COLLEGIATE BOARD

RESOLUTION - RDC No.**16 OF MARCH 28, 2013**

Approves the Technical Regulation for Good Manufacturing Practices of Medical Devices and In Vitro Diagnostic Devices and gives other provisions.

The Collegiate Board of the National Health Surveillance Agency, in the exercise of the attributions granted by item IV of Article 11 of the Regulation approved by Decree No. 3029 of April 16, 1999, and in view of the provisions of item II and 1st and 3rd Paragraph of Article 54 of the Internal Rules approved pursuant to Annex I of the ANVISA Ordinance No. 354, of August 11, 2006, republished in the Federal Official Gazette of August 21, 2006, in a meeting held on March 7, 2013,

Whereas the Law No. 6360 of September 23, 1976 and its regulations, the Decree No. 79094 of January 5, 1977;

Whereas the need to internalize the Resolution MERCOSUL / GMC / RES. No. 20/11, which approved the " MERCOSUL Technical Regulation of Good Manufacturing Practices of Medical Devices and In Vitro Diagnostic Devices (revocation of Resolution GMC No. 04/95, 38/96, 65/96 and 131/96)";

Whereas the regulation of Good Manufacturing Practices of Medical Devices and In Vitro Diagnostic Devices shall seek quality assurance, safety and efficacy of the products marketed in Brazil;

Whereas it is fundamental to promote the improvement of national systems aimed to regulate and control Medical Devices and In Vitro Diagnostic Devices;

Adopts the following Collegiate Board Resolution and I, the President-Director, determine its publication:

Article 1 - To approve the "Technical Regulation of Good Manufacturing Practices of Medical Devices and In Vitro Diagnostic Devices", which is included as Annex and is part of this Resolution.

Sole paragraph. This regulation incorporates to the national legal system the Resolution GMC MERCOSUL No. 20/2011 "MERCOSUL Technical Regulation on Good Manufacturing Practices of Medical Devices and In Vitro Diagnostic Devices (revocation of Resolution GMC Nos. 04/95, 38/96, 65/96 and 131/96)".

Article 2 - Revokes the Ordinance No. 686 of August 27, 1998; Resolution RDC No. 59 of June 27, 2000; and Resolution RDC No. 167 of July 2, 2004.

Article 3 - Distributors and storage agents of Medical Devices and In Vitro Diagnostic Devices shall meet the requirements of this Resolution, as applicable.

Article 4 - It is granted 180 days period from the date of incorporation of the normative instrument, in order to adopt necessary measures for the application of the Technical Regulation.

Article 5 - This Resolution enters into force on the date of its publication.

DIRCEU BRÁS APARECIDO BARBANO

ANNEX

TECHNICAL REGULATION OF GOOD MANUFACTURING PRACTICES OF MEDICAL DEVICES AND IN VITRO DIAGNOSTIC DEVICES

CONTENT

CHAPTER 1 - GENERAL PROVISIONS

1.1 - Applicability

1.1.1. This Technical Regulation establishes requirements applicable to the manufacture of Medical Devices and In Vitro Diagnostic Devices. These requirements describe the Good Manufacturing Practices (GMP) for methods and controls used in the design, purchasing, manufacturing, packaging, labeling, storage, distribution, installation, and servicing of Medical Devices and In Vitro Diagnostic Devices. The requirements of this Technical Regulation are intended to ensure that Medical Devices and In Vitro Diagnostic Devices are safe and effective.

1.1.1.2. The requirements of this Technical Regulation are applicable to manufacturers and importers of Medical Devices and In Vitro Diagnostic Devices that are marketed in Brazil.

1.1.1.3. Whenever the manufacturer understands that some of the requirements of this resolution are not applicable to its processes, it shall document the justification for such understanding.

1.1.1.4. Importers of Medical Devices and In Vitro Diagnostic Devices shall meet the requirements of this Resolution, as applicable.

1.1.2. Definitions

For the purposes of this Technical Regulation, it is understood by:

1.2.1. Servicing: Maintenance or repair of a finished product in order to return it to its specifications.

1.2.2. Quality audit: means an established, systematic, and independent examination of the manufacturer quality system, that runs at regular intervals and with sufficient frequency to ensure that both the activities of the quality system and its results meet the procedures specified in its quality system, that these procedures are efficiently implemented and that are suitable for achieving the goals of the quality system. The quality audit is different from other activities of the quality system required by this Technical Regulation.

1.2.3. Component: raw material, substance, piece, part, software, hardware, package, label or instructions for use used during the manufacture of a medical device and in vitro diagnostic device, intended to be included as part of the finished product.

