures for in-process controls, ensuring that in-process products are controlled until required inspections and tests are completed. They must validate computer software for its intended use according to an established protocol, document validation activities and results, and establish procedures for finished device acceptance to ensure each production run meets acceptance criteria.

9.17 In-process controls should be performed within the production area. The performance of such in-process controls should not have any negative effect on the quality of the product or another product (e.g. cross-contamination or mix up).

9.18 Production areas where susceptible products are processed should undergo periodic environmental monitoring (e.g. for microbiological monitoring and particulate matter where appropriate).

9.19 Manufacturers must ensure the accuracy and reliability of inspection, measuring, and test equipment by establishing and maintaining procedures for routine calibration, inspection, and maintenance, as well as handling, preservation, and storage to maintain equipment fitness.

9.20 Calibration procedures must include specific directions and limits for accuracy and precision, along with remedial actions for non-compliance and evaluation of potential device quality impact.

9.21 Calibration standards should be traceable to national or international standards, independent and reproducible, or in-house when no applicable standard exists.

9.22 Calibration records must be maintained, including equipment identification, calibration dates and personnel, and the next calibration date. These records must be readily accessible to equipment users and calibrators, ensuring that equipment used in production processes is reliable, accurate, and properly maintained to guarantee product quality.

9.23 **Device History Record**: Manufacturers must maintain device history records (DHRs) for each batch, lot, or unit to demonstrate compliance with the device master record (DMR) procedure. The DHR should include manufacturing dates, quantities manufactured and released for distribution, acceptance records, primary identification labels and labeling used, and any device identification and control numbers.

9.24 **Device master record**.: Manufacturers must ensure that each DMR is prepared and approved. The DMR foreach type of device must include,

a) Device specifications including appropriate drawings, composition, formulation, component specifications, and software specifications.
b) Production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications
c) Quality assurance procedures and specifications including acceptance criteria and the quality assurance equipment to be used
d) Packaging and labelling specifications, including methods and processes used
e) Installation, maintenance, and servicing procedures and methods.

9.25 Manufacturers should ensure that finished medical devices and related products are not released for distribution until all activities in the Device Medical Records (DMR) are completed, associated data and documentation are reviewed, released and dated by authorized individuals.

9.26 Manufacturers should determine the most appropriate method for achieving the required sterility assurance level (SAL) for a particular device.

9.27 Manufacturers must prepare evidence that the device complies with essential principles and, for devices supplied sterile, ensure compliance with essential principles for sterilizing devices.

9.28 Manufacturers should establish and maintain Device Master Records (DMRs). These records must include device specifications, production process specifications, quality assurance procedures and specifications, packaging and labeling specifications, and installation, maintenance, and servicing procedures and methods. Manufacturers must ensure that each DMR is prepared and approved

10.0 QUALITY CONTROL

10.1 The manufacturers must ensure that medical devices and related products are designed and manufactured to be safe and perform as intended

10.2 Manufacturers of medical devices and related products should establish quality control to ensure products meet specified requirements. The Quality control should involve sampling, inspecting, and testing of starting materials, in-process, intermediate, bulk, and finished products. It also includes environmental monitoring programs, review of batch documentation, sample retention programs, stability studies, and maintaining correct specifications of materials and products.

10.3 Manufacturers should ensure adequate laboratory facilities, with trained personnel and approved procedure for sampling, inspecting and testing starting materials, packaging materials and intermediate, bulk and finished products and for monitoring environmental conditions for GMP purposes. Records of testing, assay results, and the release or rejection of products must be maintained

10.4 Devices must be labeled with essential information, including intended use, instructions for use, and any warnings or precautions.

10.5 Medical devices and related products that are labeled as sterile, having a specific microbial state, or being pyrogen-free, must be designed, manufactured, and packaged to maintain that state throughout their shelf life. This includes ensuring their microbial state during transportation and storage, in accordance with the manufacturer's specified conditions.

10.6 Medical devices and IVD medical devices labeled as sterile must undergo rigorous processing, manufacturing, packaging, and sterilization procedures to ensure their sterility.

a) **Sterilization methods**: Sterilization processes must be validated to ensure they can achieve a Sterility Assurance Level (SAL) of 10^-6, meaning there is less than one chance in a million of a device being non-sterile.
b) Sterilization methods, such as steam sterilization, ethylene oxide sterilization, or radiation sterilization, must be validated to ensure they can achieve sterility
c) Devices must be processed and manufactured in a controlled environment to prevent contamination.
d) Packaging must be designed to maintain sterility during transportation, storage, and handling.
e) The shelf-life of sterile medical devices and IVDs must be determined using validated methods, such as real-time aging or accelerated aging studies, to ensure the device remains sterile over its specified shelf-life

10.7 Calibration of instruments, apparatus, gauges, and recording devices should be done at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met.

