

COLLEGIATE BOARD RESOLUTION - RDC NO. 672 OF 30 MARCH 2022

Provides for the criteria for Good Manufacturing Practices Certification and establishes the inspection program for international establishments that manufacture active pharmaceutical ingredients.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency (Anvisa), in the use of the attributions vested in it under Article 15, items III and IV of Law no. 9,782 of 26 January 1999, and considering item VI, Paragraph 1 of Article 187 of the Internal Regulation approved by Collegiate Board Resolution – RDC no. 585 of 10 December 2021, as decided upon in Extraordinary Meeting – Rextra no. 6 held on 30 March 2022, adopts the following Resolution, and I, 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 establishments that manufacture Active Pharmaceutical Ingredients (APIs) obtained through plant extraction, chemical synthesis, classical fermentation, or semi-synthesis and establishes the international API inspection program.

Section II

Definitions

Article 2. For the purposes of this Resolution, the following definitions are applicable:

I – active pharmaceutical ingredient manufacturer: all establishments involved in API manufacture as from the introduction of starting material; and

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

CHAPTER II

APPLICATION DOCUMENTS

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

I – specific application form for Good API Manufacturing Practices Certification, duly completed;

II – certificate or document proving compliance with current Good Manufacturing Practices, issued by the health authority of the country where the manufacturing establishment is located;

III – site master file (SMF) of the company to be inspected, containing at least:

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

b) type and capacity of the main equipment used in the manufacture of the pharmaceutical ingredient requested;

c) floor plans of the buildings, on a large scale, in color, with captions and identification of the areas;

d) production flowchart of each pharmaceutical ingredient requested;

e) water system diagram; and

f) air system diagram.

IV – last complete report(s) generated of product quality review (PQR) or validation of manufacturing process for the active pharmaceutical ingredient(s) applied for, when PQR is not available;

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

VI – a list of all ingredients manufactured at the establishment subject to certification, with an indication of those that are or will be exported to Brazil;

VII – a statement indicating the countries in which the ingredients requested in the application for certification are regularized; and

VIII – when available, copy of the conclusive inspection report issued by the country's health authority recognized by Anvisa as equivalent regarding the measures and controls used to confirm the Good API Manufacturing Practices, together with the statement from the API manufacturing company 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.

Paragraph 1. The protocol of the documents referred to in this article must comply with the provisions in the specific regulations in force for application procedures.

Paragraph 2. In case the certificate referred to in item II of this article has not been issued in English, Spanish, or Portuguese, a copy of the original certificate and a translated version must be submitted.

Article 4. The manufacturing establishment that is the object of certification may send the documents referred to in items III to VIII of Article 3 of this Resolution directly to Anvisa, provided they are duly identified and as an addendum to the related process.

Paragraph 1. The deadline to protocol the documents referred to in the caption of this article is up to thirty (30) days after the date of certification application protocol.

Paragraph 2. At the end of the term provided for in Paragraph 1 of this article, the absence of the protocol of the mandatory application documents listed in Article 3 of this Resolution shall result in application rejection.

CHAPTER III

GOOD MANUFACTURING PRACTICES CERTIFICATION

Article 5. The decision regarding the certification provided for in this Resolution depends on verification of effective compliance with the requirements recommended by the Good API Manufacturing Practices standards in force, through one of the following measures:

I – analysis of the documents listed in Article 3 of this Resolution for companies inspected by the country's health authority recognized by Anvisa as equivalent regarding the measures and controls used to confirm the Good API Manufacturing Practices;

II – analysis of the documents listed in Article 3 of this Resolution and performance of risk assessment supporting the issuance of the Good Manufacturing Practices Certification; or

III – analysis of the inspection report issued by Anvisa as a result of on-site inspection, prompted by the conduction of risk assessment or by the absence of inspection report in accordance with item VIII of Article 3 of this Resolution.

Paragraph 1. Manufacturers of sterile APIs must additionally comply with the GMP technical regulation for sterile medicinal products as from the sterilization stage.

Paragraph 2. Anvisa may determine, upon requirement, the request for Good Manufacturing Practices Certification for API intermediates.

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

Paragraph 1. In the event of nonconformities listed in the inspection reports, action plans analyzed and deemed satisfactory by the issuer of the report or proof of completion of corrective actions must be submitted.

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

Article 7. The decision regarding the certification through the mechanism provided for in item II of Article 5 of this Resolution must be made by means of a risk assessment tool, which considers the result of the analysis of the documents listed in Article 3 of this Resolution, the complexity of the manufacturing site, the technologies involved, and the intrinsic risk of the inputs.

Article 8. The certification through the mechanism provided for in item III of Article 5 must result from the 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, carry out routine health inspections or health inspections to investigate complaints 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 on-site inspection by Anvisa at any time, even during the validity of the Good Manufacturing Practices Certificate granted.

Paragraph 2. Refusal to receive an inspection by Anvisa shall result in the opening of a health administrative process, and importation, commercialization, and use of the products involved may be suspended. Anvisa may also determine the recall of such products.

CHAPTER V

FINAL PROVISIONS

Article 10. The administrative procedures to grant the Good Manufacturing Practices Certification are established in Collegiate Board Resolution – RDC no. 497 of 20 May 2021, or any other Resolution that may come to succeed it.

Article 11. Failure to comply with the provisions contained in this Resolution constitutes a health infraction, in accordance with Law No. 6,437 of 20 August 1977, without prejudice to the applicable civil, administrative, and criminal liabilities.

Article 12. Collegiate Board Resolution – RDC no. 362 of 27 March 2020, published in Federal Official Gazette no. 63 of 1 April 2020, Section 1, page 100, is hereby revoked.

Article 13. This Resolution enters into force on 2 May 2022.

ANTONIO BARRA TORRES