1.2.4. Design input: descriptions of physical attributes, indication of use, performance, compatibility, safety, efficacy, ergonomics, usability, information from previous designs and results of risk management, among other requirements of a medical device or in vitro diagnostic device that are used as the basis for the design.

1.2.5. Design output: result of the work in each phase of the design and its final result. The finished design output is the basis for the device master record (DMR)..

1.2.6. Damage: physical lesion or injury to the health of a person, or injury to property or environment.

1.2.7. Specifications: requirements to which products, components, production activities, servicing, services, quality system or any other activity shall conform.

1.2.8. Establish: define, document (by written or electronic means) and implement.

1.2.9. Manufacturer: any person who designs, manufacture, assemble or process a finished product, including those who perform functions by contract for sterilizing, labeling, packaging.

1.2.10. Executive Management: high management of the company, responsible for providing resources, with authority to establish or amend the policy and the quality system of the company.

1.2.11. Risk Management: systematic application of policies, procedures and practices of managing analysis, assessments, controls, and monitoring of risks associated with a particular finished product or process.

1.2.12. Lot or batch: quantity of a product produced in a manufacturing or sterilization cycle, whose fundamental feature is the homogeneity.

1.2.13. Manufacture material: material or substance employed in the process of manufacture or to facilitate this process, including cleaning agents, mold detach agents, lubricating oils, sterilizing agents, or other byproducts of the manufacturing process.

1.2.14. Non-conformity: failure to comply with a previously specified requirement.

1.2.15. Serial number or batch: combination of different letters or numbers, or both, from which can be determined the full history of purchasing, manufacturing, packaging, labeling and distribution of finished products.

1.2.16. Hazard: Potential source of harm.

1.2.17. Quality policy: all intentions and guidelines of an organization, with respect to quality, expressed by the executive management.

1.2.18. Special process: any process whose outcome cannot be fully verified by inspections and subsequent tests.

1.2.19. Production: all operations involved in the manufacture of a particular product, from receipt of components, through processing and packaging, up to obtaining the finished product.

1.2.20. Finished product: any product or accessory suitable for use, packaged, labeled.

1.2.21. Quality: all aspects and characteristics enabling a medical device or in vitro diagnostic device to meet the requirements of use suitability, including safety and performance.

1.2.22. Complaints: written, oral or electronic communication regarding the non-acceptance of identity, quality, durability, reliability, safety, effectiveness or performance of a product.

1.2.23. Record: physical or electronic document, which evidence data, facts, specific events and results achieved in relation to compliance of procedures and standards of the quality system.

1.2.24. Device history record: compilation of records containing the full production history of a finished product.

1.2.25. Design history file: compilation of documents containing the full design history of a finished product.

1.2.26. Device master record (DMR): compilation of documents containing specifications, instructions and procedures for obtaining a finished product, as well as installation, servicing and maintenance of the same.

1.2.27. Rework: partial or total manufacturing operation intended to correct a non-conformity of a component, intermediate product or finished product, so that it meets the specifications defined in the DMR

1.2.28. Design Review: documented, systematic and complete examination performed during the design development to assess the suitability to the planning and the objectives established.

1.2.29. Risk: combination between probability of occurrence and severity of damage.

1.2.30. Quality system: organizational structure, responsibilities, procedures, specifications, processes and resources needed for quality management.

1.2.31. Validation: confirmation by analysis and objective evidence that the requirements defined for a particular purpose consistently lead to the expected result. With respect to a design, it means to establish and document objective evidences that the product specifications meet the needs of the user and the intended use. With respect to a process, it means to establish and document objective evidence that the process will consistently produce a result that meets the predefined specifications.

1.2.32. Verifications: confirmation by analysis and submittal of objective evidences that the specified requirements have been met. The verification includes the process of examining the results of an activity to determine the compliance to the specifications established.

1.2.33. Shelf life: period of time estimated by the manufacturer during which the product correctly meets the functions to which it was designed.

CHAPTER 2 - GENERAL QUALITY SYSTEM REQUIREMENTS

2.1. General Provisions

2.1.1. Each manufacturer shall establish and maintain a quality system to ensure that the requirements of this Technical Regulation are met and that the products produced are safe, effective and appropriate for the intended use. As part of the activities in the quality system, each manufacturer shall:

2.1.1.1. Establish and maintain effective procedures and instructions of the quality system according to the requirements of this Technical Regulation, and

2.1.1.2. Establish procedures for meeting the established legal provisions in the current health surveillance legislation.

