

**NATIONAL AGENCY FOR FOOD AND DRUG  
ADMINISTRATION AND CONTROL ACT 1993  
(AS AMENDED)**

**CURRENT GOOD MANUFACTURING PRACTICE FOR  
MEDICINAL PRODUCTS REGULATIONS 2009**

***Commencement***

In exercise of the powers conferred on the Governing Council of the National Agency for Food and Drug Administration and Control (NAFDAC) by sections 5 and 29 of NAFDAC Act 1993 (as amended) and all the powers enabling it in that behalf, the Governing Council of NAFDAC with approval of the Honourable Minister of Health makes the following Regulations:

- 1.** These regulations prescribe the minimum current good manufacturing practice requirements for methods to be used in, and the facilities and controls to be used for, the manufacture, processing, packing, or holding of a medicinal product for human or animal use, to ensure that such medicinal product meets the requirements of safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess.
  
- 2.** Except as provided in these regulations, failure to comply with any provision set forth in these regulations in respect of manufacturing, processing, packing, or holding of a medicinal product shall render such medicinal product to be substandard and/or adulterated and such medicinal product, as well as the person who is responsible for the failure to comply, shall be subject to regulatory action.
  
- 3. a.** The provisions of these regulations as they may pertain to medicinal products shall be considered to supplement, not supersede, each other, unless the regulations explicitly provide otherwise. Where the provisions in these of the regulations are not applicable, those specifically applicable to the medicinal product in question shall supersede the more general.

***Scope***

***Prohibition***

***Applicability  
of current  
good  
manufacturing  
practice  
regulations***

b. Where a person engages in only some of the operations in these regulations and not in others, that person shall comply with the regulations applicable to the operations.

4. a. There shall be an adequate organizational structure that clearly defines the responsibility, authority, interrelationships and qualification of all personnel.

***Organization and Personnel***

b. The quality control unit shall be a distinct organizational unit that functions and reports to management independently of all other functional units.

5. a. There shall be a quality control unit that shall have the responsibility and authority to approve or reject all materials and medicinal products, and the authority to review production records to ensure that no errors have occurred or, where errors have occurred, that they have been fully investigated. The quality control unit shall be responsible for approving or rejecting medicinal products manufactured, processed, packed, or held under contract by another company.

***Responsibilities of quality control***

b. The Quality Control unit shall have the responsibility to approve Operating Procedures, Protocols and Plans that may impact product quality.

c. Adequate laboratory facilities for the testing and approval (or rejection) of materials, and medicinal products shall be available to the quality control unit.

d. The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the medicinal product.

e. The responsibilities and procedures applicable to the quality control unit shall be in writing; such standard operating procedures shall be followed.

f. There shall be an Internal Audit system to periodically verify that adequate procedures, systems and requirements to comply with this requirements as well as registered details are in-place and in use.

6. a. Each person engaged in the manufacture, processing, packing, or holding of a medicinal product shall have appropriate education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions.

***Personnel Qualifications***

b. Training shall be in the particular operations that the employee performs and in current good manufacturing practice (including the current good manufacturing practice regulations and standard operating procedures required in these regulations) as they relate to the employee's functions. Training in current good manufacturing practice shall be conducted by qualified individuals on a continuing

basis and with sufficient frequency to ensure that employees remain familiar with CGMP requirements applicable to them.

- c. Each person responsible for supervising the manufacture, processing, packing, or holding of a medicinal product shall have the education, training, and experience, or any combination thereof, to perform assigned functions in such a manner as to provide assurance that the medicinal product has the safety, identity, strength, quality, and purity that it purports or is represented to possess.
- d. There shall be an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of each medicinal product.

- 7. a. Personnel engaged in the manufacture, processing, packing, or holding of a medicinal product shall wear clean clothing appropriate for the duties they perform. Protective apparel, such as head, face, hand, feet and arm coverings, shall be worn as necessary to ensure personnel safety and protect medicinal products from contamination.

***Personnel responsibilities***

- b. Personnel shall practice good sanitation and health habits.
- c. Only personnel authorized by supervisory personnel shall enter those areas of the buildings and facilities designated as limited-access areas.
- d. Any person shown at any time (either by medical examination or supervisory observation) to have an apparent illness or open lesions that may adversely affect the safety or quality of medicinal products shall be excluded from direct contact with materials, and medicinal products until the condition is corrected or determined by competent medical personnel not to jeopardize the safety or quality of medicinal products. All personnel shall be instructed to report to supervisory personnel any health conditions that may have an adverse effect on medicinal products.

- 8. a. Consultants advising on the manufacture, processing, packing, or holding of medicinal products shall have sufficient education, training, and experience, or any combination thereof, to advise on the subject for which they are retained.
- b. Records shall be maintained stating the name, address, and qualifications of any consultants and the type of service they provide.

***Consultants***

***Buildings and Facilities***

- 9. a. Any building(s) used in the manufacture, processing, packing, or holding of a medicinal product shall be adequately located, constructed, and of suitable size to facilitate cleaning, maintenance, and proper operations and safety of operators as appropriate to the type and stage of manufacture.

***Location, design and construction***

- b. The building shall have adequate space for the orderly placement of equipment and materials to prevent mix-ups between different materials, or medicinal products, and to prevent contamination.
- c. The orderly flow of personnel, materials, and medicinal products through the building shall be designed to prevent contamination. People flow of and traffic to and from production areas shall be clearly indicated.
- d. There shall be defined areas of adequate size or other controlled systems to prevent contamination or mix-ups for the following:
  - i. Receipt, identification, sampling, storage, and quarantine of components, medicinal product containers, closures, and labeling, pending the appropriate sampling, testing, or examination by the quality control unit before release for manufacturing or packaging;
  - ii. Holding rejected components, medicinal product containers, closures, and labeling before disposition (example return, reprocessing or destruction);
  - iii. Storage of released components, medicinal product containers, closures, and labeling;
  - iv. Storage of in-process materials;
  - v. Manufacturing and processing operations;
  - vi. Packaging and labeling operations;
  - vii. Quarantine storage before release or rejection of medicinal products;
  - viii. Storage of medicinal products after release;
  - ix. Control and laboratory operations;
  - x. Aseptic processing, which includes as appropriate:
    - 1. Floors, walls, and ceilings of smooth, hard surfaces that can be easily cleaned and disinfected or sterilized routinely;
    - 2. Temperature and humidity controls
    - 3. An air supply filtered through high-efficiency particulate air filters under positive pressure, regardless of whether flow is laminar or non-laminar;
    - 4. A system for monitoring environmental conditions
    - 5. A system for cleaning and disinfecting the room and equipment to produce aseptic conditions;
    - 6. A system for preventive and breakdown maintenance of all equipment used to control and monitor the aseptic conditions.
    - 7. Operations relating to the manufacture, processing, and packing of Beta-Lactams shall be performed in facilities separate from those used for other medicinal products for human use.

- 10.** Adequate lighting shall be provided in all areas and should be appropriate to facilitate cleaning, maintenance, dispensing and other operations that may impact product quality.

