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Ministry of Health/Brazilian Health Regulatory Agency/Collegiate Board

COLLEGIATE BOARD RESOLUTION – RDC NO. 665 OF 30 MARCH 2022

Provides for the Good Manufacturing Practices for Medical Products and *In Vitro* Diagnostic Products.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the exercise of the attributions granted by art. 15, III and IV, in conjunction with art. 7, III and IV, of Law No. 9,782, of January 26, 1999, and with art. 187, VI, § 1 of the Internal Regulations approved by the Resolution of the Collegiate Board of Directors - RDC No. 585, of December 10, 2021, resolves to adopt the following Resolution, as deliberated in the Extraordinary Meeting - Rextra No. 6, held on March 30, 2022, and I, Director-President, determine its publication.

CHAPTER I

INITIAL PROVISIONS

Section I

Objective

Article 1. This regulation provides for the Good Manufacturing Practices (GMP) for Medical Products and *In Vitro* Diagnostic Products, establishing the requirements that describe the GMP for methods and controls used in the design, purchasing, manufacturing, packaging, labeling, storage, distribution, installation, and technical assistance applicable to the manufacture of medical products and *in vitro* diagnostic products.

Paragraph 1. The requirements referred to in the caput of this article is intended to ensure that medical products and *in vitro* diagnostic products are safe and effective.

Paragraph 2. This Resolution incorporates into the national legal system the Resolution issued by the Mercosur's Common Market Group (GMC, in Portuguese) No. 20 of 17 November 2011, MERCOSUR/GMC/RES. No. 20/11, "Mercosur Technical Regulation on Good Manufacturing Practices for Medical Products and *In Vitro* Diagnostic Products (Revoking GMC Resolutions No. 04/95, 38/96, 65/96, and 131/96)".

Section II

Scope

Article 2. This regulation applies to manufacturers, distributors, storers, and importers of medical products and *in vitro* diagnostic products that are commercialized in Brazil.

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Paragraph 1. When the manufacturers referred to in the caput of this article conclude that certain requirements established in this Resolution are not applicable to their processes, they shall document the justification for such understanding.

Paragraph 2. The distributors of medical products and *in vitro* diagnostic products shall comply with the following requirements of this Resolution, at least:

I - Chapters I, VII, and VIII, in full.

II - Chapter II, in full, except Section IV.

III - Chapter III, Section I.

IV - Chapter V, articles 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, and 77, in addition to Section IV.

V - Chapter VI, in full, except Article 119.

Paragraph 3. The storers of medical products and *in vitro* diagnostic products shall comply with the following requirements of this Resolution, at least:

I - Chapters I and VII, in full.

II - Chapter II, in full, except Section IV.

III - Chapter III, Section I.

IV - Chapter V, articles 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, and 77.

V - Chapter VI, in full, except Article 119.

Paragraph 4. The importers of medical products and *in vitro* diagnostic products shall comply with the following requirements of this Resolution, at least:

I - Chapters I, II, VII, VIII, and IX in full.

II - Chapter III, Section I and Section III.

III - Chapter IV, Article 63, items III, IV, and V.

IV - Chapter V, articles 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 85, 86, and 87, in addition to Sections III and IV.

V - Chapter VI, in full, except Article 119.

Paragraph 5. Companies that carry out more than one activity shall comply with the specific requirements defined for each activity.

Paragraph 6. The minimum requirements to be complied with, defined in Paragraphs 2, 3, and 4 of this Article, are applicable to distributors, storers, and importers, even if the provisions mention the word “manufacturer” only.

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Section III

Definitions

Article 3. For the purposes of this Resolution, the following definitions are adopted:

I - servicing: maintenance or repair of a finished product, in order to restore it to its specifications.

II - quality audit: an established, systematic, and independent examination of a manufacturer's entire quality system, performed at regular intervals and with sufficient frequency to ensure that the quality system's activities and its results comply with the procedures specified in its quality system.

III - component: raw material, substance, part, piece, software, hardware, packaging, label, or instruction for use, used during the manufacture of a medical product or *in vitro* diagnostic product, intended to be included as part of the finished product.

IV - design input: description of physical attributes, indication of use, performance, compatibility, safety, efficacy, ergonomics, usability, information retrieved from previous designs, and risk management results, amongst other requirements for medical products or *in vitro* diagnostic products, that are used as the basis for a design development.

V - design output: results from the work at each stage of the design development process, including its final result, which, when concluded, is the basis for the device master record (DMR).

VI - damage: a person's physical lesion or health injury or a property or environmental deterioration.

VII - specifications: requirements that products, components, production activities, technical assistance, services, quality system, or any other activity shall comply with.

VIII - to establish: to define, to document either in writing or electronically, and implement.