2.2. Management responsibility

2.2.1. Quality Policy. The executive management of each manufacturer shall establish its quality policy and objectives, which shall be measurable and coherent with the established policy. The executive management shall keep the policy at all levels of the organization. The executive management shall ensure that this policy is described in a quality manual and understood by all the employees that may affect or influence the product quality.

2.2.2. Organization. Each manufacturer shall establish and maintain an appropriate organizational structure, represented by organization chart, with sufficient personnel to ensure that the products are manufactured in accordance with the requirements of this Technical Regulation.

2.2.3. Responsibility and Authority. Each manufacturer shall establish at each chapter of this Technical Regulation, the responsibility, authority, and interrelationships of all personnel involved with managing, performing, and checking the work related to quality, with the necessary independence to perform their responsibilities.

2.2.4. Resources and personnel for verification activities. Each manufacturer shall establish functions for verification activities and provide appropriate resources and designates trained personnel to perform the activities of verification.

2.2.5. Management Representative. The executive management of each manufacturer shall designate an individual and document this designation, which, regardless of other functions, will have authority and responsibility to:

2.2.5.1. Ensure that quality system requirements are established and maintained in accordance with this Technical Regulation;

2.2.5.2. Report the performance of the quality system to the executive management for review and provide information on improvements of the quality system.

2.2.6. Management review. The executive management of each manufacturer shall evaluate the suitability and effectiveness of the quality system at defined intervals and sufficient frequency to ensure that the quality system meets the requirements of this Technical Regulation and complies with the objectives of quality policy established. The management review shall be conducted according to established review procedures and the results of each quality system review shall be documented. Audit results, post-market information, process performance and product conformity, status of corrective and preventive actions, changes that may affect the quality system or product conformity, regulatory requirements, and other data shall be considered as inputs for management reviews.

2.3. Personnel

2.3.1. General instructions. Each manufacturer shall have sufficient personnel with instruction, expertise, training and practice compatible with the attributes of the function, in order to insure that all the activities provided for in this Technical Regulation are properly performed. It shall be documented authority, responsibility and requirements necessary for the various functions of the company..

2.3.2. Training. Each manufacturer shall ensure that all personnel are adequately trained to perform the tasks assigned to them. Training shall be conducted in accordance with procedures established by qualified persons to ensure that employees have a proper understanding on their regular functions and on the requirements of these Technical Regulations applicable to their functions. As part of their training, all employees shall be warned of defects in products that may occur as a result of improper performance of their specific functions. The employee training shall be documented.

2.3.3. Consultants. Each manufacturer shall ensure that any consultant guiding employees on methods or controls used for designing, purchasing, manufacturing, packaging, labeling, storage, installation or servicing of products have sufficient qualifications (instructions, training and expertise) to advise on matters for which he was hired. The hiring of consultants will be conducted in accordance with the requirements of purchase control provided for in this Technical Regulation.

2.4. Risk Management

2.4.1. Each manufacturer shall establish and maintain an ongoing process of risk management which involves the entire product lifecycle, from the conception to decommission, to identify the hazards associated to a medical device

or in vitro diagnostic device, to estimate and evaluate the risks involved, to control the risks and evaluate the effectiveness of established controls. This program shall include the following elements: analysis, assessment, control and risk monitoring.

2.4.2. The executive management shall designate responsible personnel, establish the policy to determine the risk acceptability criteria, and determine a periodic review of risk management activities to ensure its adequacy and effectiveness.

2.5. Purchasing Controls

2.5.1. Each manufacturer shall establish and maintain procedures to ensure that the components, manufacturing materials, and finished products manufactured, processed, labeled, and packaged by third parties or stored by them under contract, comply with the specifications. Each manufacturer shall also ensure that the services performed by third parties comply with the established specifications.

2.5.2. Assessment of suppliers of products and services. Each manufacturer shall establish and maintain, according to the impact on the quality of the final product, criteria for assessing suppliers, specifying the requirements, including quality requirements, which they shall meet.

2.5.3. Each manufacturer shall evaluate and select potential suppliers according to their ability to meet established requirements, keeping records of approved suppliers. Assessment records shall be kept, as well as their results.

2.5.4. Purchase records. Each manufacturer shall maintain records of purchase orders that clearly describe or make reference to specifications, including quality requirements for components, manufacturing materials, finished products or services requested or contracted. The approval of orders, including the date and manual or electronic signature of the responsible, shall be documented.

2.5.5. An agreement shall be documented in which the suppliers undertake to notify the manufacturer about any change in the product or service, so that the manufacturer can determine if the change affects the quality of the finished product.