*Lighting*

***Heating,  
Ventilation and  
air-conditioning  
(HVAC)***

- 11.** a. Adequate ventilation, air filtration, air heating and cooling, exhaust systems shall be provided where appropriate. These systems shall be designed and constructed to minimize risks of contamination and cross contamination as well as protect the integrity of raw materials, packaging components, intermediates and finished products.
- b. Equipment for adequate control of air pressure, micro-organisms, dust, humidity, and temperature shall be provided when appropriate for the manufacture, processing, packing, or holding of a medicinal product.
- c. Air filtration systems, including pre-filters and particulate matter air filters, shall be used when appropriate on air supplies to production areas.
- d. Where air is re-circulated to production areas, appropriate measures shall be taken to control re-circulation of dust from production. In areas where air contamination occurs during production, there shall be adequate exhaust systems or other systems adequate to control contaminants.
- e. Air-handling systems for the manufacture, processing, and packing of penicillin shall be completely separate from those for other medicinal products for human use.
- f. The manufacture, processing and packing of Beta-lactam shall be in a dedicated building to prevent cross contamination.

- 12.** a. Water used in the manufacture of medicinal products shall be suitable for its intended use.
- b. Unless otherwise justified, process water shall at a minimum meet Nigerian Industrial Standard (NIS) standard for drinking (potable) water quality. Water not meeting such standards shall not be permitted in the potable water system.
- c. Where drinking (potable) water is insufficient to ensure medicinal product quality, stricter chemical and/or microbiological water quality specification are called for, appropriate specification for physical/chemical attributes, total microbial counts, objectionable organisms and endotoxins shall be established.
- d. Where water used in the process is treated by the manufacturer to achieve a defined quality, the treatment process shall be validated and monitored with appropriate action limits.
- e. Potable water shall be supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any medicinal product.
- f. Drains shall be of adequate size and, where connected directly to a sewer, shall be provided with an air break or other mechanical device to prevent back-siphonage.
- g. Open drains shall be avoided; where unavoidable, shall be easily accessible and shallow for easy cleaning and disinfection.
- h. Permanently installed pipework shall be appropriately identified. This can be accomplished by identifying individual lines, documentation, computer control systems, or alternative means. Pipework shall be located to avoid risks of contamination.

***Water supply  
and  
Plumbing***

**13.** a. Sewage, refuse, and other wastes in and from the building and immediate premises shall be disposed of in a safe and sanitary manner.

*Sewage and refuse*

b. Containers and or pipes for waste materials shall be clearly identified

**14.** a. Adequate, clean washing and toilet facilities shall be provided for personnel.

*Washing and toilet facilities*

b. Washing facilities provided shall be equipped with hot and cold water, soap or detergent, air driers or single-service towels, and disinfectants. Clean toilet facilities shall be easily accessible to working areas and shall be adequately separated from production areas.

**15.** a. Any building used in the manufacture, processing, packing or holding of a medicinal product shall be maintained in a clean and sanitary condition. There shall be standard operating procedures assigning responsibility for sanitation and describing in sufficient detail the cleaning schedules, methods, equipment, and materials to be used in cleaning the buildings and facilities; and shall be followed.

*Sanitation*

b. The building shall be free of infestation by rodents, birds, insects, and other vermin.  
c. There shall be standard operating procedures for use of suitable rodenticides, insecticides, fungicides, fumigating agents, and cleaning and sanitizing agents. Such standard operating procedures shall be designed to protect personnel and prevent the contamination of equipment, components, medicinal product containers, closures, packaging, labeling materials, or medicinal products and shall be followed. Rodenticides, insecticides, and fungicides shall not be used unless registered in accordance with the Food and Drug Act and the Pesticide Registration Regulations of the Agency.

**16.** a. Any building used in the manufacture, processing, packing, or holding of a medicinal product shall be maintained in a good state of repair.

*Equipment Maintenance*

b. Repair and maintenance operations shall not present any hazard to the quality of products.

**17.** a. Equipment used in the manufacture, processing, packing, or holding of a medicinal product shall be of appropriate design, adequate size, and suitably located to

*Equipment design, construction, size and location*

facilitate intended operations, its cleaning, sanitization (where appropriate) and maintenance.

- b. Equipment shall be constructed so that surfaces that come in contact with materials, or medicinal products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the medicinal product beyond the official or other established specifications.
- c. Any substances required for operation, such as lubricants, heating fluids or coolants, shall not come into contact with materials, or medicinal products so as to alter the safety, identity, strength, quality, or purity of the medicinal product beyond the official or other established specifications.

**18.** a. Schedules and procedures (including assignments of responsibilities) shall be established for the preventive maintenance of equipment

- b. Equipment and utensils shall be cleaned, maintained, and sanitized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the medicinal product beyond the official or other established specifications.
- c. Standard operating procedures shall be established and followed for cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing, or holding of a medicinal product. These procedures shall include, but are not necessarily limited to, the following:

- i. Assignment of responsibility for cleaning and maintaining equipment;
- ii. Maintenance and cleaning schedules, including, where appropriate, sanitizing schedules;
- iii. A description in sufficient detail of the methods, equipment, and materials used (including dilution of cleaning agents used to clean equipment) in cleaning and maintenance operations,
- iv. Where appropriate, instructions for disassembling and reassembling equipment to ensure proper cleaning and maintenance shall be provided;
- v. Instructions for the removal or obliteration of previous batch identification;
- vi. Instructions for the protection of clean equipment from contamination prior to use;
- vii. Inspection of equipment for cleanliness immediately before use.

d. Proper records shall be kept of maintenance, cleaning, sanitizing, and inspection as prescribed in sections 54 and 55.

*Equipment  
cleaning and  
maintenance*

**19.** a. Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a medicinal product. Where such equipment is so used, it shall be routinely calibrated, inspected, or checked according to a written program designed to ensure proper performance. Written records of those calibration checks and inspections shall be maintained.

*Automatic,  
mechanical, and  
electronic  
equipment*

- b. Appropriate controls shall be exercised over computer or related systems to ensure those changes in master production and control records or other records are instituted only by authorized personnel.
- c. Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system.
- d. A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data.
- e. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to ensure that backup data are exact and complete and that it is secure from alteration, inadvertent erasures, or loss shall be maintained.

**20.** a. Filters for liquid filtration used in the manufacture, processing, or packing of injectable medicinal products intended for human use shall not release fibers into such products.

*Filters*

- b. Fiber-releasing filters may not be used in the manufacture, processing, or packing of these injectable medicinal products unless it is not possible to manufacture such medicinal products without the use of such filters. Where use of a fiber-releasing filter is necessary, an additional non-fiber-releasing filter of 0.22 micron maximum mean porosity (0.45 micron where the manufacturing conditions so dictate) shall subsequently be used to reduce the content of particles in the injectable medicinal product.
- c. Use of an asbestos-containing filter, with or without subsequent use of a specific non-fiber-releasing filter, is permissible only upon submission of proof to the Agency that use of a non-fiber-releasing filter will, or is likely to, compromise the safety or effectiveness of the injectable medicinal product.

## **Material Management**

**21.** a. Standard operating procedures on the sourcing, receipt, identification, storage, handling, sampling, testing, and approval or rejection of materials shall be established and followed.

*General  
requirements*

- b. Materials shall at all times be handled and stored in a manner to prevent degradation and contamination.
- c. Bagged or boxed components of materials shall not be stored on the floor and shall be suitably spaced to permit cleaning and inspection.
- d. Each material shall be assigned and identified with a distinctive code, batch or receipt number. A system shall be in place to identify the status of each batch (quarantine, approved or rejected). Manufacturers of intermediates and/or APIs (Active Pharmaceutical Ingredients) shall have a system for evaluating suppliers of critical materials. Where the supplier of a critical material is not the manufacturer of that material, the name and address of that manufacturer shall be known by the intermediate and/or API manufacturer.
- e. Materials shall be purchased against an agreed specification, from a supplier or suppliers approved by the quality control unit (s).
- f. Changing the source of supply of raw materials shall be treated as prescribed in section 30.

