COLLEGIATE BOARD RESOLUTION – RDC NO. 16 OF 28 MARCH 2013

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

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 11, item IV of Regulation approved by Decree no. 3,029 of 16 April 1999, and considering the provisions of item II and paragraphs 1 and 3 of Article 54 of the Internal Regulation approved in the terms of Annex I of the ANVISA Administrative Rule no. 354, of 11 August 2006, republished in the Federal Official Gazette of 21 August 2006, in a meeting held on 7 March 2013,

whereas Law no. 6,360 of 23 September 1976 and its regulations, Decree no. 79,094 of 5 January 1977;

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

whereas the regulation of Good Manufacturing Practices for Medical Devices and *In Vitro* Diagnostic Devices must 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 for 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 for Medical Devices and *In Vitro* Diagnostic Devices (revocation of Resolutions GMC nos. 04/95, 38/96, 65/96, and 131/96)".

Article 2 – To revoke Administrative Rule no. 686 of 27 August 1998; Resolution RDC no. 59 of 27 June 2000; and Resolution RDC no. 167 of 2 July 2004.

Article 3 – Distributors and storage establishments of medical devices and *in vitro* diagnostic devices shall meet the requirements of this Resolution, as applicable.

Article 4 – A period of 180 days is granted, from the date the normative instrument is incorporated, for the companies to adopt the necessary measures to apply 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 FOR MEDICAL DEVICES AND *IN VITRO* DIAGNOSTIC DEVICES

CONTENTS

CHAPTER 6 – HANDLING, STORAGE, DISTRIBUTION, AND TRACEABILITY

6.1. Handling

6.2. Storage

6.3. Distribution

6.4. Identification and traceability

6.5. Non-conforming components and products

CHAPTER 7 – CORRECTIVE AND PREVENTIVE ACTIONS

7.1. Corrective and preventive actions

7.2. Complaint management

7.3. Quality audit

CHAPTER 8 – INSTALLATION AND TECHNICAL ASSISTANCE

8.1. Installation

8.2. Technical assistance

CHAPTER 9 – STATISTICAL TECHNIQUES

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, purchases, manufacture, packaging, labeling, storage, distribution, installation, and technical assistance 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.

1.1.2. The requirements of this Technical Regulation are applicable to manufacturers and importers of medical devices and *in vitro* diagnostic devices commercialized in Brazil.

1.1.3. Whenever the manufacturer understands that some of the requirements of this resolution are not applicable to its processes, a justification must be documented for such understanding.

1.1.4. Importers of medical devices and *in vitro* diagnostic devices shall meet the requirements of this Resolution, as applicable.

1.2 Definitions

For the purposes of this Technical Regulation, the following definitions apply:

1.2.1. Technical assistance: maintenance or repair of a finished product in order to return it to its specifications.

1.2.2. Quality audit: an established, systematic, and independent examination of the whole quality system of a manufacturer, running 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 also that they are adequate to achieve the quality system's objectives. 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 use instructions, 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. Project input data: description of physical attributes, indication of use, performance, compatibility, safety, efficacy, ergonomics, usability, information from previous projects, and results from risk management, among other requirements of a medical device or *in vitro* diagnostic device used as the basis of the project.

1.2.5. Project output data: result of the work in each phase of the project and its final result. The finished project output data are the basis for the product master record (PMR).

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, technical assistance, services, quality system, or any other activity shall meet.

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

1.2.9. Manufacturer: any person who designs, manufactures, assembles, or processes a finished product, including those who perform functions by contract of sterilization, 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 management policies, procedures, and practices to activities of analysis, assessment, control, and monitoring of risks associated to a determined product or process.

1.2.12. Lot or batch: quantity of a product elaborated in a manufacturing or sterilization cycle, the essential feature of which is 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, sterilants, 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: distinct combination of letters or numbers, or both, from which the full history of purchase, manufacture, packaging, labeling, and distribution of finished products can be determined.

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 the outcome of which 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 evidences data, facts, specific events, and results achieved in relation to compliance with procedures and standards of the quality system.

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

1.2.25. Project history record: compilation of documents containing the full project history of a finished product.

1.2.26. Product master record (PMR): compilation of documents containing specifications, instructions, and procedures to obtain a finished product, as well as its installation, technical assistance, and maintenance.

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 PMR.