2.5.6. Each manufacturer shall review and approve the purchase documents before their release.

CHAPTER 3 - QUALITY DOCUMENTS AND RECORDS

3.1. General requirements.

3.1.1. Each manufacturer shall establish and maintain procedures for document control to ensure that all documents required in this Technical Regulation are correct and appropriate for the intended use, and are understood by all employees who may affect or influence the quality of a product.

3.1.2. Approval and issuance of documents. Each manufacturer shall designate persons to evaluate and approve all documents established in this Technical Regulation for adequacy before its issuance. The approval, including date and manual or electronic signature of the responsible for approving the documents shall be documented.

3.1.3. Distribution of documents. The manufacturer shall insure that all documents are updated and available at the sites of use and that all unnecessary or obsolete documents are removed from use, or protected from unintentional use.

3.1.4. Changes to documents. Changes to specifications, methods or procedures related to the quality system shall be evaluated, documented, reviewed, and approved by persons whose function and level of responsibility are equivalent to those who performed the original revision and approval.

3.1.5. Records of changes to documents. Each manufacturer shall maintain records of changes to documents, including a description of the change, identification of the changed documents and the affected documents, identification of the responsible person, date of approval and date on which the change shall enter into force. A list of valid documents shall be maintained in order to identify their current status and ensure that only updated and approved documents are in use.

3.1.6. Documents and Records Archive. All quality documents and records shall be legible and be stored so as to minimize damage, prevent losses, and promote quick recovery. All documents and records electronically filed shall have backups.

3.1.6.1. Confidentiality. The documents and records considered as confidential by the manufacturer may be marked to alert the competent health authority;

3.1.6.2. Period of retention of documents and records: all the required documents and records related to a product shall be maintained for a period of time equivalent to the shelf life of the product, but in no case less than two years from the date of its distribution.

3.2. Device history record.

3.2.1. Each manufacturer shall maintain device history records. Each manufacturer shall establish and maintain procedures to ensure that the device history records are kept for each batch or series to demonstrate the products were manufactured according to the device master record and the requirements of this Technical Regulation. The device history record shall contain or make reference to the following information:

3.2.1.1. Manufacture Date;

3.2.1.2. Components used;

3.2.1.3. Quantity manufactured;

3.2.1.4. Results of tests and inspections;

3.2.1.5. Special processes parameters;

3.2.1.6. Quantity released for distribution;

3.2.1.7. Labeling;

3.2.1.8. Identification of serial number or batch of the device; and

3.2.1.9. final release of the device.

3.3. Inspections and tests records.

3.3.1. Each manufacturer shall maintain records of results of established tests and inspections, when directly related to critical quality attributes of the product. These records shall include acceptance criteria, results, equipment / instrument used, and date and manual or electronic signature of the responsible.

CHAPTER 4 - DESING CONTROL AND DEVICE MASTER RECORD (DMR)

4.1. Design Control

4.1.1. General Instructions. Each manufacturer shall establish and maintain procedures to control product design to ensure that the specified requirements for the design are met.

4.1.2. Design planning and development. Each manufacturer shall establish and maintain plans that describe or make reference to design and development activities and the responsible for each activity. The plans shall describe or make reference to design development activities, including any interaction between different organizational and technical groups that may have some interface with the design. The plans shall be evaluated, updated, and approved as the design development progresses.

4.1.3. Design input. Each manufacturer shall establish and maintain procedures to ensure that the requirements relating to a product are appropriate and meet its intended use, including the needs of the user and patient and applicable legal and regulatory requirements. Procedures shall include a mechanism by which incomplete, ambiguous or conflicting requirements are identified and handled. The design input shall be documented, evaluated and approved by a designated qualified person. The approval of requirements, including the date and manual or electronic signature of the responsible for the approval, shall be documented.

4.1.4. Design verification. Each manufacturer shall establish and maintain procedures for product design verification . The design verification shall be performed by designated personnel and shall ensure that the design output meets the input. The results of design verification, including the identification of the design verified, verification methods, date and name of the person responsible for the verification, shall be documented in the design history file.

4.1.5. Design output. Each manufacturer shall establish and document the design output in order to allow the assessment of design's compliance to the requirements established as input. The design output shall meet the requirements of the input, and shall include the acceptance criteria and identify the design features that are fundamental to the intended use of the product. These shall be documented, reviewed and approved prior to release.