**22.** a. Suppliers of raw materials, excipients, API (Active Pharmaceutical Ingredients), and Packaging components shall be approved following a documented process. The approval process shall clearly define identity, location address and GMP levels of manufacturer.

*Supplier  
certification*

b. The process shall define minimum acceptable conditions for approval. Agents and suppliers in the supply chain shall be identifiable and their activities shall be adequately controlled not to jeopardize the identity, performance or quality of the material.

**23.** a. Upon receipt and before acceptance, each material shall be examined visually for appropriate labeling as to contents, container damage or broken seals, and contamination.

*Receipt and  
storage of  
untested  
materials*

b. Materials shall be held under quarantine until they have been sampled, examined or tested, as appropriate. Storage within the area shall be as prescribed in section 21.

**24.** a. Each batch of materials shall be withheld from use until the batch has been sampled, tested, or examined, as appropriate, and released for use by the quality control unit.

*Testing and  
approval or  
rejection of  
materials*

b. Representative samples of each shipment of each batch shall be collected for testing or examination.

- c. Sampling methods shall specify the number of containers to be sampled, which part of the container to sample, and the amount of material to be taken from each container. The sampling method shall be based on appropriate criteria such as
- i. Statistical criteria (variability, confidence levels, degree of precision desired)
  - ii. Criticality of the material,
  - iii. Past quality history of the supplier,
  - iv. Quantity needed for analysis and retention as prescribed in section 52.
- d. Samples shall be collected in accordance with the following procedures:
- i. The containers of components selected shall be cleaned where necessary, by appropriate means.
  - ii. The containers shall be opened, sampled, and resealed in a manner designed to prevent contamination of their contents and contamination of other materials.
  - iii. Sterile equipment and aseptic sampling techniques shall be used when necessary.
  - iv. Where it is necessary to sample a component from the top, middle, and bottom of its container, such sample subdivisions shall not be composited for testing.
  - v. Sample containers shall be identified so that the following information can be determined:
    1. Name of the material sampled
    2. The batch number
    3. The container from which the sample was taken
    4. The date on which the sample was taken
    5. The name and signature of the person who collected the sample.
  - vi. Sampling shall be conducted at defined locations and by procedures designed to prevent contamination of the material sampled and contamination of other materials.
  - vii. Containers from which samples are withdrawn shall be opened carefully and subsequently re-closed. They shall be marked to indicate that a sample has been taken from them.
- e. Samples shall be examined and tested as follows:
- i. Tests shall be conducted to verify the identity of each material. Specific identity tests, where they exist, shall be used.
  - ii. Each component shall be tested for conformity with all appropriate written specifications for purity, strength, and quality. In lieu of such

testing by the manufacturer, a report of analysis may be accepted from the supplier of a component, provided that at least one specific identity tests are conducted on such component by the manufacturer, and provided that the manufacturer establishes the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.

- iii. Containers and closures shall be tested for conformance with appropriate standard operating procedures. In lieu of such testing by the manufacturer, a certificate of testing may be accepted from the supplier, provided that at least a visual identification is conducted on such containers/closures by the manufacturer and provided that the manufacturer establishes the reliability of the supplier's test results through appropriate validation of the supplier's test results at appropriate intervals.
- iv. When appropriate, components shall be microscopically examined.
- v. Each batch of material that is liable to contamination with filth, insect infestation, or other extraneous adulterant shall be examined against established specifications for such contamination.
- vi. Each batch of material that is liable to microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use.

f. Any batch of material that meets the appropriate written specifications of identity, strength, quality, and purity and related tests as prescribed in section 24(e) may be approved and released for use. Any batch of such material that does not meet such specifications shall be rejected.

- 25.** a. Materials approved for use shall be rotated so that the oldest approved stock is used first.
- b. Deviation from this requirement is only permitted where such deviation is temporary and appropriate.

*Use of  
approved  
materials*

**26.** Materials shall be retested or re-examined, as appropriate, for identity, strength, quality, and purity and approved or rejected by the quality control unit as prescribed in section 24 as necessary, for example, after storage for long periods or after exposure to air, heat or other conditions that might adversely affect the material.

*Retesting of  
approved  
materials*

27. a. Rejected materials shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable.

*Rejected  
Materials*

b. Disposal of rejected materials shall be conducted in accordance with standard operating procedures and environmental regulations.

28. a. Containers and closures shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the medicinal product beyond the official or established requirements.

*Containers and  
closures*

b. Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the medicinal product.

c. Product containers and closures shall be clean and, where indicated by the nature of the medicinal product, sterilized and processed to remove pyrogenic properties to ensure that they are suitable for their intended use.

d. Standards or specifications, methods of testing, and, where indicated, methods of cleaning, sterilizing, and processing to remove pyrogenic properties shall be written and followed for medicinal product containers and closures.

**Standard operating  
procedures**

29. a. There shall be standard operating procedures for production and process control designed to ensure that the medicinal products have the identity, strength, quality, and purity they purport or are represented to possess. These standard operating procedures, including any changes, shall be drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit.

*Production  
and Process  
Controls*

b. Standard operating procedures for production and process control procedures shall be followed in the execution of the various production and process control functions and shall be documented at the time of performance.

30. a. Any deviation from the standard operating procedures shall be reported, properly investigated, recorded and justified.

*Deviations*

- b. There shall be a standard operating procedure for handling deviations such that a system is in place for approving manufacturing changes that may have an impact on product quality.
- c. Deviations shall not be approved without the involvement of the quality control unit.

**31.** a. A formal change control system shall be established to evaluate all changes that may affect the production and control of the medicinal product, intermediate or API (Active Pharmaceutical Ingredients)

*Change control*

- b. Written procedures shall provide for the identification, documentation, appropriate review, and approval of changes in raw materials, specifications, analytical methods, facilities, support systems, equipment (including computer hardware), processing steps, labeling and packaging materials, computer software.
- c. Any proposals for GMP-relevant changes shall be drafted, reviewed, and approved by the appropriate organizational unit and reviewed and approved by the quality unit(s).

**32.** Standard operating production and control procedures shall include the following, which are designed to ensure that the medicinal products produced have the identity, strength, quality, and purity specifications for the intended use they purport or are represented to possess:

*Charge in of components*

- a. The batch shall be formulated with the intent to provide not less than 100 percent of the labeled or established amount of active ingredient.
- b. Components for medicinal product manufacturing shall be weighed, measured, or subdivided as appropriate. Where a component is removed from the original container to another, the new container shall be identified with the following information:
  - i. Component name or item code;
  - ii. Receiving or control number;
  - iii. Weight or measure in new container;
  - iv. Batch for which component was dispensed, including its product name, strength, and lot number.
- c. Weighing, measuring, or subdividing operations for components shall be adequately supervised. Each container of component dispensed to manufacturing shall be examined by a second person to ensure that:

- i. The component was released by the quality control unit;
  - ii. The weight or measure is correct as stated in the batch production records;
  - iii. The containers are properly identified.
- d. Each component shall be added to the batch by one person and verified by a second person.
- e. The identification of personnel performing each step of the process and of the person who checked each of these steps shall be clearly stated.

**33.** Actual yields and percentages of theoretical yield shall be determined at the conclusion of each appropriate phase of manufacturing, processing, packaging, or holding of the medicinal product. Such calculations shall be performed by one person and independently verified by a second person. Deviation from validated yield range shall be treated as prescribed in section 30.

*Calculation of yield*

**34. a.** All compounding and storage containers, processing lines, and major equipment used during the production of a batch of a medicinal product shall be properly identified at all times to indicate the product or material being processed, its strength (where applicable) batch number and, when necessary, the phase of processing of the batch.