1.2.28. Project review: documented, systematic, and complete examination performed during project development to assess its adequacy 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. Regarding a project, it means to establish and document objective evidence that the product specifications meet the needs of the user and its intended use. Regarding 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. Verification: confirmation by analysis and submission of objective evidence 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 a 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 manufactured 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 instructions and procedures of the quality system in accordance with the requirements of this Technical Regulation, and

2.1.1.2. Establish procedures to meet the legal provisions established in the health legislation in force.

2.2. Management responsibility

2.2.1. Quality Policy. The executive management of each manufacturer shall establish its quality commitment 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 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 an organization chart, with enough 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 interrelations of all personnel who manage, perform, and verify quality-related work, with the necessary independence to perform their responsibilities.

2.2.4. Resources and personnel for verification activities. Each manufacturer shall establish verification functions, provide adequate resources, and designate trained personnel to perform verification activities.

2.2.5. Management representative. The executive management of each manufacturer shall indicate an individual and document such indication, and, regardless of other functions, this individual will have authority and responsibility to:

2.2.5.1. Ensure that quality system requirements are established and kept 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 assess the suitability and effectiveness of the quality system at defined intervals and frequently enough to ensure that the quality system meets the requirements of this Technical Regulation and complies with the objectives of the 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, alterations that may affect the quality system or product conformity, regulatory requirements, among others, shall be considered as inputs for management reviews.

2.3. Personnel

2.3.1. General instructions. Each manufacturer shall have sufficient personnel with instruction, experience, training, and practice compatible with the job description, in order to ensure that all activities provided for in this Technical Regulation are properly performed. The company shall keep documents defining authority, responsibility, and requirements necessary for the various tasks of the company.

2.3.2. Training. Each manufacturer shall ensure that all personnel are trained to perform adequately the tasks assigned to them. Training shall be conducted in accordance with procedures established by qualified people to ensure the employees have a proper understanding of their regular duties and the requirements of these Technical Regulations applicable to their duties. As part of their training, all employees shall be warned about defects

in products that may occur as a result of incorrect conduction of their specific duties. Staff training shall be documented.

2.3.3. Consultants. Each manufacturer shall ensure that any consultant providing guidance on methods or controls used in project, purchase, manufacture, packaging, labeling, storage, installation, or technical assistance of products is qualified enough (through instruction, training, and experience) to advise on matters he/ she was contracted for. The contracting of consultants shall be conducted in accordance with the purchase control requirements 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 that involves the entire product lifecycle, from conception to discontinuation, to identify the hazards associated to a medical device or *in vitro* diagnostic device, to estimate and assess the risks involved, control the risks and assess the effectiveness of established controls. This program shall include the following elements: risk analysis, assessment, control, and monitoring.

2.4.2. The company's 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 their adequacy and effectiveness.

2.5. Purchase Controls

2.5.1. Each manufacturer shall establish and maintain procedures to ensure that components, manufacturing materials, and finished products manufactured, processed, labeled, or 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 meet the specifications established by it.

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 to assess suppliers, specifying the requirements, including quality requirements, they must meet.

2.5.3. Each manufacturer shall assess and select potential suppliers according to their ability to meet requirements previously established, 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 date and manual or electronic signature of the responsible person, shall be documented.

2.5.5. An agreement shall be documented in which the suppliers undertake to notify the manufacturer about any alteration in the product or service, so that the manufacturer can determine if the alteration 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 document control procedures 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 people to assess 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 person responsible for approving the documents, shall be documented.

3.1.3. Distribution of documents. The manufacturer shall ensure 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. Alterations to documents. Alterations to specifications, methods, or procedures related to the quality system shall be assessed, documented, reviewed, and approved by people whose job and level of responsibility are equivalent to those who performed the original revision and approval.

3.1.5. Records of alterations to documents. Each manufacturer shall maintain records of alterations to documents, including a description of the alteration, identification of the documents altered and the ones affected, identification of the responsible person, date of approval, and date on which the alterations 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 stored in a way 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 deemed 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 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 for less than two years from the date of its distribution.

3.2. Product history record

3.2.1. Each manufacturer shall maintain product history records. Each manufacturer shall establish and maintain procedures to ensure that the product history records are kept for each batch or series to show the products were manufactured according to the product master record and the requirements of this Technical Regulation. The product history record shall include 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 inspections and tests;

3.2.1.5. Parameters of special processes;

3.2.1.6. Quantity released for distribution;

3.2.1.7. Labeling;

3.2.1.8. Identification of serial number or production batch; and

3.2.1.9. Final release of the product.

3.3. Records of inspections and tests.

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

CHAPTER 4 – PROJECT CONTROL AND PRODUCT MASTER RECORD (PMR)

4.1. Project Control

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

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

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

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

4.1.5. Project output data. Each manufacturer shall establish and document the project output data in order to assess if the project is in compliance with the requirements established as input data. The project output data shall meet input data requirements, include acceptance criteria, and identify the project characteristics that are essential for the intended use of the product. These shall be documented, reviewed, and approved prior to release.

