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**RESOLUTION OF THE COLLEGIATE BOARD - RDC No. 205 OF DECEMBER 28, 2017**

**(Published in DOU No. 249, of December 29, 2017)**

Establishes a special procedure for approval of clinical trials, certification of good manufacturing practices and registration of new drugs for the treatment, diagnosis or prevention of diseases rare.

The **Collegiate Board of the National Health Surveillance Agency**, in the use of the attribution conferred by art. 15, III and IV, combined with art. 7, III, and IV, of Law nº 9.782, of January 26, 1999, and to art. 53, V, §§ 1 and 3 of the Internal Regulation approved pursuant to Annex I of the Resolution of the Collegiate Board - RDC No. 61, of February 3, 2016, resolves to adopt the following Resolution of the Collegiate Board, as resolved at a meeting held on December 12, 2017, and I, the Chief Executive Officer, determine its publication.

## **CHAPTER I**

### **Initial Provisions**

Art. 1 The special procedure is approved for:

I - approval of clinical trials to be carried out in Brazil to evaluate drugs for rare diseases;

II – certification of good manufacturing practices applicable to medicines for rare diseases; and

III – sanitary registration of new drugs for rare diseases.

Art. 2nd This resolution applies to new drugs for rare diseases.

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

I - rare disease: one that affects up to sixty-five people in every one hundred thousand individuals, as defined by the National Policy for Comprehensive Care for People with Rare Diseases, based on official national data or, when non-existent, on data published in technical documentation -scientific;

II - new medicine: one with an active pharmaceutical ingredient (API) unprecedented in the country for the specific rare disease;



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III - serious debilitating condition: disease or condition associated with irreversible morbidity or a high probability of death, unless the course of the disease is interrupted; and

IV - technical-scientific documentation: documentation based on bibliographical references, indexed scientific publication, Brazilian or international, and technical publication, such as those issued by health and government authorities.

## **CHAPTER II**

### **General Provisions**

Art. 4 So that the criteria of this resolution can be used, the request for approval of clinical trials, certification of good manufacturing practices and registration of a new drug must refer to a drug for a rare disease.

Single paragraph. A medicine for a rare disease will be considered one that has the purpose of treating, diagnosing or preventing the rare disease and that:

I – is used in a serious debilitating condition; and

II – proposes to change in a clinically significant way the evolution or enable disease remission.

Art. 5th When filing the petition for approval of clinical trials and registration of a new drug, the company must inform whether the request refers to a drug for a rare disease.

Art. 6 For clinical trials to be carried out in Brazil, when the subject of the petition refers to the Clinical Drug Development Dossier (DDCM), the analysis, according to the criteria of this resolution, applies only to the petitions submitted and analyzed together with the initial request.

Single paragraph. In order for specific clinical trial dossiers and substantial modifications by protocol inclusion, subsequently linked to a DDCM, to be evaluated in accordance with this resolution, the company must inform whether the request refers to a drug for a rare disease at the time of the protocol.

Art. 7 Petitions for approval of clinical trials and registration of a new drug referring to a drug for a rare disease must be accompanied by the following documentation:

I - description of the rare disease for which the drug will be indicated;



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II - relevance of the medicine for the treatment, diagnosis or prevention of the disease;

III - global and national data on the prevalence and incidence of the rare disease for which the medicine will be indicated; and

IV - supporting document of drug designation for rare disease by another regulatory authority, when available.

Art. 8 If it is not confirmed during the technical analysis of the petitions for approval of clinical trials and registration of a new medicine that the request refers to a medicine for a rare disease, the petition will be rejected.

### Section I

#### The approval of clinical trials to be carried out in Brazil

Art. 9 The submission of a clinical drug development dossier (DDCM), specific clinical trial dossier, substantial modification by inclusion of a protocol must be carried out in accordance with specific legislation regarding the performance of clinical trials with drugs in Brazil, plus the documentation described in art. 7th.

Single paragraph. The approval of clinical trials to be carried out in Brazil with a drug for a rare disease can be granted without presenting a substantiated opinion from the Research Ethics Committee (CEP).