*Equipment identification*

b. Major equipment shall be identified by a distinctive identification number or code that shall be recorded in the batch production record to show the specific equipment used in the manufacture of each batch of a medicinal product. In cases where only one of a particular type of equipment exists in a manufacturing facility, the name of the equipment may be used in lieu of a distinctive identification number or code.

**35 a.** To ensure batch uniformity and integrity of medicinal products, standard operating procedures that describe the in-process controls and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch shall be established and followed. Such control procedures shall be established to monitor the output and to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the medicinal product.

*Sampling and testing of in-process materials and medicinal products*

b. Valid in-process specifications shall be consistent with medicinal product final specifications and shall be derived from previous acceptable process average and process variability estimates where possible and determined by the application of suitable statistical procedures where appropriate. Examination and testing of

samples shall ensure that the medicinal product and in-process material conform to specifications.

- c. In-process materials shall be tested for identity, strength, quality, and purity as appropriate, and approved or rejected by the quality control unit, during the production process, for example, at commencement or completion of significant phases or after storage for long periods.
- d. Rejected in-process materials shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable.

- 36.** a. When appropriate, time limits for the completion of each phase of production shall be established to ensure the quality of the medicinal product.
- b. Deviation from established time limits may be acceptable where such deviation does not compromise the quality of the medicinal product. Such deviation shall be justified and documented.

*Time limitations  
on production*

- 37.** a. Standard operating procedures designed to prevent objectionable micro-organisms in medicinal products not required to be sterile, shall be established and followed.
- b. Standard operating procedures designed to prevent microbiological contamination of medicinal products purporting to be sterile, shall be established and followed. Such procedures shall include validation of any sterilization process.

*Control of  
microbiological  
contamination*

- 38.** a. Standard operating procedures prescribing a system for reprocessing batches that do not conform to standards or specifications and the steps to be taken to ensure that the reprocessed batches will conform to all established standards, specifications, and characteristics shall be established and followed.
- b. Reprocessing shall not be performed without the review and approval of the quality control unit.

*Reprocessing*

## **Packaging and Labeling Control**

- 39.**a. Standard operating procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials shall be established and followed.

*Material  
examination and  
usage criteria*

- b. Labeling and packaging materials shall be representatively sampled, and examined or tested upon receipt and before use in packaging or labeling of a medicinal product.
- c. Any labeling or packaging materials meeting appropriate written specifications may be approved and released for use. Any labeling or packaging materials that do not meet such specifications shall be rejected to prevent their use in operations for which they are unsuitable.
- d. Records shall be maintained for each shipment received of each different labeling and packaging material indicating receipt, examination or testing, and whether accepted or rejected.

- 40.**
- a. Containers shall provide adequate protection against deterioration or contamination of the intermediate, API or finished medicinal product that may occur during transportation and recommended storage.
  - b. Containers shall be clean and, where indicated by the nature of the Intermediate, API or finished medicinal product, sanitized to ensure that they are suitable for their intended use.
  - c. These containers shall not be reactive, additive, or absorptive so as to alter the quality of the intermediate, API or finished medicinal product beyond the specified limits.
  - d. Where containers are re-used during production process, they shall be cleaned in accordance with documented procedures and all previous labels shall be removed or defaced.

***Packaging  
Materials***

- 41.**
- a. Labels and other labeling materials for each different medicinal product, strength, dosage form, or quantity of contents shall be stored separately with suitable identification.
  - b. Obsolete and outdated labels, labeling, and other packaging materials shall be destroyed.
  - c. Use of gang printing of labeling for different medicinal products or different strengths or net contents of the same medicinal product, is prohibited unless the labeling from gang-printed sheets is adequately differentiated by size, shape, or color.
  - d. Where cut labeling is used, packaging and labeling operations shall include one of the following special control procedures:
    - i. Dedication of labeling and packaging lines to each different strength of each different medicinal product.
    - ii. Use of appropriate electronic or electromechanical equipment to conduct a 100- percent examination for correct labeling during or after completion of finishing operations; or
    - iii. Use of visual inspection to conduct a 100- percent examination for correct labeling during or after completion of finishing operations for hand- applied labeling. Such examination shall be performed by one person and independently verified by a second person.

***Label Issuance  
and Control***

- e. Printing devices on/or associated with, manufacturing lines used to imprint/overprint labeling upon the medicinal product unit label or case shall be monitored to ensure that all imprinting/overprinting conform to the print specified in the batch production record.
- f. Procedures shall be used to reconcile the quantities of labels issued, used, and returned and to evaluate discrepancies found between the number of containers labelled and the number of labels issued. Such discrepancies shall be investigated, documented and approved by the quality control unit(s).
- g. All excess labeling bearing lot or control numbers shall be destroyed.
- h. Returned labeling shall be maintained and stored in a manner to prevent mix-ups and provide proper identification.

**42.** a. Standard operating procedures designed to ensure that correct labels, labeling, and packaging materials are used for medicinal products shall be established and followed. These procedures shall incorporate the following features:

- i. Designs to prevent mix-ups and cross-contamination by physical or spatial separation from operations involving other medicinal products.
- ii. Identification and handling of filled medicinal product containers that are set aside and held in unlabeled condition for future labeling operations to preclude mislabeling of individual containers, batches, or portions of batches. Identification need not be applied to each individual container but shall be sufficient to determine name, strength, quantity of contents, and batch or control number of each container.
- iii. Identification of the medicinal product with a lot or control number that permits determination of the history of the manufacture and control of the batch.
- iv. Examination of packaging and labeling materials for suitability and correctness before packaging operations, and documentation of such examination in the batch production record.
- v. Inspection of the packaging and labeling facilities immediately before use to ensure that all medicinal products have been removed from previous operations. Inspection shall also be made to ensure that packaging and labeling materials not suitable for subsequent operations have been removed. Results of inspection shall be documented in the batch production records.

b. Holders of product license for medicinal products shall obtain approval from the Agency for changes in packaging and labeling.

*Packaging and  
labeling  
operations*

**43.a.** A medicinal product (except a dermatological, dentifrice, insulin, or throat lozenge product) for sale that is not packaged in a tamper-resistant package or that is not properly labeled as prescribed under this section shall be considered adulterated.

*Tamper-resistant packaging*

- b. The tamper-resistant packaging shall be designed to and shall remain intact when handled in a reasonable manner during manufacture, distribution, and retail display.
- c. There shall be a statement that is prominently placed so that consumers are alerted to the specific tamper-resistant feature of the package
- d. The tamper-resistant labeling shall be so placed that it will be unaffected where the tamper-resistant feature of the package is breached or missing.
- e. To reduce the likelihood of successful tampering and to increase the likelihood that consumers will discover where a product has been tampered with, tamper-resistant packaging shall not be easily duplicated by the use of commonly available materials or through use of commonly available processes.

**44. a.** Packaged and labeled products shall be examined during finishing operations to provide assurance that containers and packages in the batch have the correct label.

*Medicinal product inspection*

- b. A representative sample of units shall be collected at the completion of finishing operations and shall be visually examined for correct labeling.
- c. Results of these examinations shall be recorded in the batch production or control records.

**45. a.** To ensure that a medicinal product meets applicable standards of identity, strength, quality, and purity at the time of use, it shall bear an expiration date determined by appropriate stability testing.

*Expiration dating*

- b. Expiration dates shall be related to any storage conditions stated on the labeling, as determined by stability studies.
- c. Where the medicinal product is to be reconstituted at the time of dispensing, its labeling shall bear expiration information for both the reconstituted and un-reconstituted medicinal products.
- d. Expiration dates shall appear on labeling in accordance with the NAFDAC labelling Regulations for Drug Products.