IX - manufacturer: any person who design, manufacture, assemble, or process a finished product, including those who execute sterilization, labeling, and packaging activities by contract.

X - executive management: a company's senior management team, responsible for providing resources and with authority to establish or modify the company's quality policy and system.

XI - risk management: policies, procedures, and management practices applied systematically to the tasks of analysis, assessment, control, and risk monitoring associated to a given product or process.

XII - lot or batch: quantity of a product elaborated in a manufacturing or sterilization cycle, the essential characteristic of which is homogeneity.

XIII - manufacturing material: material or substance used during the manufacturing process or to support this process, including cleaning agents, molding releasing agents, lubricating oils, sterilizing agents, or other subproducts from the manufacturing process.

XIV - non-conformity: failure to comply with a previously specified requirement.

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XV - serial number or batch: unique combination of letters and/ or numbers, from which the complete purchase, manufacture, packaging, labeling, and distribution history of the finished products may be determined.

XVI - hazard: potential source of harm.

XVII - quality policy: totality of an organization's intentions and guidelines related to quality, expressed by the executive management.

XVIII - special process: any process the results of which cannot be fully verified by subsequent inspections and tests.

XIX - production: all activities involved in the manufacturing of a given product, from the receipt of components, through processing and packaging, until the obtention of the finished product.

XX - finished product: any product or accessory already packaged and labeled and ready for use.

XXI - quality: all the aspects and characteristics that allow a medical product or *in vitro* diagnostic product to meet suitability, safety, and performance requirements.

XXII - complaint: written, oral or electronic communication, related to non-acceptance of a product's identity, quality, durability, reliability, safety, efficacy, or performance.

XXIII - record: document set down in writing or electronically, which evidences data, facts, specific events, and the results achieved regarding compliance with the quality system procedures and standards.

XXIV - device history record: compilation of records comprising the complete production history of a finished product.

XXV - design history record: compilation of documents comprising the complete design history of a finished product.

XXVI - device master record (DMR): compilation of documents including specifications, instructions, and procedures for the obtention of a finished product, in addition to its installation, servicing and maintenance.

XXVII - rework: partial or total manufacturing activities intended to correct non-conformities of a component, intermediary product, or finished product, so that it complies with the specifications defined in the DMR.

XXVIII - design review: documented systematic and complete examination performed during the design development to assess its compliance to the design development planning and the objectives established.

XXIX - risk: combination of occurrence probability and damage severity.

XXX - quality system: organizational structure, responsibilities, procedures, specifications, processes, and resources required for quality management.

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XXXI - validation: proof by analysis and objective evidence that the requirements defined for a given purpose consistently lead to the expected result.

XXXII - verification: proof by analysis and presentation of objective evidence that the requirements specified have been met, including the process of assessing the results of an activity to determine compliance with the specifications established.

XXXIII - lifespan: manufacturer's estimated time length during which a product correctly performs its originally intended functions.

Paragraph 1. The procedures referred to in item II of the caput of this article shall be implemented efficiently and be adequate so the quality system's objectives can be achieved.

Paragraph 2. The quality audit referred to in item II of the caput of this article differs from other quality system's activities required by this Resolution.

Paragraph 3. When applied to a project, the validation mentioned in item XXXI of the caput of this article means establishing and documenting objective evidence that the product specifications meet the user's needs and its intended use.

Paragraph 4. When applied to a process, the validation referred to in item XXXI of the caput of this article means establishing and documenting objective evidence that the process will consistently produce a result that meets the predetermined specifications.

CHAPTER II

QUALITY SYSTEM GENERAL REQUIREMENTS

Section I

General requirements

Article 4. Each manufacturer shall establish and maintain a quality system to ensure that the requirements of this Resolution are met, and the products manufactured are safe, effective, and adequate for the intended use.

Sole paragraph. As part of quality system activities referred to in the caput of this article, each manufacturer shall:

I - establish and maintain effective quality system instructions and procedures in accordance with this regulation's requirements.

II - establish procedures to meet the legal requirements determined by current health surveillance regulations.

Section II

Management responsibility

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Subsection I

Quality policy

Article 5. The executive management of each manufacturer shall establish its quality policy and objectives, which shall be measurable and consistent with the policy established.

Article 6. The executive management shall keep the quality policy at all levels of the organization.

Article 7. The executive management shall ensure that the quality policy is described in a quality manual and that this policy is understood by all employees who may affect or influence the quality of a product.

Subsection II

Organization and responsibilities

Article 8. Each manufacturer shall:

I - establish and maintain an adequate organizational structure, expressed by an organizational chart, with sufficient personnel to ensure that the products are manufactured in accordance with this regulation's requirements.