10.8 Animals used for testing materials or products should be quarantined before use. They should be maintained and controlled in a manner that ensures their suitability for the intended use. They should be identified, and adequate records should be maintained, showing the history of their use.

10.9 Out-of-specification (OOS)/out-of-trend (OOT) results obtained during testing of materials or products should be investigated in accordance with an approved procedure. Records should be maintained.

10.10 **Environmental Monitoring:** Manufacturers must implement key practices to maintain environmental controls of equipment and core processing areas for the production of medical devices and related products,

a) Regular monitoring of air quality, including controlling particulate and microbial contamination through HEPA filters and maintaining appropriate air pressure differentials, is essential.
b) Consistent monitoring and control of temperature and humidity levels are crucial to prevent degradation of materials and ensure optimal production conditions.
c) Adhering to Standards for cleanroom classification to ensure that the environment meets the required cleanliness levels for different stages of production.

d) Regular cleaning and maintenance of cleanrooms, including surfaces, equipment, and air handling systems, help maintain the required environmental conditions
e) Implementing validated sterilization processes, such as autoclaving and gamma irradiation, for equipment and materials used in production ensure they remain free from contaminants.
f) Continuous monitoring of sterility through environmental sampling and testing helps detect and address any deviations promptly.
g) Developing and adhering to Standard Operating Procedures (SOPs) for all critical processes ensures consistency and control over environmental conditions.
h) Regular training for personnel on proper handling and maintenance of equipment and cleanroom protocols is essential to prevent contamination.
i) Maintaining detailed records of environmental monitoring, maintenance activities, and any corrective actions taken is crucial for compliance and continuous improvement.
j) Regular internal audits and inspections help identify potential issues and ensure that environmental controls are effectively implemented.
k) Conducting regular risk assessments to identify potential sources of contamination and implementing mitigation strategies helps maintain a controlled environment.
l) Using data from environmental monitoring and audits to continuously improve processes and controls ensures ongoing compliance and product safety.

11.0 NON-CONFORMING PRODUCT

11.1A non-conforming product refers to any product that fails to meet specified requirements. This can include deviations from design specifications, manufacturing defects, labelling errors, or any other discrepancies that prevent the product from fulfilling its intended purpose.

11.2A non-conforming product refers to any product that fails to meet specified requirements. This can include deviations from design specifications, manufacturing defects, labelling errors, or any other discrepancies that prevent the product from fulfilling its intended purpose.

11.3Manufacturers must have procedures in place to manage products that fail to meet specified requirements. These procedures should cover identifying and documenting nonconforming products, evaluating the nonconformance to determine if an investigation is needed, notifying relevant parties responsible for the nonconformance, segregating and disposing of nonconforming products, and documenting the evaluation and any subsequent investigation.

11.4Manufacturers must establish and maintain clear procedures for managing nonconforming products. These procedures should include defined responsibilities and authorities for reviewing and disposing of nonconforming products, a documented review and disposition process, and justification and authorization for using nonconforming products.

11.5 Manufacturers must establish and maintain procedures for rework, which shall include retesting and reevaluation of the nonconforming product after rework, to ensure that the product meets its current approved specifications.

11.6 Manufacturers should establish and maintain procedures for rework, ensuring these procedures include retesting and reevaluation of nonconforming products, documenting all rework and reevaluation activities in the DHR, determining and documenting any adverse effects of rework on the product, and ensuring the product meets approved specifications after rework

11.7 Manufacturers should establish and maintain procedures for implementing corrective and preventive action. The procedures shall include requirements for:

a) Analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned products, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems.
b) Employing appropriate statistical methodology where necessary to detect recurring quality problems.
c) Investigating the cause of nonconformities relating to product, processes, and the quality system.
d) Identifying the action(s) needed to correct and prevent recurrence of nonconforming products and other quality problems.
e) Verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device.