## **Storage and Distribution**

**46. a.** Standard operating procedures describing the warehousing of medicinal products shall be established and followed. They shall include:

*Warehousing procedures*

- i. Quarantine of medicinal products before release by the quality control unit.

- ii. Storage of medicinal products under appropriate conditions of temperature, humidity, and light so that the identity, strength, quality, and purity of the medicinal products are not affected.

b. Records shall be maintained of special storage conditions where required for some medicinal products.

**47.** Standard Operating Procedures for the distribution of medicinal products shall be established, and followed. They shall include:

*Distribution procedures*

- a. A procedure whereby the oldest approved stock of a medicinal product is distributed first. Deviation from this requirement is only permitted where such deviation is temporary, appropriate and documented.
- b. A system by which the distribution of each lot of medicinal product can be traceable to facilitate its recall where necessary.

## Laboratory Controls

**48.** a. The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this section, including any change in such specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms, shall be drafted by the appropriate organizational unit and reviewed and approved by the quality control unit. The requirements in this section shall be followed and shall be documented at the time of performance. Any deviation from the written specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms shall be recorded and justified.

*General requirements*

b. Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to ensure that materials and medicinal products conform to appropriate standards of identity, strength, quality, and purity. Laboratory controls shall include:

- i. Determination of conformance to appropriate written specifications for the acceptance of each lot within each shipment of materials used in the manufacture, processing, packing, or holding of medicinal products. The specifications shall include a description of the sampling and testing procedures used. Samples shall be representative and adequately identified. Such procedures shall also require appropriate retesting of any material that is subject to deterioration.
- ii. Determination of conformance to written specifications and a description of sampling and testing procedures for in-process materials. Such samples shall be representative and properly identified.

- iii. Determination of conformance to written descriptions of sampling procedures and appropriate specifications for medicinal products. Such samples shall be representative and properly identified.
- iv. Calibration of instruments, apparatus, gauges, and recording devices 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. Instruments, apparatus, gauges, and recording devices not meeting established specifications shall not be used.

- 49.** a. For each batch of medicinal product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the medicinal product, including the identity and strength of each active ingredient, prior to release. Where sterility and/or pyrogen testing are conducted on specific batches of short-lived radiopharmaceuticals, such batches may be released prior to completion of sterility and/or pyrogen testing, provided such testing shall be completed as soon as possible.
- b. There shall be appropriate laboratory testing, as necessary, of each batch of medicinal product required to be free of objectionable microorganisms.
  - c. Standard operating procedures describing sampling and testing plans that shall include the method of sampling and the number of units per batch to be tested, shall be established and followed.
  - d. Acceptance criteria for the sampling and testing conducted by the quality control unit shall be adequate to ensure that batches of medicinal products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release. The statistical quality control criteria shall include appropriate acceptance levels and/or appropriate rejection levels.
  - e. The accuracy, sensitivity, specificity, and reproducibility of test methods employed shall be established and documented. Such validation and documentation may be accomplished as prescribed in section 61 a(ii).
  - f. Medicinal products failing to meet established standards or specifications and any other relevant quality control criteria shall be rejected. Reprocessing may be performed. Prior to acceptance and use, reprocessed material must meet appropriate standards, specifications, and any other relevant criteria.

***Testing and release  
for distribution***

- 50 .** a. There shall be a written testing program designed to continuously assess the stability characteristics of medicinal products. The results of such stability testing shall be used in determining appropriate storage conditions and expiration dates. The written program shall be followed and shall include:
- i. Sample size and test intervals based on statistical criteria for each attribute examined to ensure valid estimates of stability;
  - ii. Storage conditions for samples retained for testing;

***Stability testing***

- iii. Reliable, meaningful, and specific test methods;
- iv. Testing of the medicinal product in the same container-closure system as that in which the medicinal product is marketed;
- v. Testing of medicinal products for reconstitution at the time of dispensing (as directed in the labeling) as well as after they are reconstituted.

**b.** An adequate number of batches of each medicinal product shall be tested to determine an appropriate expiration date and a record of such data shall be maintained.

c. Accelerated studies, combined with basic stability information on the components, medicinal products, and container-closure system, may be used to support tentative expiration dates provided full shelf life studies are not available and are being conducted.

d. Where data from accelerated studies are used to project a tentative expiration date that is beyond a date supported by actual shelf life studies, there must be stability studies conducted, including medicinal product testing at appropriate intervals, until the tentative expiration date is verified or the appropriate expiration date determined.

e. For homeopathic medicinal products, the requirements of this section are as follows:

- i. There shall be a written assessment of stability based at least on testing or examination of the medicinal product for compatibility of the ingredients, and based on marketing experience with the medicinal product to indicate that there is no degradation of the product for the normal or expected period of use.
- ii. Evaluation of stability shall be based on the same container-closure system in which the medicinal product is being marketed.

**51.a.** For each batch of medicinal product purporting to be sterile and/or pyrogen-free, there shall be appropriate laboratory testing to determine conformance to such requirements. The test procedures shall be in writing and shall be followed.

***Special testing requirements***

b. For each batch of ophthalmic ointment, there shall be appropriate testing to determine conformance to specifications regarding the presence of foreign particles and harsh or abrasive substances. The test procedures shall be in writing and shall be followed.

c. For each batch of controlled-release dosage form, there shall be appropriate laboratory testing to determine conformance to the specifications for the rate of release of each active ingredient. The test procedures shall be in writing and shall be followed.

**52.** a. An appropriately identified retention sample that is representative of each lot in each shipment of each active ingredient shall be retained. The retention sample consists of at least twice the quantity necessary for all tests required to determine whether the active ingredient meets its established specifications, except for sterility and pyrogen testing.

b. The retention time for an active ingredient is as follows:

- i. For an active ingredient in a medicinal product other than those described in sections 52 b(ii) of this section, the retention sample shall be retained for 1 year after the expiration date of the last lot of the medicinal product containing the active ingredient.
- ii. For an active ingredient in a radioactive medicinal product, except for non-radioactive reagent kits, the retention sample shall be retained for:
  - a) Three months after the expiration date of the last lot of the medicinal product containing the active ingredient where the expiration dating period of the medicinal product is 30 days or less; or
  - b) Six months after the expiration date of the last lot of the medicinal product containing the active ingredient where the expiration dating period of the medicinal product is more than 30 days.

c. An appropriately identified retention sample that is representative of each lot or batch of medicinal product shall be retained and stored under conditions consistent with product labeling. The retention sample shall be stored in the same immediate container-closure system in which the medicinal product is marketed or in one that has essentially the same characteristics. The retention sample consists of at least twice the quantity necessary to perform all the required tests, except those for sterility and pyrogens.

e.d. Except for those medicinal products described in section 52(c)ii of this section, retention samples from representative sample lots or batches selected by acceptable statistical procedures shall be examined visually at least once a year for evidence of deterioration unless visual examination would affect the integrity of the retention sample.

e. Any evidence of medicinal product deterioration shall be investigated as prescribed in section 60. The results of examination shall be recorded and maintained with other stability data on the medicinal product.

f. Retention samples of compressed medical gases need not be retained.

e.g. The retention time for a medicinal product is as follows:

- i. For a medicinal product other than those described in section 52 (b) (i) of this section, the retention sample shall be retained for 1 year after the expiration date of the medicinal product.
- ii. For a radioactive medicinal product, except for non-radioactive reagent kits, the retention sample shall be retained for:

- a) Three months after the expiration date of the medicinal product where the expiration dating period of the medicinal product is 30 days or less; or
- b) Six months after the expiration date of the medicinal product where the expiration dating period of the medicinal product is more than 30 days.