II - establish the responsibility, authority, and interrelation of all personnel who manages, executes, and verifies quality-related work, with the necessary independence to carry out their responsibilities. and

III - establish verification functions, provide adequate resources, and assign trained personnel to perform verification activities.

Article 9. Each manufacturer's executive management team shall assign a person from the executive management team itself, who, regardless of other activities, has authority and responsibility to:

I - ensure that the quality system requirements are established and maintained in accordance with this regulation.

II - report the quality system performance to the executive management for review and provide information on the quality system improvement.

Sole paragraph. The assignment referred to in the caput of this article shall be documented.

Subsection III

Management review

Article 10. The executive management of each manufacturer shall assess the quality system adequacy and effectiveness at defined intervals and with sufficient frequency to ensure that the quality system meets this regulation's requirements and the objectives of the quality policy established.

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Article 11. The management review shall be conducted in accordance with the review procedures established and the results from each quality system review shall be documented.

Article 12. Matters related to audit results, post-marketing information, process performance and product compliance, status of corrective and preventive actions, changes that could affect the quality system or a product compliance, and regulatory requirements, amongst others, shall be considered for management review.

Section III

Personnel

Article 13. Each manufacturer shall have sufficient personnel with instruction, experience, training, and practice compatible with their job description, to ensure that all activities provided for in this Resolution are correctly performed.

Article 14. Descriptions defining authority, responsibility, and necessary requirements of all personnel for the various tasks of the company shall be kept.

Article 15. Each manufacturer shall ensure that all personnel are trained to perform their assigned tasks properly.

Paragraph 1. The training referred to in the caput of this article shall be conducted by qualified personnel, in accordance with the established procedures, to ensure that employees have an adequate understanding of their jobs and of the requirements in this regulation that are applicable to their activities.

Paragraph 2. As part of the training mentioned in the caput of this article, all employees shall be warned about product defects that may occur as a result of incorrect execution of their specific duties.

Paragraph 3. Personnel training shall be documented.

Article 16. Each manufacturer shall ensure that any external consultant that advises on applied methods or utilized controls for a product's design, purchase, manufacture, packaging, labeling, storage, installation, or servicing activities has sufficient qualifications – education, training, and experience – to advise on matters for which the consultant was hired.

Article 17. The consultant's hiring process shall be conducted in accordance with the purchase control requirements determined in this regulation.

Section IV

Risk management

Article 18. Each manufacturer shall establish and maintain a continuous risk management process that covers the entire life cycle of a medical device or *in vitro* diagnostic product, from conceiving to discontinuation, to:

I - identify the associated hazards.

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II - estimate and assess the risks involved.

III - control the associated risks.

IV - assess the effectiveness of the controls established.

Article 19. The continuous risk management process shall include the following elements:

I - analysis.

II - evaluation.

III - control.

IV - risk monitoring.

Article 20. The company's executive management team shall designate the responsible professionals, establish the policy to determine the risk acceptability criteria, as well as determine a periodic review of risk management activities, to ensure the adequacy and effectiveness of such activities.

Section V

Purchase controls

Article 21. 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.

Sole paragraph. Each manufacturer shall ensure that the services performed by third parties referred to in the caput of this article comply with the specifications established.

Article 22. Each manufacturer shall establish and maintain, according to the impact on the quality of the finished product, criteria for suppliers' evaluation, specifying the requirements that shall be complied with by suppliers, including quality requirements.

Article 23. Each manufacturer shall evaluate and select potential suppliers, according to their ability to meet the previously established requirements, maintaining a record of approved suppliers.

Sole paragraph. Supplier evaluation's records and results shall be maintained.

Article 24. An agreement shall be documented in which the suppliers agree 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.

Article 25. Each manufacturer shall keep records of the purchase orders that clearly describe or refer to specifications, including quality requirements for components, manufacturing materials, finished goods, or services requested or hired.

Article 26. Each manufacturer shall review and approve purchase orders prior to their release.

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Article 27. Approval of purchasing orders, including the date and the handwritten or digital signature of the in-charge person, shall be documented.

CHAPTER III

QUALITY DOCUMENTS AND RECORDS

Section I

General requirements

Article 28. Each manufacturer shall establish and maintain document control procedures to ensure that all the documents mentioned to in this regulation are correct and adequate for the intended use and are understood by everyone who may affect or influence the product's quality.

Article 29. Each manufacturer shall designate personnel to evaluate and approve all documents mentioned in this regulation for its adequacy before its issuance.

Sole paragraph. The approval referred to in the caput of this article, including the date and handwritten or digital signature of the person responsible for approving the documents, shall be documented.

Article 30. Each manufacturer shall ensure that all documents are updated and available at the use points and that all unnecessary or obsolete documents are withdrawn from use or protected from unintended use.