12.0 DEVICE LABELLING

12.1 Medical device manufacturers must ensure their quality assurance (QA) program includes elements related to labeling to meet GMP requirements. The QA program must ensure labeling meets device master record standards for legibility and adhesion, and that labeling operations are controlled to ensure correct labeling is always used. Labeling encompasses equipment labels, control labels, package labels, directions for use, maintenance manuals, and electronic displays providing instructions or warnings.

12.2 Manufacturers of medical devices must provide Standard Operating Procedures (SOPs) for the creation, approval, and control of labeling materials, detailed specifications for labels including content, format, and placement, master records for each device detailing all labeling components and versions, documentation of any changes made to labeling with justifications and approvals, physical or digital samples of current and past labels, records showing where and when labeled products were distributed, documentation of any complaints related to labeling issues and the investigations conducted, evidence of training for personnel involved in labeling processes, and copies of labeling submitted to regulatory authorities along with any related correspondence.

12.3 Labels must include the device name, intended use, manufacturer's name and address, batch or serial number, and expiry date.

12.4 Instructions for use (IFU) must be clear, concise, and in the local language(s) of the market where the device is sold.

12.5All labels must be designed and applied to ensure they remain in place and legible during distribution, storage, and use. User instructions and other labeling should also remain legible under customary conditions. Manufacturers must ensure that printed labels, such as those on plastic in vitro diagnostic media plates, are legible and remain so until used.

12.6Devices must have a UDI to enhance traceability. The UDI must be included on the packaging.

12.7All packaging and labeling materials must be examined upon receipt and acceptance activities performed to ensure they meet specifications. Samples of labels must be proofread by designated individuals. Once accepted, these components can be placed into inventory or production. These activities must be recorded in the device history record to confirm inspection and proofreading were completed, with the acceptance record maintain.

12.8 Labelling and packaging operations should be separated to prevent mixups between similar products or labels. This can be achieved through physical or spatial separation, or by scheduling labeling and packaging at different times for different devices. Separation is not needed when mix-ups are impossible, such as with labels that only fit specific instruments or devices. Access to labeling should be limited to authorized personnel.

12.9Unused labeling with pre-coded information like serial numbers, manufacturing dates, expiration dates, and control numbers should be destroyed rather than returned to storage, especially when packaging or labeling different sizes of the same product.

12.10 Special attention should be given to the labeling of sterile devices. Devices that are not sterile in their entirety must be labeled to properly inform users what is intended to be "sterile" in the package. In the case of single-use sterile devices, manufacturers must include labeling to advise against resterilization and reuse.

13.0 COMPLAINT AND RECALL

13.1 Complaint

a) The Manufacturers must provide adequate resources and trained personnel to handle complaints.

b) Written procedures (SOPs) must be in place to describe the handling, investigation, and documentation of complaints.

c) Implementation of root cause analysis to identify the underlying issues and prevent recurrence must be incorporated into a written procedure.

d) Effectiveness and monitoring of CAPA must be assured by the manufacturers

e) Manufacturers must ensure that all complaints are logged and reviewed promptly, conduct thorough investigations to determine the cause, maintain detailed records of

the complaint, investigation, and actions taken, and communicate timely with regulatory authorities and stakeholders.

f) Manufacturers must ensure that all decisions and actions related to product quality are thoroughly documented and linked to medical device records. Complaint records should be reviewed regularly to identify and address recurring issues, and regulatory agencies must be promptly informed of any serious quality problems. All relevant records must be maintained for a minimum of one year after the device's expiration date or the date of complaint receipt, whichever is longer.

13.2 **Product recall**

a) Written procedures must be established for initiating and managing recalls.

b) Manufacturers must assess the risk posed by the defective product and determine the extent of the recall.

c) Conducting mock recalls to evaluate the effectiveness of recall procedure**.**

d) Manufacturers must promptly initiate recall procedures upon identifying a quality defect, inform regulatory authorities, healthcare professionals, and customers about the recall, efficiently execute the recall to remove defective products from the market, and monitor the recall process to ensure all affected products are accounted for.

13.0 STORAGE AND DISTIBUTION

13.1 Manufacturers must establish and maintain robust procedures for managing storage areas and stock rooms to prevent product mix-ups, damage, deterioration, contamination, or other adverse effects, ensure timely use or distribution of products, and prevent the use or distribution of obsolete, rejected, or deteriorated products.