4.1.6. Project review. Each manufacturer shall establish and keep procedures to ensure that the assessments of project results are planned, conducted, and documented in the various stages of project development. The procedures shall ensure that representatives from all jobs directly related to the project stage under review, as well as individuals from related areas and experts needed, are involved. The results from project review shall be documented in the project history record.

4.1.7. Project transfer. Each manufacturer shall establish and keep procedures to ensure that the product project is correctly translated into production specifications.

4.1.8. Project validation. Each manufacturer shall establish and keep a procedure to validate the product project. Project validation shall be performed under pre-determined operational conditions, in the initial production of batches or unit. Project validation shall ensure that the product meets user needs and indication of use, and shall include tests of the products under real or simulated conditions of use. Project validation shall include software validation when appropriate. The results from project validation, including its identification, methods, data, and manual or electronic signature of the people responsible for it shall be documented in the project history file. Stability studies shall be conducted whenever applicable.

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

4.1.10. Project alterations. Each manufacturer shall establish and keep procedures to identify, document, validate, review, and approve project alterations before its implementation, including a risk assessment within the risk management process.

4.1.11. Project history file. Each manufacturer shall establish and keep a project history file for each product. The project history file shall contain or make reference to all records necessary to show that the project was developed in accordance with the approved project plan and the requirements of this Technical Regulation.

4.2. Product master record (PMR)

4.2.1. Each manufacturer shall keep product master records (PMRs). The PMR for each type of product shall include or make reference to the following information:

4.2.1.1. Product specifications, including the respective drawings, composition, formulation, component specifications, software project specifications, and its source codes;

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

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

4.2.1.4. Procedures for inspection and tests with the respective acceptance criteria; and

4.2.1.5. Methods and procedures for installation, maintenance, and technical assistance.

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 complies with its specifications. Where any deviation may occur in product specifications, as a result of the manufacturing process, the manufacturer shall establish and keep process control procedures that describe any process controls necessary to ensure compliance with specifications. Process controls shall include:

5.1.1.1. Documented instructions, standard operational procedures, and methods that define and control the method of production, installation, and maintenance;

5.1.1.2. Monitoring and control of process parameters;

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

5.1.1.4. Instructions for process start release;

5.1.2. The company facilities shall be properly designed to provide the performance of all operations, prevent exchanges or contamination of components, manufacturing materials, intermediate products, and finished products, and ensure the proper handling thereof, including adequate 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 operation of the established environmental control systems shall be monitored, and the corresponding records shall be kept.

5.1.3.1. Cleaning and sanitization. Each manufacturer shall establish and keep appropriate cleaning and sanitization procedures, as well as a program that meets the requirements of manufacturing process specifications. Each manufacturer shall ensure that the employees involved understand such procedures.

5.1.3.2. Personnel health and hygiene. Each manufacturer shall ensure that the employees and/ or other people in contact with the product or its 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 kept away from the operations until his or her health conditions are back to normal. Each manufacturer shall instruct its 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 so production areas are not affected.

5.1.3.4. Contamination control. Each manufacturer shall establish and keep procedures to prevent the contamination of equipment, components, manufacturing materials, intermediate products, and finished products with 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 chemical waste and sewage. Treatment and destination of waste, chemical effluents, and by-products shall occur in accordance with the applicable legislation in force.

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

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

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

5.1.5.1. Maintenance program. Each manufacturer shall establish and keep 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 maintenance and use of the equipment. A record of maintenance activities shall be made, with date of conduction and identification of the people 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 such adjustments.

5.1.5.3. Manufacturing materials. Each manufacturer shall establish and keep procedures for use and removal of manufacturing materials, to ensure that such materials are removed from the product or limited to a specified quantity 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 ensure compliance with specifications. Critical parameters shall be monitored and recorded in the product history record.

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

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

5.2.2. Product labeling

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

5.2.2.2. Each manufacturer shall ensure that labels are designed, printed, and, if applicable, applied in a way they remain legible and adhered to the product during processing, storage, handling, and use steps.

5.2.2.3. Inspection of labels and instructions of use. Labels and instructions of use shall not be released for use until an authorized person has examined their compliance with the information

contained therein. The approval, including date, name, and manual or electronic signature of the person responsible for it, shall be documented in the product history record.

5.3. Inspection and tests

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

5.3.2. The authority over 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 their compliance with the established requirements are verified. Each manufacturer shall establish and keep procedures for retention of components, manufacturing materials, intermediate products, and returned products until inspections, tests, or other established types of verification have been completed and documented.