Art. 10. The following procedures must be followed for purposes of approval of clinical trials to be carried out in Brazil with drugs for diseases rare:

~~I - request by the interested party for a pre-submission meeting for the presentation of the DDCM, specific clinical trial dossier or substantial modification due to protocol inclusion;~~

~~- request for a pre-submission meeting, if the interested party deems it necessary, for the presentation of the DDCM, specific clinical trial dossier or substantial modification due to protocol inclusion;~~

~~(Wording given by Resolution -~~

~~RDC No. 763, of November 25, 2022)~~

I - request for a pre-submission meeting, if the interested party deems it necessary, for the presentation of the DDCM, specific clinical trial dossier or substantial modification due to protocol inclusion;

(Wording given by Resolution -

RDC No. 763, of November 25, 2022, republished in DOU No. 226, of December 2, 2022)



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~~II - holding the pre-submission meeting for the presentation of the DDCM, specific clinical trial dossier or substantial modification by inclusion of the protocol, within sixty days after the request by the interested party;~~

~~\* - holding a pre-submission meeting, if the interested party deems it necessary, for the presentation of the DDCM, specific clinical trial dossier or substantial modification by inclusion of the protocol, within sixty days after the request by the interested party; (Wording provided by Resolution - RDC No. 763, of November 25, 2022)~~

" - holding a pre-submission meeting, if the interested party deems it necessary, for the presentation of the DDCM, specific clinical trial dossier or substantial modification by inclusion of the protocol, within sixty days after the request by the interested party; (Wording provided by Resolution - RDC No. 763, of November 25, 2022, republished in DOU No. 226, of December 2, 2022)

III - submission of DDCM, specific clinical trial dossier or substantial modification by inclusion of protocol, by the interested party, using a specific subject code;

IV - evaluation of the DDCM, specific dossier of clinical trial or substantial modification by inclusion of protocol, by Anvisa, within thirty days after submission, with issuance of notification of requirement or statement of conclusion;

V - holding a meeting, if the interested party deems it necessary, for discussion of the requirements;

VI - fulfillment of the requirements by the interested party within thirty days after reading of the notification; and

VII - assessment of compliance with the requirements, by Anvisa, within thirty days after submission to the agency.

Art. 11. Secondary petitions, referring to DDCM, specific dossier of clinical trial or substantial modification by inclusion of protocol evaluated according to the criteria of this resolution, will have the same treatment.

## Section II

### Certification of good manufacturing practices

Art. 12. The request for certification of good manufacturing practices must be carried out in compliance with the specific legislation regarding the procedures for granting certification of good manufacturing practices.



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Art. 13. The following procedures must be followed for certification purposes of good manufacturing practices:

I - request for certification of good manufacturing practices for the plants where the medicine will be produced by the interested party; and

II – publication of the decision regarding the certification of good manufacturing practices, by Anvisa, within one hundred and twenty days after the submission of the certification request.

**Section III**

**from the registry**

Art. 14. The request for registration of a new drug for a rare disease must be carried out in accordance with specific legislation for each regulatory category, plus the documentation described in art. 7th.

§ 1 In the case of drugs already registered in other countries, a technical report on the evaluation of the drug issued by the respective regulatory authorities, when available, must be presented.

§ 2 The submission of the registration request may be accepted with the presentation of the inspection request protocol for the purpose of issuing the certificate of good manufacturing practices.

§ 3 When submitting the registration request, a long-term stability study in progress may be accepted, conducted in accordance with the temperature and humidity conditions required by specific legislation, with the results that are available up to the date of the protocol.

§ 4 Safety and efficacy reports may be accepted with the presentation of completed phase II studies and phase III studies in progress, or without the presentation of phase III clinical studies, when carrying out these studies is not feasible.

§ 5 In the case of imported drugs, the suppression of quality control in Brazil is permitted, provided that the quality control is carried out by the drug manufacturer and a summary report of the qualification of the operation of the transport system is presented.

§ 6 The registration request may be filed in accordance with the *Common Technical Document* (CTD) format, provided for in the M4 guide of the *International Conference on Harmonization* (ICH).



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Art. 15. Submission of supplementary data and additional evidence after granting the registration may be accepted, through the signature of a term of commitment between Anvisa and the company requesting the registration.

Single paragraph. Failure to fulfill the commitments assumed may result in the cancellation of the drug registration.

