

COLLEGIATE BOARD RESOLUTION – RDC NO. 362 OF 27 MARCH 2020

Provides for the criteria for Good Manufacturing Practices certification and institutes the inspection program for international manufacturers of active pharmaceutical ingredients.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 15, items III and IV, and Article 7, items III and IV of Law no. 9,782 of 26 January 1999, and item V, paragraphs 1 and 3 of Article 53 of the Internal Regulation approved by the Collegiate Board Resolution – RDC no. 255 of 10 December 2018, adopts the following Collegiate Board Resolution, as decided upon in a meeting held on 25 March 2020, and I, Deputy Director-President, determine its publication.

CHAPTER I

INITIAL PROVISIONS

Section I

Objective and Scope

Article 1 This Resolution provides for the criteria for the Good Manufacturing Practices Certification (GMPC) for international manufacturers of active pharmaceutical ingredients (APIs) obtained from plant extraction, chemical synthesis, classic fermentation, or semi-synthesis, and institutes the API international inspection program.

Section II

Definitions

Article 2 For the purposes of this Resolution, the following definitions apply:

I – manufacturer of active pharmaceutical ingredients: all establishments involved in API manufacture as of the introduction of starting materials; and

II – conclusive report: report that clearly describes the status of the company regarding compliance with good manufacturing practices, in accordance with the regulations referred to in the report scope.

CHAPTER II

PETITION DOCUMENTS

Article 3 All petitions for Good Manufacturing Practices Certification provided for in this Resolution must be submitted with the following documents:

I – specific petition form for API Good Manufacturing Practices certification, completed accordingly;

II – certificate or document that proves the compliance with the Good Manufacturing Practices in force, issued by the health authority of the country where the manufacturing establishment is installed (if the certificate has not been issued in English, Spanish, or Portuguese, a copy of the original certificate and a translated version must be sent);

III – plant master file (PMF) of the company to be inspected, including at least:

general information: types of products manufactured by the company, including information on non-pharmaceutical ingredients and products, handling and production of highly active, sensitizing, toxic, or dangerous substances, describing how they are produced (whether in dedicated facilities, separate buildings, among other relevant information);

type and capacity of the main equipment used in the manufacture of the pharmaceutical ingredients requested;

enlarged-scale colored blue prints of the buildings, with subtitles and identification of the areas;

production flowchart for each pharmaceutical ingredient requested;

water system diagram; and

air system diagram.

IV – latest full report(s) generated from product quality review (PQR) or manufacturing process validation for the active pharmaceutical ingredient(s) requested, when the PQR is not available;

V – list of all regulatory inspections conducted in the establishment subject to certification in the last 3 (three) years, including the period of each inspection, name of the authority responsible for its conduction, conclusion and details of any resulting regulatory action;

VI – list of all ingredients manufactured in the establishment subject to certification, including those that are or will be exported to Brazil;

VII – declaration indicating in which countries the ingredients petitioned for certification are regulated; and

VIII – when available, copy of the conclusive inspection report issued by the health authority of a country acknowledged by Anvisa as equivalent regarding the measures and controls applied to prove compliance with API good manufacturing practices, together with a statement by the API manufacturer attesting that there is no divergence in the manufacture and controls adopted for the API that will be supplied for the manufacture of medicinal products intended for the Brazilian market.

Sole paragraph. Document submission must comply with the provisions in the specific legislation in force regarding petitioning procedures.

Article 4 The manufacturing establishment requesting certification may send directly to Anvisa the documents referred to in items III to VIII of Article 3, as long as they are appropriately identified and attached to the related process.

Paragraph 1 The period to submit the documents referred to in the caption of this article is up to 30 (thirty) days after the certification petition submission.

Paragraph 2 At the end of the period provided for in Paragraph 1 of this article, the absence of the compulsory documents listed in Article 3 of this Resolution will lead to petition rejection.

CHAPTER III

GOOD MANUFACTURING PRACTICES CERTIFICATION

Article 5 Decision on the certification provided for in this Resolution will depend on the verification of the effective compliance with the requirements in the legislation in force on API Good Manufacturing Practices (GMP), through one of the following measures:

I – assessment of the documents listed in Article 3 of this regulation for companies inspected by a health authority of a country acknowledged by Anvisa as equivalent regarding the measures and controls applied to prove compliance with API GMP;

II – assessment of the documents listed in Article 3 of this regulation and risk analysis conduction to support the issue of a GMPC; or

III – assessment of inspection report issued by Anvisa as a result of *in loco* inspection, motivated by risk analysis conduction or the absence of an inspection report in the terms of item VIII of article 3 of this Resolution.

Paragraph 1 Sterile API manufacturers must also comply with the GMP technical regulation for sterile medicinal products from the stage of sterilization.

Paragraph 2 Anvisa may require a GMPC request for API intermediates.

Article 6 For certification through the mechanism provided for in item I of Article 5 of this Resolution, inspection reports must include the API(s) object of certification petition and allow for the conclusion that the establishment complies with the GMP.

Paragraph 1 In case there are non-conformities listed in the inspection reports, plans of action assessed and deemed satisfactory by the report issuer, or evidence of conclusion of corrective actions, must be presented.

Paragraph 2 If the inspection report does not include the API(s) object of certification petition, the certification analysis shall follow the mechanism provided for in item II of Article 5 of this Resolution.

Article 7 Decision on certification through the mechanism provided for in item II of Article 5 of this Resolution shall be made through a risk analysis tool, which considers the result from the assessment of documents listed in Article 3 of this Resolution, the manufacturing unit complexity, the technologies involved, and the intrinsic risk of ingredients.

Article 8 Certification through the mechanism provided for in item III of Article 5 shall result from elimination of the possibilities provided for in items I and II of the referred article of this Resolution.

CHAPTER IV

INSPECTION PROGRAM

Article 9 Anvisa may, at any time, conduct routine health inspection or health inspection resulting from an investigation of a denunciation or possible irregularities in any manufacturer of APIs used in medicinal products in Brazil, regardless of the Certification process.

Paragraph 1 The certification issued based on the documentation provided for in items I and II of Article 5 of this Resolution does not exempt the company from receiving *in loco* inspection by Anvisa, at any time, even during the validity of the Good Manufacturing Practices Certificate granted.

Paragraph 2 Refusal to receive Anvisa inspection will lead to a health administrative process, with possible suspension of import, commercialization, and use, as well as possible determination of withdrawal of the products involved.

CHAPTER V

FINAL PROVISIONS

Article 10 Failure to comply with the provisions in this Resolution constitutes a health infraction, in the terms of Law no. 6,437 of 20 August 1977, without prejudice to the applicable civil, administrative, and criminal responsibilities.

Article 11 The administrative procedures to grant the Good Manufacturing Practices Certification are established in Collegiate Board Resolution – RDC no. 39 of 14 August 2013 and its updates.

Article 12 Up to 1 March 2021, only GMPC petitions by companies that have requested the Active Pharmaceutical Ingredient Dossier Adequacy Letter (*Carta de Adequação de Dossiê de Insumo Farmacêutico Ativo – CADIFA*, in Portuguese), in the terms of Collegiate Board Resolution – RDC no. 359 of 27 March 2020, or a registration of API under analysis at Anvisa, in the terms of Collegiate Board Resolution – RDC no. 57 of 17 November 2009, shall be covered by this Resolution.

Article 13 This Resolution enters into force on 3 August 2020.

ANTONIO BARRA TORRES