Article 31. Changes related to quality system specifications, methods, or procedures shall be evaluated, documented, reviewed, and approved by personnel whose role and level of responsibility are equivalent to those who performed the original review and approval.

Article 32. Each manufacturer shall keep records of document changes that shall include:

I - description of the change.

II - identification of the altered documents.

III - identification of the affected documents.

IV - identification of the person responsible for the change.

V - change's approval date.

VI - change's effectiveness date.

Article 33. A list of current documents shall be maintained to identify the documents' status and to ensure that only updated and approved documents are in use.

Article 34. All quality documents and records shall be legible and stored in a way to minimize damage, prevents loss, and allow quick recovery.

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Article 35. All digital documents and records shall have backup copies.

Article 36. Documents and records considered confidential by the manufacturer may be flagged to alert the competent health authority.

Article 37. All necessary documents and records related to a product shall be kept for a time length equivalent to the product's lifespan, counted from the date of its distribution and in no situation this time length can be less than two years.

Section II

Device history record

Article 38. Each manufacturer shall keep device history records.

Article 39. Each manufacturer shall establish and maintain procedures to ensure that the device history records are kept for each batch or series, to evidence that the products were manufactured in accordance with the device master record and the requirements in this resolution´s requirements.

Article 40. The device history records shall include or refer to the following information:

I - manufacturing date.

II - components used.

III - quantity manufactured.

IV - inspections and tests results.

V - special processes' parameters.

VI - quantity released for distribution.

VII - labeling.

VIII - serial number or batch number identification.

IX - product's final release.

Section III

Inspection and test records

Article 41. Each manufacturer shall keep a record of the results from established inspections and tests when these are directly related to product critical quality attributes.

Article 42. The records of established inspections and tests shall include the acceptance criteria, the results, the used equipment/instrument identification, the date, and in-charge person's handwritten or digital signature.

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CHAPTER IV

DESIGN CONTROL AND DEVICE MASTER RECORD (DMR)

Section I

Design control

Article 43. Each manufacturer shall establish and maintain product design control procedures to ensure that that the specified design requirements are met.

Article 44. Each manufacturer shall establish and maintain plans that describe or refer to design and development activities, as well as the personnel responsible for each activity.

Paragraph 1. The plans referred to in the caput of this article shall include any interaction between the various organizational and technical groups that have interface with the design.

Paragraph 2. The plans referred to in the caput of this article shall be evaluated, updated, and approved during design development.

Article 45. Each manufacturer shall establish and maintain procedures to ensure that product requirements are appropriate and meet its intended use, including user and patient needs, as well as the applicable legal and regulatory requirements.

Sole paragraph. The procedures referred to in the caput of this article shall include a mechanism that allows incomplete, ambiguous, or conflicting requirements to be identified and addressed.

Article 46. Design input data shall be documented, evaluated, and approved by a qualified assigned person.

Article 47. The design requirements approval, including the responsible person´s handwritten or digital signature and the date, shall be documented.

Article 48. Each manufacturer shall establish and maintain procedures for product design verification.

Paragraph 1. The design verification shall be performed by a designated person and shall ensure that the design output data matches the design input data.

Paragraph 2. The design verification results, including the identification of the design verified, the verification methods, the date, and the name of the person in charge of the verification, shall be documented in the design history record.

Article 49. Each manufacturer shall define and document the design output data in a way that allows the assessment of the design's conformity to the requirements established as input data.

Paragraph 1. The design output data shall meet the input data requirements, include the acceptance criteria, and identify the design characteristics that are essential for the product intended use.

Paragraph 2. The design output data shall be documented, reviewed, and approved before its release.

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Article 50. Each manufacturer shall establish and maintain procedures to ensure that the design reviews are planned, conducted, and documented during the various stages of design development.

Sole paragraph. The procedures referred to in the caput of this article shall ensure that representatives of all activities directly related to the design stage being reviewed, as well as representatives from related areas and the necessary specialists are involved.

Article 51. The design review results shall be documented in the design history record.

Article 52. Each manufacturer shall establish and maintain procedures to ensure that product design is correctly translated into production specifications.

Article 53. Each manufacturer shall establish and maintain a procedure to validate the product design.

Article 54. Design validation shall be performed under predetermined operational conditions, during the initial batch or unit manufacturing.

Article 55. Design validation shall ensure that the product meets the user's needs and intended use, and it shall include products trials under real or simulated use conditions.

Article 56. Design validation shall include software validation, where appropriate.

Article 57. The project's validation results, including identification, methods, date, and handwritten or digital signature of those responsible, shall be documented in the design history record.

Article 58. When applicable, stability studies shall be performed during design validation.