- 53.** a. Animals used in testing components, in-process materials, or medicinal products for compliance with established specifications shall be maintained and controlled in a manner that ensures their suitability for their intended use.
- b. Laboratory animals shall be identified, and adequate records shall be maintained showing the history of their use.

*Laboratory animals*

- 54.** Where a reasonable possibility exists that a non-beta-lactam medicinal product has been exposed to cross-contamination with beta-lactam the non-beta-lactam medicinal product shall be tested for the presence of beta-lactam. Such medicinal product shall not be marketed where detectable levels are found when tested by methods as prescribed by the Agency.

*Beta-lactam contamination*

## **Records and Reports**

- 55.** a. Records shall provide appropriate history of each batch of product, including its distribution, and all other relevant circumstances pertinent to the quality of the final product.
- b. The records shall be made or completed at the time each action is taken and in such a way that all significant activities concerning the manufacture of medicinal products are traceable. Any production, control, or distribution record that is required to be maintained in compliance with this section and is specifically associated with a batch of a medicinal product shall be retained for at least 1 year after the expiration date of the batch.
- c. Records shall be maintained for all materials for at least 1 year after the expiration date of the medicinal product.
- d. All records required under this section, or copies of such records, shall be readily available for authorized inspection during the retention period at the establishment where the activities described in such records occurred. These records or copies thereof shall be subject to photocopying or other means of reproduction as part of such inspection. Records that can be immediately retrieved from another location

*General requirements*

by computer or other electronic means shall be considered as meeting the requirements of this section.

- e. Records required under this section may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records and the accuracy of the records shall be checked. Where reduction techniques, such as microfilming, are used, suitable reader and photocopying equipment shall be readily available.
- f. Written records required by this section shall be maintained so that data therein can be used for evaluating, at least annually, the quality standards of each medicinal product to determine the need for changes in medicinal product specifications or manufacturing or control procedures. Standard operating procedures shall be established and followed for such evaluations and shall include provisions for:
  - i. Review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch.
  - ii. Review of complaints, recalls, returned or salvaged medicinal products, and investigations conducted under section 60 for each medicinal product.
- g. Procedures shall be established to ensure that the responsible officials of the firm, where they are not personally involved in or immediately aware of such actions, are notified in writing of any investigations conducted under sections 63, 65, or 66 of these regulations, any recalls, reports of inspectional observations issued by the Agency, or any regulatory actions relating to good manufacturing practices brought by the Agency.

- 56.a. Written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and number of each batch processed. In cases where dedicated equipment is employed, the records of cleaning, maintenance, and use shall be part of the batch record.
- b. Persons performing and double-checking the cleaning and maintenance shall date and sign or initial the log indicating that the work was performed. Entries in the log shall be in chronological order.

*Equipment  
cleaning and use  
log*

57. These records shall include the following:

*Materials records*

- a. Identity and quantity of each shipment of each lot of materials, shall include the following:
  - i. Name of the supplier;
  - ii. Supplier's batch number(s) where known;
  - iii. The receiving code as prescribed in section 21 and
  - iv. The date of receipt.

- b. Name and location of the prime manufacturer, where different from the supplier, shall be listed.
- c. Results of any test or examination performed (including those performed as required by section 23 (a), 24 (e), or 39 (a) and the conclusions derived therefrom.
- d. Individual inventory record of each material and record of reconciliation of the use of each lot of such component. The inventory record shall contain sufficient information to allow determination of any batch or lot of medicinal product associated with the use of each component, medicinal product container, and closure.
- e. Documentation of the examination and review of labels and labeling for conformity with established specifications as prescribed in section 39 (d), and 42a (iii)
- f. The disposition of rejected materials.

**58.** a. To ensure uniformity from batch to batch, master production and control records for each medicinal product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person. The preparation of master production and control records shall be described in a standard operating procedure which shall be followed.

*Master production  
and control  
records*

- b. Master production and control records shall include:
  - i. The name and strength of the product and a description of the dosage form;
  - ii. The unit of weight or measure of the medicinal product, and a statement of the total weight or measure of any dosage unit;
  - iii. A complete list of components designated by names or codes sufficiently specific to indicate any special quality characteristic;
  - iv. An accurate statement of the weight or measure of each component, using the same weight system for each component. Reasonable variations may be permitted, however, in the amount of components necessary for the preparation in the dosage form, provided they are justified in the master production and control records;
  - v. A statement concerning any calculated excess of component;
  - vi. A statement of theoretical weight or measure at appropriate phases of processing;
  - vii. A statement of theoretical yield, including the maximum and minimum percentages of theoretical yield beyond which investigation is required in section 60.
  - viii. A description of the medicinal product containers, closures, and packaging materials, including a specimen or copy of each label and all

other labeling signed and dated by the person or persons responsible for approval of such labeling;

- ix. Complete manufacturing and control instructions, sampling and testing procedures, specifications, special notations, and precautions to be followed.

**59.** Batch production and control records shall be prepared for each batch of medicinal product produced and shall include complete information relating to the production and control of each batch. These records shall include:

*Batch production  
and control records*

- a. An accurate reproduction of the appropriate master production or control record, checked for accuracy, dated, and signed;
- b. Documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished, including:
  - i. Date and time;
  - ii. Identity of individual major equipment and lines used;
  - iii. Checks that the equipment and work station are clear of previous products, documents or materials not required for the planned process, and that equipment is clean and suitable for use.
  - iv. Specific identification of each batch of component or in-process material used;
  - v. Weights and measures of components used in the course of processing;
  - vi. In-process and laboratory control results;
  - vii. Inspection of the packaging and labeling area before and after use;
  - viii. A statement of the actual yield and a statement of the percentage of theoretical yield at appropriate phases of processing;
  - ix. Complete labeling control records, including specimens or copies of all labeling used;
    - x. Description of medicinal product containers and closures;
    - xi. Any sampling performed;
    - xii. Identification of the persons performing and directly supervising or checking each significant step in the operation;
    - xiii. Any investigation made as prescribed in section 60.
    - xiv. Results of examinations made as prescribed in section 44.

**60.** a. All medicinal product production and control records, including those for packaging and labeling, shall be reviewed and approved by the quality control unit to determine compliance with all established, approved standard operating procedures before a batch is released or distributed.

*Production  
record review*

- b. Any unexplained discrepancy (including a percentage of theoretical yield exceeding the maximum or minimum percentages established in master production and control records) or the failure of a batch or any of its components to meet any of its specifications shall be thoroughly investigated, whether or not the batch has already been distributed. The investigation shall extend to other batches of the same medicinal product and other medicinal products that may have been associated with the specific failure or discrepancy. A written record of the investigation shall be made and shall include the conclusions and follow-up.