13.2 Manufacturers must ensure that the key responsibilities of those authorizing product receipt and dispatch include:

a) Ensuring all incoming and outgoing products have the correct documentation, such as purchase orders, delivery notes, and invoices.

b) Checking the quality and quantity of products received or dispatched to confirm they meet the required standards.

c) Communicating with warehouse staff and other departments to ensure smooth operations and resolve any issues that arise during receipt or dispatch.

d) Keeping accurate records of all transactions to ensure traceability and accountability

13.3 To ensure product quality and safety during storage and transportation of medical devices and related products, manufacturers should adhere to these key requirement

13.2.1 **Storage Conditions**:

a) **Temperature and Humidity Control**: Maintain appropriate temperature and humidity levels as specified for each product. Use calibrated monitoring devices to ensure these conditions are consistently met.
b) **Environmental Monitoring**: Implement alarm systems for temperature and humidity deviations. Regularly calibrate and verify these monitoring devices.
c) **Cleanliness and Hygiene**: Ensure storage areas are clean and free from contaminants. Implement pest control measures and maintain a high standard of hygiene.

13.2.2 Transportation Requirements:

a) **Temperature-Controlled Transport**: Use temperature-controlled vehicles and containers for products sensitive to temperature variations. Ensure these vehicles and containers are qualified and regularly maintained.
b) **Monitoring During Transit**: Continuously monitor temperature and humidity during transportation. Use data loggers and other monitoring devices to ensure conditions remain within specified limits.
c) **Handling Procedures**: Establish and follow standard operating procedures (SOPs) for handling products during loading, unloading, and transportation to prevent damage and contamination.

13.3 Documentation and Record-Keeping:

a) **Comprehensive Records**: Maintain detailed records of storage conditions, transportation logs, and any deviations.

13.4 Manufacturers should establish and maintain comprehensive procedures for controlling and distributing finished devices, ensuring that only devices approved for release are distributed. Reviewing purchase orders to resolve any ambiguities and errors before device release and ensuring that only approved devices are distributed.

13.5 Manufacturers should maintain accurate and complete distribution records, including the name and address of the initial consignee, the identification and quantity of devices shipped, the date shipped, and any control numbers used.

14.0 SELF EVALUATION

14.1 Manufacturers must ensure adherence to key practices for performing internal evaluation and its effectiveness. Regular internal audits must be conducted to assess adherence to standards, identifying any gaps or areas for improvement.

14.2 Manufacturers should conduct internal audits at planned intervals to ensure conformity to quality management system requirements. They must document procedures for planning and conducting audits, recording, and reporting results. The audit program should consider the status and importance of processes and areas to be audited, define criteria, scope, intervals, and methods, ensure objectivity and impartiality, and maintain records of audits and their result

14.3 Manufacturers must develop and document detailed compliance policies and procedures, ensuring these are regularly updated to reflect any changes in regulations.

14.4Manufacturers should implement robust monitoring and auditing systems to continuously evaluate compliance processes.

14.5Manufacturers can engage external auditors to provide an unbiased assessment of their compliance programs, offering insights and recommendations for further improvement.

14.6Manufacturers should appoint a self-inspection team consisting of experts in their respective fields and are familiar with GMP. The members of the team may be appointed from inside or outside the company. Frequency of self-inspection

14.7The frequency at which self-inspections are conducted may depend on company requirements but should preferably be at least once a year. The frequency should be stated in the procedure.

14.8Self-inspection report

a) A report should be made at the completion of a self-inspection.
b) The report should include Self-inspection results; Evaluation and conclusions; and recommended corrective actions.
c) There should be an effective follow-up programme to ensure the implementation of all corrective actions recommended. The company management should evaluate both the self-inspection report and the corrective actions as necessary.

15.0 STABILITY STUDIES

15.1 A manufacturer of a medical device or related product is expected to design and manufacture a product that is safe and performs as intended throughout its life cycle.

15.2 Manufacturers should have effective stability procedures to ensure quality and safety performance of devices through their shelf-life, during the time of use after being opened (for IVDs, including after being installed in the instrument), and during transportation or dispatch (for IVDs, including samples).