Article 59. Each manufacturer shall ensure that the design is released for production only after approval by the manufacturer's designated personnel.

Paragraph 1. The designated personnel, referred to in the caput of this article, shall review all records required for the design history record, to ensure that it is complete, and the final design is compatible with the approved plans, before its release.

Paragraph 2. The release referred to in the caput of this article shall be documented, including the date and the in-charge person handwritten or digital signature.

Article 60. Each manufacturer shall establish and maintain procedures for the identification, documentation, validation, review, and approval of design changes prior to their implementation, including a risk assessment as within the risk management process.

Article 61. Each manufacturer shall establish and maintain a design history record for each product.

Sole paragraph. The design history record shall contain or refer to all records necessary to demonstrate that the design was developed in accordance with the design plan approved and approved design plan and this resolution's requirements.

Section II

Device Master Record (DMR)

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Article 62. Each manufacturer shall keep device master records (DMRs).

Article 63. The DMR for each product's type shall include or refer to the following information:

I - product specifications, including the respective designs, composition, formulation, component specifications, software design specifications, and their source codes.

II - production process specifications, including infrastructure specifications, equipment, production methods and instructions, and environmental production specifications.

III - packaging and labeling specifications, including methods and processes used.

IV - inspection and testing procedures, with the respective acceptance criteria.

V - installation, maintenance, and servicing methods and procedures.

CHAPTER V

PROCESS AND PRODUCTION CONTROLS

Section I

General requirements

Article 64. Each manufacturer shall design, conduct, control, and monitor all production processes to ensure that the manufactured products complies with its specifications.

Article 65. Each manufacturer shall establish and maintain process control procedures that describe the process controls necessary to ensure compliance with product specifications.

Sole paragraph. Process controls shall be established at any stage where deviation from product specifications may occur as a result of the manufacturing process.

Article 66. Process controls shall include:

I - documented instructions, standard operational procedures, and methods that define and control the production flow, installation, and maintenance.

II - process parameters' monitoring and control.

III - compliance with technical regulations, standards, or reference codes.

IV - process initiation's release instructions.

Article 67. The company's facilities shall be properly designed to:

I - ensure adequate personnel flow.

II - allow for the execution of all operations.

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III - prevent components, manufacturing materials, intermediate and finished products swaps, or contamination, and ensure the correct handling of these materials.

Article 68. Each manufacturer shall provide suitable environmental conditions for production operations, in a way to prevent contamination or other adverse effects on the product.

Sole paragraph. For the purposes of the provisions in the caput of this article, the correct functioning of the established environmental control systems shall be monitored, and the corresponding records shall be kept.

Article 69. Each manufacturer shall establish and maintain appropriate cleaning and sanitization procedures, as well as a schedule that meets the manufacturing process specifications requirements.

Sole paragraph. Each manufacturer shall ensure that the personnel involved in cleaning activities understand the cleaning and sanitization procedures.

Article 70. Each manufacturer shall ensure that personnel who are in contact with the product or its environment are clean, healthy, and dressed appropriately for the activity to be performed.

Article 71. Any person that, after clinical exam or supervisor observation, might be considered in a health condition that could affect the product, shall be suspended from manufacturing operations until the health condition is considered adequate.

Sole paragraph. Personnel shall be instructed to report to supervisors whenever they have a health condition that could affect the product.

Article 72. Each manufacturer shall restrict food and beverage consumption to specific locations, so it does not affect production areas.

Article 73. Each manufacturer shall establish and maintain procedures to prevent equipment, components, manufacturing materials, intermediate and finished products contamination by cleaning and disinfecting materials, including hazardous substances or contaminants generated by the manufacturing process.

Article 74. A pest control program shall be established, and it shall ensure that, whenever chemical agents are used, such agents do not affect the quality of the product.

Article 75. The waste, chemical effluents and by-products treatment and disposal shall occur in accordance with applicable current regulations.

Article 76. Biological safety standards shall be followed in cases where there is a biological risk.

Article 77. Each manufacturer shall ensure compliance with the applicable standards related to workers' health, including personal protective equipment wearing that is compatible with the executed work processes. Article 78. Each manufacturer shall ensure that all equipment used in the manufacturing process is suitable for its intended use and where correctly designed, built, and installed to facilitate maintenance, adjustment, cleaning, and use.

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Article 79. Each manufacturer shall establish and maintain a program for equipment maintenance, adjustment and, when necessary, cleaning, to ensure that all manufacturing specifications are complied with.

Sole paragraph. The maintenance program shall be easily accessible to the personnel responsible for the equipment maintenance and operation.

Article 80. Maintenance activities shall be recorded, with the completion date and in-charge personnel identification.