4.1.6. Design Review. Each manufacturer shall establish and maintain procedures to ensure that the assessments of design results are planned, conducted and documented in the various stages of design development. The procedures shall ensure that representatives from all functions directly related to the design stage being reviewed, as well as the individuals from related areas and experts needed, are involved. The results of design review shall be documented in the device history record.

4.1.7. Design Transfer. Each manufacturer shall establish and maintain procedures to ensure that the product design is correctly translated into production specifications.

4.1.8. Design validation. Each manufacturer shall establish and maintain procedure to validate the product design. The design validation shall be performed under pre-determined operation conditions, in the initial production of a batch or unit. The design validation shall ensure that the product meets the needs of the user and indication of use, and shall include tests of the products under real or simulated conditions of use. The design validation shall include software validation when appropriate. The results of design validation, including its identification, methods, data and manual or

electronic signature of the responsible shall be documented in the design history file. Stability studies shall be conducted whenever applicable.

4.1.9. Design release. Each manufacturer shall ensure the design will not be released for production until its approval by the persons assigned by the manufacturer. The persons assigned shall review all records required to the design history file in order to ensure it is complete and the final design is compatible with the approved plans, prior to its release. This release, including date and manual or electronic signature of the responsible shall be documented.

4.1.10. Design changes. Each manufacturer shall establish and maintain procedures to identify, document, validate, review and approve design changes before its implementation, including an assessment of the risks within the risk management process.

4.1.11. Design history file. Each manufacturer shall establish and maintain a design history file for each product. The design history file shall contain or make reference to all records necessary to demonstrate that the design was developed in accordance to the approved design plan and the requirements of this Technical Regulation.

4.2. Device master record (DMR)

4.2.1. Each manufacturer shall maintain device master records (DMR's). The DMR for each type of product shall include or make reference to the following information:

4.2.1.1. Product specifications, including the corresponding drawings, composition, formula, components specifications, and software design specifications, and its source codes;

4.2.1.2. Production process specifications, including infrastructure specifications, equipment, production methods and instructions, and environmental specifications of production;

4.2.1.3. Packaging and labeling specifications, including methods and processes used;

4.2.1.4. Procedures for inspecting and testing with the respective acceptance criteria; and

4.2.1.5. Methods and procedures for installation, maintenance, and servicing.

CHAPTER 5 - PROCESS AND PRODUCTION CONTROLS

5.1. General Instructions

5.1.1. Each manufacturer shall design, conduct, control and monitor all production processes in order to ensure that the product comply with the specifications. Where any deviation in the product specifications may occur as a result of the manufacturing process, the manufacturer shall establish and maintain procedures of process control, which describe any process controls necessary to ensure compliance to the specification. The process controls shall include:

5.1.1.1. Documented instructions, standard operating procedures, and methods defining and controlling the method of production, installation and maintenance;

5.1.1.2. Monitoring and control of process parameters;

5.1.1.3. Compliance to technical rules, standards or reference codes; and

5.1.1.4. Instructions for releasing the beginning of the process;

5.1.2. The company facilities shall be properly designed to provide the performance of all operations, to prevent exchanges or contamination of components, manufacturing materials, intermediate products, and finished products, and ensure the proper handling thereof, including proper flow of people.

5.1.3. Environmental Control. Each manufacturer shall provide appropriate environmental conditions to production operations in order to prevent contamination or other adverse effects on the product. The correct functioning of established environmental control systems shall be monitored, keeping the corresponding records.

5.1.3.1. Clean and sanitization. Each manufacturer shall establish and maintain appropriate cleaning and sanitization procedures, as well as a program that meet the requirements of manufacturing process specifications. Each manufacturer shall insure that the employees involved understand these procedures.

5.1.3.2. Personal health and hygiene. Each manufacturer shall ensure that the employees and or others who are in contact with the product or with the environment are clean, healthy, and appropriately dressed for the activity to be performed. Any person who, by medical examination or observation of supervisors, seems to be in a health condition that may affect the product, shall be removed from the operations. Each manufacturer shall instruct the personnel to report such conditions to the supervisors.

5.1.3.3. Personnel habits. Each manufacturer shall limit the consumption of foods and beverages to specific locations in order not to affect the production areas.

5.1.3.4. Contamination control. Each manufacturer shall establish and maintain procedures to prevent the contamination of equipment, components, manufacturing materials, intermediates and finished products by cleaning and disinfection materials, including hazardous substances or contaminants generated by the production process. A pest control program shall be established, and whenever chemical agents are used, the company shall ensure they do not affect the product quality.