**61.** a. Laboratory records shall include complete data derived from all tests necessary to ensure compliance with established specifications and standards, including examinations and assays, as follows:

*Laboratory records*

- i. A description of the sample received for testing with identification of source (that is, location from where sample was obtained), quantity, batch number or other distinctive code, date sample was taken, and date sample was received for testing.
- ii. A statement of each method used in the testing of the sample. The statement shall indicate the location of data that establish that the methods used in the testing of the sample meet proper standards of accuracy and reliability as applied to the product tested. Where the method employed is in the current edition of a recognized standard reference (e.g. British Pharmacopoeia, United States Pharmacopoeia, International Pharmacopoeia), and the referenced method is not modified, a statement indicating the method and reference will suffice. The suitability of all testing methods used shall be verified under actual conditions of use.
- iii. A statement of the weight or measure of sample used for each test, where appropriate.
- iv. A complete record of all data secured in the course of each test, including all graphs, charts, and spectra from laboratory instrumentation, properly identified to show the specific component, medicinal product container, closure, in-process material, or medicinal product, and batch tested.
- v. A record of all calculations performed in connection with the test, including units of measure, conversion factors, and equivalency factors.
- vi. A statement of the results of tests and how the results compare with established standards of identity, strength, quality, and purity for the component, medicinal product container, closure, in-process material, or medicinal product tested.
- vii. The initials or signature of the person who performs each test and the date(s) the tests were performed.

viii. The initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.

- b. Complete records shall be maintained of any modification of an established method employed in testing. Such records shall include the reason for the modification and data to verify that the modification produced results that are at least as accurate and reliable for the material being tested as the established method.
- c. Complete records shall be maintained of all out-of-specification investigations carried out as prescribed in section 55.
- d. Complete records shall be maintained of any testing and standardization of laboratory reference standards, reagents, and standard solutions.
- e. Complete records shall be maintained of the periodic calibration of laboratory instruments, apparatus, gauges, and recording devices as prescribed in section 48b(iv).
- f. Complete records shall be maintained of all stability testing performed as prescribed in section 50.

**62.** Distribution records shall contain the following:

- a. Name, strength and dosage form of the product
- b. Description of the dosage form,
- c. Name and address of the consignee,
- d. Date and quantity shipped,
- e. Batch or control number of the medicinal product.
- f. Date of Manufacture and Expiration date.

*Distribution records*

**63.** a. Standard operating procedures describing the handling of all written and oral complaints regarding a medicinal product shall be established and followed. Such procedures shall include provisions for review by the quality control unit, of any complaint involving the possible failure of a medicinal product to meet any of its specifications and, for such medicinal products, a determination as to the need for an investigation as prescribed in section 60. Such procedures shall include provisions for review to determine whether the complaint represents a serious and unexpected adverse drug event which shall be reported to the Agency in accordance with the Good Pharmacovigilance Practice (GVP) regulations.

*Complaint files*

- b. Written record of each complaint shall be maintained in a file designated for medicinal product complaints. The file regarding such medicinal product complaints shall be maintained at the establishment where the medicinal product involved was manufactured, processed, or packed, or such file may be

maintained at another facility where the written records in such files are readily available for inspection at that other facility.

- c. Written records involving a medicinal product shall be maintained until at least 1 year after the expiration date of the medicinal product, or 1 year after the date that the complaint was received, whichever is longer.
- d. The written record shall include the following information where known:
  - i. Name, strength and dosage form of the medicinal product,
  - ii. Batch number,
  - iii. NAFDAC registration number,
  - iv. Name and address of complainant,
  - v. Nature of complaint, and
  - vi. Reply to complainant.
  - vii. Date of Manufacture and Expiration date.
- e. Where an investigation is conducted, the written record shall include the findings of the investigation and follow-up. The record or copy of the record of the investigation shall be maintained at the establishment where the investigation occurred as prescribed in section 55.
- f. Where an investigation as prescribed in section 60 is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.

- 64.**
- a. All product recall activities whether voluntarily or directed by the Agency shall be carried out expeditiously and the records kept.
  - b. There shall be a standard operating procedure describing a product recall and shall define the circumstances under which a recall of a medicinal product shall be considered as prescribed by the Agency.
  - c. The recall procedure shall designate:
    - i. Who shall be involved in evaluating the information,
    - ii. How a recall should be initiated,
    - iii. Who shall be informed about the recall, and
    - iv. How the recalled material shall be treated.
  - d. In the event of a voluntarily recall or serious and/ or potentially life-threatening situation, local, national, and/or international authorities shall be informed and their advice sought.
  - e. Appropriate investigation for reason for the recall shall be conducted as prescribed in section 60.
  - f. Where an investigation under section 60 is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.

*Recall records*

## Returned and Salvaged Medicinal Products

- 65.** a. Returned medicinal products shall be identified as such and held. Where the conditions under which returned medicinal products have been held, stored, or shipped before or during their return, or where the condition of the medicinal product, its container, carton, or labeling, as a result of storage or shipping, casts doubt on the safety, identity, strength, quality or purity of the medicinal product, the returned medicinal product shall be destroyed unless examination, testing, or other investigations prove the medicinal product meets appropriate standards of safety, identity, strength, quality, or purity.
- b. A medicinal product may be reprocessed provided the subsequent medicinal product meets appropriate standards, specifications, and characteristics.
- c. Records of returned medicinal products shall be maintained and shall include the name and labeled potency of the medicinal product dosage form, batch number or control number, reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned medicinal product.
- d. Where the reason for a medicinal product being returned implicates associated batches, an appropriate investigation shall be conducted as prescribed in section 60.
- e. Procedures for the holding, testing, and reprocessing of returned medicinal products shall be in writing and shall be followed.

*Returned  
medicinal  
products*

- 66.** a. Medicinal products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, expiry, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace.

*Medicinal  
product  
salvaging*

- b. Whenever there is doubt whether medicinal products have been subjected to such conditions, salvaging operations may be conducted only where there is:
- i. Evidence from laboratory tests and assays (including animal feeding studies where applicable) that the medicinal products meet all applicable standards of identity, strength, quality, and purity and
  - ii. Evidence from inspection of the premises that the medicinal products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident.
- c. Organoleptic examinations shall be acceptable only as supplemental evidence that the medicinal products meet appropriate standards of identity, strength, quality, and purity.
- d. Records including name, batch number, and disposition shall be maintained for medicinal products subject to this section.

- 67.** a. A person who contravenes a provision of these regulations is guilty of an offence and liable on conviction:-
- i. in the case of an individual, to imprisonment for a term not exceeding two years or to a fine not exceeding ₦50,000 or to both imprisonment and fine.
  - ii. In the case of body corporate, to a fine not exceeding N100,000.
- b. Where an offence under these Regulations is committed by a body corporate or firm or other association of individuals:-
- i. every director, manager, secretary or other similar officer of the body corporate; or
  - ii. every partner or officer of the firm; or
  - iii. every trustee of the body concerned; or
  - iv. every person concerned in the management of the affairs of the association; or
  - v. every person who was purporting to act in a capacity referred to in paragraphs (i) to (iv), is severally guilty of that offence and liable to be proceeded against and punished for that offence in the same manner as if he had himself committed the offence unless he proves that the act or omission constituting the offence took place without his knowledge, consent or connivance.