5.3.4. Finished products shall not be released until the activities specified in the PMR 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 date and manual or electronic signature of the person responsible for it shall be documented.

5.4. Inspection, measurement, and test equipment

5.4.1. Each manufacturer shall ensure that all measurement and test equipment, including mechanical, automated, or electronic equipment, is suitable for its intended purposes and capable of producing valid results. Each manufacturer shall establish and keep procedures to ensure that the equipment is calibrated, inspected, and controlled on a routine basis. The measurement equipment shall be identified so the calibration status can be determined.

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

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

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

5.4.5. Maintenance. Each manufacturer shall establish and keep procedures to ensure that handling, preservation, and custody of equipment for tests, inspection, and measurement are performed in order to preserve its precision and suitability for use.

5.4.6. Facilities. Each manufacturer shall protect facilities and equipment for inspection, tests, and measurement, including hardware and test software, from adjustments that may invalidate 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 from validations, including date and identification of the person responsible for the approval, shall be recorded.

5.5.2. Analytical methods, auxiliary systems supporting the process 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 process or environment control, automated computerized systems, and validated software, and, when applicable, establish the frequency for revalidation.

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

5.6.1. The procedure shall describe the actions to be taken, including the need of requalification or revalidation, when appropriate.

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

CHAPTER 6 – HANDLING, STORAGE, DISTRIBUTION, AND TRACEABILITY

6.1. Handling

6.1.1. Each manufacturer shall establish and keep 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 keep procedures to identify the conformity 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 expired are not distributed or used.

6.2. Storage

6.2.1. Each manufacturer shall establish and keep procedures to identify 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 keep distribution records that include or make reference to:

6.3.1.1. Names and addresses of the consignee;

6.3.1.2. Identification and quantity 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 keep procedures to identify 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 fulfillment of orders.

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 product history record.

6.5. Non-conforming components and products

6.5.1. Each manufacturer shall establish and keep procedures to ensure that components, manufacturing materials, intermediate products, finished products, and returned products not in conformity with the requirements established are not installed or used inadvertently. The procedures shall contain prescriptions to identify, document, assess, segregate, and dispose non-conforming components, manufacturing materials, intermediate products, and finished products. Non-conformity assessment shall include the need to investigate and notify people

and/ or organizations involved in such non-conformity. The results from assessments and eventual investigations shall be recorded.

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

6.5.3. Each manufacturer shall establish and keep procedures for re-work, re-inspection, and reassessment of intermediate or finished products after re-work, to ensure that they meet their 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 product history record.

CHAPTER 7 – CORRECTIVE AND PREVENTIVE ACTIONS

7.1. Corrective and preventive actions

7.1.1. Each manufacturer shall establish and keep procedures to:

7.1.1.1. Analyze processes, work operations, quality audit reports, quality records, technical assistance records, complaints, returned products, and other sources of quality data in order to identify existing and potential causes 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 cause 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, correct the event, and 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 alterations made, when applicable, shall observe alteration 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 the prevention of such problems;

7.1.1.7. Submit relevant information on the 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 withdrawals and other field actions relevant in the case of products already distributed.

7.2. Complaint Management

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

7.2.1.1. Complaints are received, documented, examined, assessed, 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 conducted, the unit shall keep a record including the reason why the investigation was not conducted and the name of the person responsible for the decision not to investigate;

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

7.2.1.5. When an investigation is conducted, 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 of and results from the investigation, 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 with the requirements established.

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

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

CHAPTER 8 – INSTALLATION AND TECHNICAL ASSISTANCE

8.1. Installation. Each manufacturer shall establish and keep appropriate instructions and procedures for the correct installation of products. When the manufacturer or his authorized representative installs a product, the representative shall verify if it operates according to the 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 person responsible for installing the product.

8.2. Technical assistance. Each manufacturer shall establish and keep procedures to ensure that finished products submitted to technical assistance by the manufacturer or his representative meet the specifications.

8.2.1. Technical assistance records. Each manufacturer shall establish and keep procedures to ensure the technical assistance records are kept and identify:

8.2.1.1. Product subjected to technical assistance;

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 service approval.

8.2.2. Each manufacturer shall review the technical assistance records on a regular basis. Where the analysis identifies trends of failure representing 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 keep procedures to identify valid statistical techniques to assess the quality system performance and process capability to meet the specifications established.

9.2. Sampling plans shall be formalized in writing and based on valid statistical logic. Each manufacturer shall establish and keep procedures to ensure that the sampling methods are adequate for their intended use and reviewed on a regular basis. The revision of sampling plans shall consider the occurrence of non-conformities of products, quality audit reports, complaints, and other indicators.