5.1.3.5. Removal of garbage and chemical waste. The treatment and destination of garbage, chemical wastes and by-products shall occur in accordance with the applicable legislation in force.

5.1.3.6. Biological safety standards shall be observed in the cases where there is biological risk.

5.1.4. Worker health. Each manufacturer shall ensure the compliance to applicable standards related to the health of workers, including the use of personal protective equipment, which is compatible with the labor processes performed.

5.1.5. Equipment. Each manufacturer shall ensure that all equipment used in the manufacturing process are appropriate for the intended use and properly designed, constructed, and installed to facilitate the maintenance, adjustments, cleaning and use.

5.1.5.1. Maintenance program. Each manufacturer shall establish and maintain a program for maintenance, adjustments, and, when appropriate, cleaning of equipment to ensure that all manufacturing specifications are being achieved. The maintenance program shall be in a place of easy access to the personnel responsible for the maintenance and use of the equipment. A record of the maintenance activities shall be performed, with date of performance and identification of the persons in charge.

5.1.5.2. Adjustments. Each manufacturer shall ensure that any acceptable tolerances or inherent limitations are attached in a visible place or near the equipment requiring periodic adjustment, or are easily available to the personnel in charge of these adjustments.

5.1.5.3. Manufacturing materials. Each manufacturer shall establish and maintain procedures for use and removal of manufacturing materials, to ensure that such materials are removed from the product or limited to a specified amount that does not adversely affect the product quality.

5.1.6. Special processes shall be conducted in accordance with established procedures and parameters in order to assure the compliance to the specifications. The critical parameters shall be monitored and recorded in the device history record.

5.2. Controls of packaging, labeling and instructions for use.

5.2.1. Product packaging. Each manufacturer shall establish procedures for product packaging in order to protect the product from any change, damage or contamination during the processing, storage, handling, and distribution processes.

5.2.2. Product labeling.

5.2.2.1. Each manufacturer shall establish and maintain procedures to ensure the integrity and prevent accidental mixing of labels, instructions for use, packaging materials or identification tags.

5.2.2.2. Each manufacturer shall ensure that labels are designed, printed, and, if applicable, applied so as to remain legible and attached to the product during processing, storage, handling, and use steps.

5.2.2.3. Inspection of labels and instructions for use. The labels and instructions for use shall not be released for use until an authorized person has examined their compliance to the information contained therein. The approval, including date, name and manual or electronic signature of the responsible, shall be documented in the device history record.

5.3. Inspection and tests

5.3.1. General Instructions. Each manufacturer shall establish and maintain procedures for inspections, tests or other means of verification, so as to ensure compliance to the specified requirements in the entire production chain. The results of the acceptance activities during the receipt of components and manufacturing materials, as well as intermediate production stages and final acceptance of the finished product, shall be documented, including its conclusion (accepted or rejected).

5.3.2. The authority and responsibility for such activities shall be defined by the manufacturer.

5.3.3. The components and manufacturing materials received, as well as components, intermediate products, and returned products shall not be used or processed until the verification of their compliance to the requirements. Each manufacturer shall establish and maintain procedures for the retention of components, manufacturing materials, intermediate products, and returned products until the inspections, tests or other verification have been completed and documented.

5.3.4. The finished products shall not be released until the activities specified in the DMR have been completed and until the documentation and the associated data have been reviewed by a person assigned to ensure that all acceptance criteria have been met. The release, including the date and manual or electronic signature of the responsible shall be documented.

5.4. Inspection, measurement and testing equipment.

5.4.1. Each manufacturer shall ensure that all measurement and testing equipment, including mechanical, automated or electronic equipment, are suitable for its intended purposes and are capable of producing valid results. Each manufacturer shall establish and maintain procedures to ensure that equipment is routinely calibrated, inspected and controlled. The measurement equipment shall be identified so as the calibration status can be determined.

5.4.2. Calibration. Each manufacturer shall establish and maintain calibration procedures that include special guides and precision and accuracy limits, as well as prescriptions for corrective actions when the precision and accuracy limits are not achieved. The calibration shall be performed by personnel who have the necessary instruction, training, practice and expertise.

5.4.3. Calibration standards. Each manufacturer shall establish and maintain calibration standards for measurement equipment that are traceable to the official national or international standards. If there is no applicable standard available, the manufacturer shall establish and maintain its own standard.

5.4.4. Calibration records. Each manufacturer shall insure the maintenance of calibration records, including dates, measurements obtained, employee in charge of this task, and the next date for this operation. Records shall be maintained by the manufacturer and shall be available for the personnel using this equipment and for those responsible for calibrating it.