Article 81. Each manufacturer shall ensure that any acceptable tolerances or inherent limitations are posted in a visible location or near the equipment requiring periodic adjustments, or readily available to the in-charge personnel of such adjustments.

Article 82. Each manufacturer shall establish and maintain procedures for the 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's quality.

Article 83. Special processes shall be conducted in accordance with established procedures and parameters to ensure compliance with the specifications.

Sole paragraph. The critical parameters of special processes shall be monitored and recorded in the device history record.

Section II

Controls for packaging, labeling, and instructions for use

Article 84. Each manufacturer shall establish procedures for packaging, in a way to protect the product from any alteration, damage, or contamination during the processing, storage, handling, and distribution activities. Article 85. 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.

Article 86. Each manufacturer shall ensure that labels are designed, printed and, where applicable, applied so that they remain legible and adhered to the product during processing, storage, handling, and use.

Article 87. Labels and instructions for use shall not be released for use until an authorized person has examined their compliance with the information they contain.

Paragraph 1. The approval of labels and instructions for use shall be documented in the device history record, including the date, name and handwritten or digital signature of the in-charge person.

Paragraph 2. In case of importers, the approval documentation referred to in Paragraph 1 of this article may be recorded in a specific document instead of the device history record.

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Inspection and tests

Article 88. Each manufacturer shall establish and maintain inspection and testing procedures, or other verification methods, to ensure product compliance with specified requirements throughout the manufacturing process.

Article 89. The product's conformity to the specified requirements must be evaluated upon components and manufacturing materials receiving, as well as during intermediate production steps and at finished product´s final acceptance.

Paragraph 1. The activities result mentioned in the caput of this article must be documented, including the acceptance or rejection conclusion. caput

Paragraph 2. The manufacturer shall delegate the authority and responsibility for carrying out the activities referred to in the caput of this article.

Article 90. Incoming components and manufacturing materials, as well as components, intermediate products, and returned products, shall not be used or processed until their compliance with the established requirements has been verified.

Article 91. Each manufacturer shall establish and maintain retention procedures components, manufacturing materials, intermediate products, and returned products, until inspections, tests, or other established verifications have been performed and documented.

Article 92. Finished products shall only be released when the activities specified in the DMR have been completed and the associated documentation and data have been reviewed by a designated person to ensure that all acceptance criteria have been met.

Sole paragraph. The finished product's release shall be documented, including the date and handwritten or digital signature of the in-charge person.

Section IV

Measuring and testing equipment

Article 93. Each manufacturer shall ensure that all measurement and testing equipment, including mechanical, automated, or electronic equipment, is adequate for its intended purpose and capable of producing valid results.

Article 94. Each manufacturer shall establish and maintain procedures to ensure that measurement and testing equipment is routinely calibrated, inspected, and controlled.

Article 95. Each manufacturer shall establish and maintain calibration procedures that include specific guidelines and precision and accuracy limits, as well as requirements for corrective actions when the precision and accuracy limits are not achieved.

Article 96. Calibration shall be carried out by personnel who have the necessary education, training, practice, and experience.

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Article 97. Measuring and testing equipment shall be identified to allow the calibration status to be determined.

Article 98. Each manufacturer shall establish and maintain calibration standards for measuring equipment that are traceable to official national or international standards.

Sole paragraph. The manufacturer shall establish and maintain its own calibration standard when there is no applicable calibration standard available.

Article 99. Each manufacturer shall ensure that calibration dates, obtained measurements, in-charge person's name and next calibration date records are kept.

Paragraph 1. The manufacturer shall keep the records referred to in the caput of this article.

Paragraph 2. The records referred to in the caput of this article shall be available to the personnel that uses the equipment and to those responsible for its calibration.

Article 100. Each manufacturer shall establish and maintain procedures to ensure that handling, preservation, and storage of test, inspection, and measurement equipment are carried out in a manner that preserves its accuracy and adequacy for use.

Article 101. Each manufacturer shall protect facilities and inspection, test, and measurement equipment, including testing hardware and software, from adjustments that could invalidate calibration.

Article 102. Each manufacturer shall establish procedures to assess the impact of previous measurement results, when non-conformities are found in measurement and testing equipment, and the result of such assessment shall be documented.

Section V

Validation

Article 103. Special processes shall be validated according to previously established protocols and the validation results, including the date and identification of the person responsible for its approval, shall be recorded.

Article 104. Analytical methods, auxiliary systems to support the manufacturing process or environmental control, automated computerized systems, and software that may adversely affect product quality or the quality system shall be validated.

Article 105. Each manufacturer shall establish procedures to verify periodically its processes, analytical methods, auxiliary systems to support the manufacturing process or environmental control, automated computerized systems, and validated software and, when applicable, establish the revalidation frequency.