*Penalty*

- 68.** In these regulations, unless the context otherwise requires the following terms shall have the meaning specified:

*Interpretations*

Acceptance/rejection criteria	The product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units).
Act	The NAFDAC Act 1993 as amended
Active ingredient	Any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those

	components that may undergo chemical change in the manufacture of the medicinal product and be present in the medicinal product in a modified form intended to furnish the specified activity or effect.
Active pharmaceutical ingredients (API) (or Medicinal Substances)	Any substance(s) or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, which when used in the production of a drug, becomes an active ingredient of the medicinal product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.
Actual yield	The quantity that is actually produced at any appropriate phase of manufacture, processing, or packing of a particular medicinal product.
Agency	National Agency for Food and Drug Administration and Control
Air-lock	An enclosed space with two or more doors, and which is interposed between two or more rooms, e.g. of differing class of cleanliness, for the purpose of controlling the air-flow between those rooms when either people or goods need to enter or leave them. .
Aseptic area	A zone or zones within a clean area where grade A or B conditions are maintained.
Aseptic process	A method of producing a sterile product in which sterile bulk drug or sterile raw materials are compounded and assembled with sterile packaging components under grade A or B conditions.
Authorized personnel	The person recognised by the Agency as having the necessary basic scientific and technical background and experience; and who is responsible for ensuring critical operations or/and processes are maintained in compliance with the Good Manufacturing Practice (GMP) Regulations.
Batch (or lot)	<p>A batch of a medicinal product that comprises all the units of a drug form which are made from the same initial mass of material and have undergone a single series of manufacturing operations or a single sterilization operation or, in the case of a continuous production process, all the units manufactured in a given period of time during the same cycle of manufacture.</p> <p>A lot can also be a batch, or a specific identified portion of a batch, having uniform character and quality within specified limits.</p>
Bulk product	Any product which has completed all processing stages up to, but not including, final packaging.
Calibration	The set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by a material measure and the corresponding known values of a reference standard.
Component	Any ingredient intended for use in the manufacture of a medicinal product, including those that may not appear in such medicinal

	product.
Computer system	A group of hardware components and associated software, designed and assembled to perform a specific function or group of functions.
Computerised system	A system including the input of data, electronic processing and the output of information to be used either for reporting or automatic control.
Contamination	The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or unto a starting material, intermediate or finished product during production, sampling, packaging or repackaging, storage or transport.
Cross contamination	Contamination of a material or product with another material or product.
Fiber	Any particulate contaminant with a length at least three times greater than its width.
Finished product	A finished dosage form that has undergone all stages of manufacture, including packaging in its final container and labelling.
Gang-printed labeling	Labeling derived from a sheet of material on which more than one item of labeling is printed.
Inactive ingredient	Any component other than an "active ingredient."
In-process material	Any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the medicinal product.
Intermediate product	Partly processed material which must undergo further manufacturing steps before it becomes a bulk product.
Lot number, control number, or batch number	Any distinctive combination of letters, numbers, or symbols, or any combination of them, for identification such that the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of medicinal product or other material can be determined.
Manufacture, processing, packing, or holding of a medicinal product	Includes packaging and labeling operations, testing, and quality control of medicinal products.
Manufacturer	A company that carries out operations such as production, packaging, repackaging, labelling and re-labelling of pharmaceuticals.
Marketing authorization (product license, registration certificate)	A legal document issued by the Agency that establishes the detailed composition and formulation of the product and the pharmacopoeial or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, labelling and shelf-life.
Master formula	A document or set of documents specifying the starting materials with their quantities and the packaging materials, together with a

	description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process.
Master record	A document or set of documents that serve as a basis for the batch documentation (blank batch record).
Materials	A general term used to denote components, raw materials (starting materials, reagents, solvents), process aids, intermediates, APIs (Active Pharmaceutical Ingredients), product containers, closures, packaging and labelling materials and in-process materials.
Medicinal product	Any substance or combination of substances which may be administered to human beings or animals with a view to preventing diseases, making a medical diagnosis or restoring, correcting or modifying physiological functions in human beings or in animals.
Non-fiber-releasing filter	Any filter, which after any appropriate pretreatment such as washing or flushing, will not release fibers into the component or medicinal product that is being filtered. All filters composed of asbestos are deemed to be fiber-releasing filters.
Packaging	All operations, including filling and labelling, which a bulk product has to undergo in order to become a finished product.  Note: Filling of a sterile product under aseptic conditions or a product intended to be terminally sterilized, would not normally be regarded as part of packaging
Packaging material	Any material employed in the packaging of a medicinal product, excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.
Percentage of theoretical yield	The ratio of the actual yield (at any appropriate phase of manufacture, processing, or packing of a particular medicinal product) to the theoretical yield (at the same phase), stated as a percentage.
Production	All operations involved in the preparation of a medicinal product, from receipt of materials, through processing and packaging, to its completion as a finished product.
Qualification	Action of proving that any premises, systems and items of equipment work correctly and actually leads to the expected results.  The word <i>validation</i> is sometimes widened to incorporate the concept of qualification.
Quality assurance (QA)	The sum total of the organised arrangements made with the object of ensuring that all medicinal products are of the quality required for their use and that quality systems are maintained.
Quality control (QC)	The part of GMP that is concerned with sampling, specifications, testing, documentation, and release procedures which ensures that materials are not released for use, and that medicinal products are

	not released for sale or supply, until their quality has been deemed satisfactory.
Quality control unit	An organizational unit independent of production designated by the firm to be responsible for the duties relating to both quality control and quality assurance functions. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.
Quality unit(s)	An organizational unit independent of production which fulfils both Quality Assurance and Quality Control responsibilities. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.
Quarantine	The status of starting or packaging materials, intermediate, bulk or finished products isolated physically or by other effective means whilst awaiting a decision on their release or refusal.
Recovery	The introduction of all or part of previous batches of the required quality into another batch at a defined stage of manufacture.
Regulatory action	Includes but not limited to product hold, recall, forfeiture, or destruction, sealing of manufacturing line or facility, withdrawal of GMP certificate or product license/registration certificate, prosecution.
Representative sample	A sample that consists of a number of units that are drawn based on rational criteria such as random sampling and intended to ensure that the sample accurately portrays the material being sampled.
Reprocessing	The reworking of all or part of a batch of product of an unacceptable quality from a defined stage of production so that its quality may be rendered acceptable by one or more additional operations.
Retention or Reserve sample	Retained sample of each batch of starting materials and finished medicinal product and that is representative of the batch.
Signed (signature)	The record of the individual who performed a particular action or review. This record can be initials, full handwritten signature, personal seal, or authenticated and secure electronic signature.
Specifications	A list of detailed requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation.
Standard operating procedures (SOP)	An authorized written procedure giving instructions for performing operations not necessarily specific to a given product or material (example equipment operation, maintenance and cleaning; validation; cleaning of premises and environmental control; sampling and inspection). Certain SOPs may be used to supplement product-specific master and batch production documentation.
Starting material	Any substance used in the production of a medicinal product excluding packaging materials.

Strength	<ol style="list-style-type: none"> <li>1. The concentration of the drug substance (for example, weight/weight, weight/volume, or unit dose/volume basis), and/or</li> <li>2. The potency, that is, the therapeutic activity of the medicinal product as indicated by appropriate laboratory tests or by adequately developed and controlled clinical data (expressed, for example, in terms of units by reference to a standard).</li> </ol>
System	A regulated pattern of interacting activities and techniques which are united to form an organised whole.
Tamper-resistant package	<p>A package having one or more indicators or barriers to entry which, where breached or missing, can reasonably be expected to provide visible evidence to consumers that tampering has occurred.</p> <p>A tamper-resistant package may involve an immediate-container and closure system or secondary- container or carton system or any combination of systems intended to provide a visual indication of package integrity.</p>
Theoretical yield	The quantity that would be produced at any appropriate phase of manufacture, processing, or packing of a particular medicinal product, based upon the quantity of components to be used, in the absence of any loss or error in actual production.
Validation	A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting pre-determined criteria.

69. These Regulations may be cited as Current Good Manufacturing Practice for Medicinal Products Regulations 2009.

*Citation*

MADE AT ABUJA THIS.....DAY OF.....2009

Chairman  
Governing Council  
National Agency for Food and  
Drug Administration and Control  
(NAFDAC).

Director-General,  
National Agency for Food  
and Drug Administration and  
Control (NAFDAC)