5.4.5. Maintenance. Each manufacturer shall establish and maintain procedures to ensure that the handling, preservation, and custody of equipment for testing, measuring, and inspecting are performed in order to preserve its precision and suitability for use.

5.4.6. Facilities. Each manufacturer shall protect the facilities and equipment for inspection, testing, and measurement, including hardware and test software, from adjustments that would invalidate the calibration.

5.4.7. The manufacturer shall establish procedures to assess the impact of results from previous measurements when identifying non-conformities in testing and measurement equipment. The result of the assessment shall be documented.

5.5. Validation

5.5.1. Special processes shall be validated according to previously established protocols. The results of validations, including the date and identification of the responsible for the approval shall be recorded.

5.5.2. Analytical methods, auxiliary systems supporting the processes or environmental control, automated computerized systems, and software that may adversely affect the quality of the product or the quality system shall be validated.

5.5.3. The manufacturer shall establish procedures to periodically verify their processes, analytical methods, auxiliary systems supporting the processes and environment control, automated computerized systems, and validated software, and, when applicable, to establish the frequency for revalidation.

5.6. Change control. The manufacturer shall establish procedures for change control in order to control the changes in auxiliary systems, software, equipment, processes, methods or other changes that may influence the quality of the products, including a risk assessment within the risk management process.

5.6.1. The procedure shall describe the actions to be taken, including, when appropriate, the need to re-qualify or revalidate.

5.6.2. The changes shall be formally requested, documented and approved before their implementation.

CHAPTER 6 - HANDLING, STORAGE, DISTRIBUITION AND TRACEABILITY

6.1. Handling

6.1.1. Each manufacturer shall establish and maintain procedures to ensure inversions (exchanges), damages, deterioration or other adverse effects affecting components, manufacturing materials, intermediate products, finished products, and samples for quality control do not occur during any stage of handling.

6.1.2. Each manufacturer shall establish and maintain procedures to identify the compliance of components, manufacturing materials, intermediate products, and finished products, in order to ensure that only those duly approved are used or distributed.

6.1.3. The procedures shall ensure that when the quality or condition of suitable for use of a component, manufacturing material, intermediate product or finished product, deteriorate over time, they are not used or distributed.

6.1.4. The procedures shall ensure that components, manufacturing materials, intermediate products or finished products nearest the expiry date are distributed or used firstly, and those out of the expiry date are not distributed or used.

6.2. Storage

6.2.1. Each manufacturer shall establish and maintain procedures to identify the components, manufacturing materials, intermediate products, finished products, and samples for quality control, in order to prevent inversions (exchanges). These shall be stored in physical and environmental conditions that prevent damages, deterioration or other adverse effects during the period of storage.

6.3. Distribution

6.3.1. Each manufacturer shall maintain distribution records, including or making reference to:

6.3.1.1. Names and addresses of the consignee;

6.3.1.2. Identification and amount of products shipped, with shipment date; and

6.3.1.3. Any numerical control used for traceability.

6.4. Identification and traceability

6.4.1. Each manufacturer shall establish and maintain procedures for identifying components, manufacturing materials, intermediate products, and finished products during all stages of storage, production, distribution and installation in order to prevent confusion and to ensure the correct order fulfillment.

6.4.2. Each manufacturer shall identify each unit, batch or lot of products with a serial or batch number. This identification shall be recorded in the device history record.

6.5. Non-conforming components and products

6.5.1. Each manufacturer shall establish and maintain procedures to ensure that components, manufacturing materials, intermediate products, finished products, and returned products, which do not comply with the requirements, are not installed or used inadvertently. The procedures shall contain prescriptions to identify, document, evaluate, segregate, and dispose non-conforming components, manufacturing materials, intermediate products, and finished products. The assessment of non-conformity shall include the need for investigation and notification of those people and organizations involved in such non-conformity. The results of assessments and eventual investigations shall be recorded.

6.5.2. The responsibility for the review and the authority for the decision on non-conforming components, manufacturing materials, intermediate products, finished products, and returned products shall be defined. The review and decision process shall be described in an established procedure. The decision shall be documented and the record of the rationale and manual or electronic signature(s) of the responsible(s) shall be kept. In case of authorization of use, the decision shall be based on risk assessment technically justifiable.

6.5.3. Each manufacturer shall establish and maintain procedures for re-work, re-inspection, and re-assessment of intermediate or finished products after re-work, to ensure that they meet the original specifications. The activities related to re-work and re-assessment of the product, including problems resulting from re-work, shall be documented in the device history record.