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Article 106. Each manufacturer shall establish a change control procedure to control changes in auxiliary systems, software, equipment, processes, methods, or other changes that may influence the products quality, including a risk assessment within the risk management process.

Paragraph 1. The procedure referred to in the caput of this article shall describe the actions to be taken, including, when applicable, the need for requalification or revalidation.

Paragraph 2. The changes mentioned in the caput of this article shall be formally requested, documented, and approved before implementation.

CHAPTER VI

HANDLING, STORAGE, DISTRIBUTION, AND TRACEABILITY

Section I

Handling

Article 107. Each manufacturer shall establish and maintain procedures to ensure that inversions (swaps), damage, deterioration, or other adverse effects that affect components, manufacturing materials, intermediate products, finished products, and quality control samples do not occur during any step of handling.

Article 108. Each manufacturer shall establish and maintain procedures to identify components, manufacturing materials, intermediate products, and finished products conformity, to ensure that only those duly approved are used or distributed.

Article 109. The procedures referred to in Article 107 and Article 108 of this regulation shall ensure that components, manufacturing materials, intermediate products, or finished products:

I - are not used or distributed, when their quality or the “fit for use” status has been lost over time.

II - closest to the expiration date are distributed or used first.

III - are not distributed or used if the expiration date was achieved.

Section II

Storage and distribution

Article 110. Each manufacturer shall establish and maintain procedures to identify components, manufacturing materials, intermediate products, finished products, and quality control samples, in a way to prevent inversions (swaps) during storage.

Article 111. Components, manufacturing materials, intermediate products, finished products, and quality control samples shall be stored in physical and environmental conditions that prevent damage, deterioration, or other adverse effects during the period in which they remain in storage.

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Article 112. Each manufacturer shall keep distribution records that include or refer to:

I - the consignee's name and address.

II - the products' identification and quantity shipped, with the shipment date.

III - any numerical control used for traceability.

Section III

Identification, traceability, and non-conformities

Article 113. Each manufacturer shall establish and maintain procedures to identify components, manufacturing materials, intermediate products, and finished products during all stages of storage, production, distribution, and installation, to avoid mixing and to ensure the correct order fulfillment.

Article 114. Each manufacturer shall identify each product unit, lot, or batch with a serial or batch number, and such identification shall be included in the device history record.

Sole paragraph. For distributors, storer, and importer, the identification referred to in the caput of this article may be recorded in a specific document instead of the device history record.

Article 115. Each manufacturer shall establish and maintain procedures to ensure that components, manufacturing materials, intermediate products, finished products, and returned products, which are not in conformity with the established requirements, are not used or installed inadvertently.

Sole paragraph. The procedures referred to in the caput of this article shall contain requirements for the identification, documentation, evaluation, segregation, and disposal of non-conforming components, manufacturing materials, intermediate products, and finished products.

Article 116. The assessment of non-conforming components, manufacturing materials, intermediate products, and finished products shall include the need for investigation and notification of the persons and/ or organizations involved with the non-conformity.

Sole paragraph. The evaluation results and eventual investigations referred to in the caput of this article shall be recorded.

Article 117. Responsibility for review and authority to dispose of components, manufacturing materials, intermediate products, finished products, and non-conforming returned products, shall be defined.

Article 118. The review and disposal process for non-conforming components, manufacturing materials, intermediate products, finished products, and returned products shall be described in an established procedure.

Paragraph 1. The disposal of the products referred to in the caput of this article shall be documented, and a record of the decision's rationale and a handwritten or digital signature of the person or people responsible for the disposal shall be kept.

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Paragraph 2. In case of authorization to use the products referred to in the caput of this article, the decision shall be based on a technically justifiable risk assessment.

Article 119. Each manufacturer shall establish and maintain procedures for the rework, re-inspection, and intermediate or finished products re-evaluation after rework, to ensure that the products meet their original specifications.

Sole paragraph. Activities related to rework and products reassessment referred to in the caput of this article, including issues related to rework activities, shall be documented in the device history record.

CHAPTER VII

CORRECTIVE AND PREVENTIVE ACTIONS

Section I

General requirements

Article 120. Each manufacturer shall establish and maintain procedures to:

I - analyze processes, work operations, quality audit reports, quality records, servicing records, complaints, returned products, and other quality data sources, to identify existing and potential non-conformities causes related to a product, process, or to the quality system.

II - investigate the non-conformities causes related to a product, process, or to the quality system.

III - identify and execute the necessary actions to prevent and correct the occurrence and prevent the non-conformities recurrence.

IV - verify or validate the corrective action effectiveness and ensure that such corrective action does not adversely affect the product.

V - record the activities related to corrective and preventive actions.