15.3 Manufacturers of medical devices should consider the following key practices in developing a stability programme for their devices.

a) Stability Testing Protocols: Ensure that stability testing protocols are in place and comply with regulatory guidelines. These protocols should outline the testing methods, conditions, and intervals.

b) Sample Storage Conditions: Verify that samples are stored under appropriate conditions that mimic the intended storage environment of the product. This includes temperature, humidity, and light exposure.

c) Testing Methods: Confirm that validated testing methods are used to assess the stability of the product. These methods should be scientifically sound and reproducible**.**

d) Documentation and Record Keeping: Ensure that all stability testing activities are thoroughly documented. This includes test results, deviations, and corrective actions.

e) Shelf-Life Determination: Check that the shelf-life of the product is determined based on stability data and is supported by scientific evidence.

f) Change Control Procedures: Verify that any changes to the product, process, or testing methods are evaluated for their impact on stability and are documented through a formal change control process.

g) Periodic Review: Ensure that stability data is periodically reviewed to confirm that the product remains stable throughout its shelf-life

16.0 **TERMS AND DEFINITION**

a) **Complaint** means any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

b) **Component** means any raw material, substance, piece, part, software, firmware, labeling, or assembly which is intended to be included as part of the finished, packaged, and labeled device.

c) **Control number** means any distinctive symbols, such as a distinctive combination of letters or numbers, or both, from which the history of the manufacturing, packaging, labeling, and distribution of a unit, lot, or batch of finished devices can be determined.

d) **Design history file (DHF)** means a compilation of records which describes the design history of a finished device.

e) **Design input** means the physical and performance requirements of a device that are used as a basis for device design.

f) **Design output** means the results of a design effort at each design phase and at the end of the total design effort. The finished design output is the basis for the device master record. The total finished design output consists of the device, its packaging and labeling, and the device master record.

g) **Design review** means a documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements, and to identify problems.

h) **Device history record (DHR**) means a compilation of records containing the production history of a finished device.

i) **Device master record (DMR)** means a compilation of records containing the procedures and specifications for a finished device.
j) **Establish** means define, document (in writing or electronically), and implement.
k) **Finished device** means any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled, or sterilized.
l) **In vitro diagnostic (IVD)** means a medical device, whether used alone or in combination, intended by the manufacturer for the in vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes. This includes reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles.
m) **Lot or batch** means one or more components or finished devices that consist of a single type, model, class, size, composition, or software version that are manufactured under essentially the same conditions and that are intended to have uniform characteristics and quality within specified limits.
n) **Management with executive responsibility** means those senior employees of a manufacturer who have the authority to establish or make changes to the manufacturer's quality policy and quality system.
o) **Manufacturer** means any person who designs, manufactures, fabricates, assembles, or processes a finished device. Manufacturer includes but is not limited to those who perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions.
p) **Manufacturing material** means any material or substance used in or used to facilitate the manufacturing process, a concomitant constituent, or a byproduct constituent produced during the manufacturing process, which is present in or on the finished device as a residue or impurity not by design or intent of the manufacturer.
q) **Medical device** means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material, or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings or animals, for one or more of the specific medical purpose(s) of:
    a. diagnosis, prevention, monitoring, treatment, or alleviation of disease,
    b. diagnosis, monitoring, treatment, alleviation of, or compensation for an injury,
    c. investigation, replacement, modification, or support of the anatomy or of a physiological process, supporting or sustaining life,
    d. control of conception,
    e. disinfection of medical devices,
    f. providing information by means of in vitro examination of specimens derived from the human body;
    g. and does not achieve its primary intended action by pharmacological, immunological, or metabolic means, in or on the human body, but which may be assisted in its intended function by such means

r) **Nonconformity** means the nonfulfillment of a specified requirement.
s) **Product** means components, manufacturing materials, in- process devices, finished devices, and returned devices.
t) **Quality** means the totality of features and characteristics that bear on the ability of a device to satisfy fitness-for-use, including safety and performance.
u) **Quality audit** means a systematic, independent examination of a manufacturer's quality system that is performed at defined intervals and at sufficient frequency to determine whether both quality system activities and the results of such activities comply with quality system procedures, that these procedures are implemented effectively, and that these procedures are suitable to achieve quality system objectives.
v) **Quality policy** means the overall intentions and direction of an organization with respect to quality, as established by management with executive responsibility.
w) **Quality system** means the organizational structure, responsibilities, procedures, processes, and resources for implementing quality management.
x) **Remanufacturer** means any person who processes, conditions, renovates, repackages, restores, or does any other act to a finished device that significantly changes the finished device's performance or safety specifications, or intended use.
y) **Rework** means action taken on a nonconforming product so that it will fulfill the specified DMR requirements before it is released for distribution.
z) **Specification** means any requirement with which a product, process, service, or other activity must conform.
aa) **Validation** means confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.

REFERENCES

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