CHAPTER 7 - CORRECTIVE ACTIONS

7.1. Corrective and preventive actions.

7.1.1. Each manufacturer shall establish and maintain procedures to:

7.1.1.1. Analyze processes, work operations, quality audit reports, quality records, servicing records, complaints, returned products, and other sources of quality data in order to identify existing and potential sources of non-conformities related to the product, process or quality system. When applicable, the analysis shall be based on valid statistical technique to detect recurrent quality problems;

7.1.1.2. Investigate the source of non-conformities related to the product, process or quality system;

7.1.1.3. Identify and implement the necessary actions to prevent the occurrence, to correct the event, and to prevent the recurrence of non-conformities;

7.1.1.4. Verify or validate the effectiveness of the corrective action to ensure it does not adversely affect the product. For this purpose, any changes made, when applicable, shall observe change control procedures and validation protocols established;

7.1.1.5. Record activities related to corrective and preventive actions;

7.1.1.6. Ensure the information concerning quality issues or non-conforming products are properly disseminated to those directly involved in the maintenance of product quality or in preventing the occurrence of such problems;

7.1.1.7. Submit relevant information on quality issues identified, and preventive and corrective actions, to the executive management for information and monitoring, as well as the competent health authority, when applicable;

7.1.1.8. Determine product recalls and other field actions that are relevant for products already distributed.

7.2. Complaints Management.

7.2.1. Each manufacturer shall establish and maintain procedures to receive, examine, evaluate, investigate, and file complaints. Such procedures shall ensure that:

7.2.1.1. Complaints are received, documented, examined, evaluated, investigated, and filed by a formally designated unit;

7.2.1.2. When applicable, the complaints are notified to the competent health authority;

7.2.1.3. Complaints are examined to evaluate whether an investigation is necessary. When no investigation is performed, the unit shall maintain a record including the reason why the investigation has not been performed and the name of the responsible for the decision to not investigate;

7.2.1.4. Each manufacturer shall examine, evaluate, and investigate all complaints involving possible product non-conformity. Any complaints related to death, injury or threaten to public health shall be immediately reviewed, evaluated and investigated.

7.2.1.5. When an investigation is performed, a record shall be kept, containing the following information:

7.2.1.5.1. Product name;

7.2.1.5.2. Date of receipt of the complaint;

7.2.1.5.3. Any control number used;

7.2.1.5.4. Name, address and telephone number of the claimant;

7.2.1.5.5. Nature of the complaint; and

7.2.1.5.6. Date and investigation results, including the actions taken.

7.3. Quality Audit.

7.3.1. Each manufacturer shall conduct and document quality audits to assess the quality system compliance to the requirements established.

7.3.2. Quality audits shall be conducted by trained persons, according to audit procedures established, with no direct responsibility for the matters being audited.

7.3.3. Those responsible for the audited areas shall be notified on non-conformities identified.

CHAPTER 8 - INSTALLATION AND SERVICING

8.1. Installation. Each manufacturer shall establish and maintain appropriate instructions and procedures to correctly install the products. When the manufacturer or his authorized representative installs a product, it shall be verified for operation according to established criteria. The results of this verification shall be recorded. The manufacturer shall ensure the installation instructions and procedures are distributed along with the product or otherwise available to the responsible for installing the product.

8.2. Servicing. Each manufacturer shall establish and maintain procedures to ensure that finished products undergoing servicing by the manufacturer or his representative meet the specifications.

8.2.1. Servicing records. Each manufacturer shall establish and maintain procedures to ensure the servicing records are maintained and identify:

8.2.1.1. Product subject of service;

8.2.1.2. Control number used;

8.2.1.3. Date of service;

8.2.1.4. Identification of service provider;

8.2.1.5. Description of service performed; and

8.2.1.6. Results of tests and inspections for approving the service.

8.2.2. Each manufacturer shall regularly review the servicing records. Where the analysis identifies failure trends, which represent hazards, or records involving death or severe injury, the corrective / preventive action shall be implemented according to the requirements of this Technical Regulation.

CHAPTER 9 - STATISTICAL TECHNIQUES

9.1. Each manufacturer shall establish and maintain procedures for identifying valid statistical techniques to assess the performance of the quality system and capability of the process to meet the established specifications.

9.2. Sampling plans shall be formalized in writing and based on valid statistical logic. Each manufacturer shall establish and maintain procedures to ensure that sampling methods are adequate for their intended use and are regularly

reviewed. The revision of sampling plans shall consider the occurrence of non-conformities of products, quality audit reports, complaints, and other indicators.