VI - ensure that information about quality problems or non-conforming products is properly disseminated amongst those directly involved in maintaining the product's quality or preventing the occurrence of such problems.

VII - submit relevant information about identified quality issues, as well as preventive and corrective actions to the executive management for acquaintance and follow-up, and also to the competent health authority, when applicable.

VIII - determine products' recall and other field actions that are relevant in case of products already distributed.

Paragraph 1. The analysis referred to in item I of this article shall be based on a valid statistical technique to detect recurring quality problems, when applicable.

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Paragraph 2. To comply with the provisions in item IV of this article, any change made shall follow the change control procedures and established validation protocols, when applicable.

Section II

Complains Management

Article 121. Each manufacturer shall establish and maintain procedures for receiving, examining, evaluating, investigating, and filing complaints, ensuring that:

I - complaints are received, documented, examined, evaluated, investigated, and filed by a formally designated department.

II - complaints are notified to the competent health authority, when applicable.

III - complaints are examined to verify the need for an investigation.

IV - all complaints involving a possible product non-conformity are examined, evaluated, and investigated.

V - when an investigation is conducted, records containing the following information are kept:

a) product’s name.

b) complaint’s date of receipt.

c) any control number used.

d) complainant’s name, address, and telephone number.

e) nature of the claim.

f) investigation date and results, including actions taken.

Paragraph 1. When the investigation referred to in item III of this article is not conducted, the department shall record the reason why the investigation was not carried out and who was responsible for the decision of not to investigate.

Paragraph 2. When any complaint referred to in item IV of this article is related to death, injury, or threat to public health, it shall be immediately examined, evaluated, and investigated.

Section III

Quality audit

Article 122. Each manufacturer shall conduct and document quality audits to assess the quality system's compliance with the established requirements.

Article 123. Quality audits shall be conducted by trained personnel, in accordance with the established audit procedures, and by who have no direct responsibility for the process being audited.

Sole paragraph. Those responsible for conducting the quality audit cannot have direct responsibility for the process being audited.

Article 124. Those responsible for the audited areas shall be notified about identified non-conformities.

CHAPTER VIII

INSTALLATION AND SERVICING

Article 125. Each manufacturer shall establish and maintain adequate instructions and procedures for the correct product installation.

Article 126. During the product installation, either by the manufacturer or its authorized representative, there shall be a verification whether the product's operation parameters meet the criteria established.

Sole paragraph. The verification results referred to in the caput of this article shall be recorded.

Article 127. Each manufacturer shall ensure that installation instructions and procedures are distributed with the product or are otherwise available to the person responsible for the product installation.

Article 128. Each manufacturer shall establish and maintain procedures to ensure that finished products submitted to servicing by the manufacturer or his representative meet the specifications.

Article 129. Each manufacturer shall establish and maintain procedures to ensure that servicing records are maintained and include the following information:

I - the product submitted to servicing.

II - the control number used.

III - the servicing date.

IV - the servicing provider´s identification.

V - the description of the service performed.

VI - the inspections and tests results for the service´s approval.

Article 130. Each manufacturer shall evaluate the servicing records periodically.

Sole paragraph. In the cases where the evaluation referred to in the caput of this article identifies failure trends, which represent danger, or records involving death or serious injury, a corrective/ preventive action shall be initiated in accordance with the requirements in this regulation.

CHAPTER IX

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STATISTICAL TECHNIQUES

Article 131. Each manufacturer shall establish and maintain procedures to identify valid statistical techniques to verify the quality system performance and the process ability to meet the established specifications.

Article 132. Sampling plans shall be registered and be based on valid statistical logics.

Article 133. Each manufacturer shall establish and maintain procedures to ensure that sampling methods are suitable for their intended use and that they are regularly reviewed.

Article 134. The sampling plans review shall consider the occurrence of product non-conformities, quality audit reports, complaints, and other indicators.

CHAPTER X

FINAL PROVISIONS

Article 135. The documentation that proves compliance with the requirements established in this regulation shall be available whenever requested by health surveillance authorities.

Article 136. Failure to comply with the requirements established by this regulation shall be considered an infraction of health regulations, pursuant to Law No. 6,437 of 20 August 1977 and its updates, without prejudice to the applicable civil, administrative, and criminal liabilities.

Article 137. The following regulations are hereby revoked:

I - Collegiate Board Resolution – RDC No. 16 of 28 March 2013, published in the Federal Official Gazette No. 61 of 1 April 2013, Section 1, page 75.

II - Normative Instruction – IN No. 8 of 26 December 2013, published in the Federal Official Gazette No. 252 of 30 December 2013, Section 1, page 758.

Article 138. This Resolution enters into force on May 2, 2022.

ANTONIO BARRA TORRES

Director-President