Art. 16. In cases where the company requesting the registration does not have the complete clinical development of the drug for rare disease with new active pharmaceutical ingredient (API) in the country, a clinical report containing:

I - safety and efficacy data based on bibliographical references from indexed scientific publications, Brazilian or international;

II - *in vitro* or *in vivo* comparability studies using international comparator medicine;

III - relative bioequivalence/bioavailability studies using international comparator medicine, when applicable;

IV - leaflet and public opinion on the evaluation of the comparator drug international issued by regulatory authority;

V - pharmacovigilance plan or risk minimization plan, when applicable, in accordance with specific legislation; and

~~VI - updated pharmacovigilance report of the drug, in the case of drugs marketed in other countries.  
(Revoked by Resolution - RDC No. 406, of July 22, 2020)~~

§ 1 For the purposes of registration under the condition provided for in the *caput*, Anvisa may allow the use of an international comparator drug registered with another regulatory authority when:

I - there is an agreement or agreement entered into with Anvisa, and there is similarity of sanitary measures between the regulatory authority and Anvisa; and

II - registration of the comparator drug has been in effect for at least ten years in the regulatory authority and the drug is being marketed.

§ 2 Before submitting the registration, the company must consult Anvisa regarding the proposed international comparator drug to be used.



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§ 3 The leaflet of the drug to be registered with Anvisa must have the same indications, route of administration and dosage as the leaflet of the international comparator drug, and may only differ in terms of additional safety information.

§ 4 The medicine registered under the terms of the *caput* cannot be elected to reference medicine.

§ 5 The provisions of the *caput* do not apply to biological products.

Art. 17. Anvisa may allow the use of an international comparator medicine registered in another regulatory authority, under the terms provided for in § 1 of art. 16 in the case of a request for registration of a rare disease drug with the same APIs as an already registered drug.

Single paragraph. Medications that fit the situation described in the *caput* will only follow the criteria of this resolution with regard to the possibility of using an international comparator medication, not applying the other special procedures.

Art. 18. The following procedures must be followed for the purpose of registering new drug for rare disease:

I - request for a pre-submission meeting by the interested party to present the product;

II - holding the pre-submission meeting for the presentation of the product, within 60 days after the request by the interested party;

III - submission of the registration request by the interested party, using a specific subject code, within thirty days after the pre-submission meeting;

IV - evaluation of the request for registration of the medicine by Anvisa within sixty days after submission, with issuance of notification of requirement or conclusive opinion;

V - holding a meeting, if the interested party deems it necessary, for discussion of the requirements;

VI - compliance with the requirements, by the interested party, within thirty days after reading of the notification; and

VII - assessment of compliance with the requirements, by Anvisa, in up to forty-five five days after submission to the agency.

**This text does not replace the one(s) published in the Official Gazette.**



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§ 1 The absence of a request for a pre-submission meeting, pursuant to item I of the *caput*, will prevent the analysis of the registration request according to this resolution.

§ 2 In the case of drugs for national development, the request for a pre-submission meeting may be held at any time, provided that registration with another regulatory authority has not been requested.

§ 3 In the case of imported drugs, the request for a pre-submission meeting must be carried out within sixty days after the first request for registration in another regulatory authority, unless it is not attributable to the interested company.

§ 4 In cases where registrations of drugs for rare diseases have been requested or if the drugs are already registered with other authorities prior to the publication of this resolution, requests for pre-submission meetings provided for in item I of the *caput* will be accepted at *any time* .

### CHAPTER II

#### Final and Transitional Provisions

~~Art. 19. Companies that submit a request for registration of new drugs according to the criteria of this resolution must submit a dossier defining the maximum price concomitantly with the registration request protocol.~~

Art. 19. Companies that submit a request for registration of new drugs according to the criteria of this resolution, will have a period of up to 30 (thirty) days to submit the maximum price definition dossier, counted from the first business day after the publication of the registration of the medicine. **(Wording provided by Resolution - RDC No. 293, of July 15, 2019)**

Art. 20. Medicines registered through the criteria of this resolution will have a period of up to three hundred and sixty-five days to be marketed, counted from the date of publication of the registration.

Art. 21. For requests for registration of new drugs for rare diseases, the provisions of art. 2 of the Resolution of the Collegiate Board - RDC No. 20, of April 10, 2013.

Art. 22. Item "e" of item IV of art. 3, and item "e" of item VIII of art. 38 of the Resolution of the Collegiate Board - RDC No. 9, of February 20, 2015.





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Art. 23. § 2 of art. 47 of the Resolution of the Collegiate Board - RDC No. 9, of 2015 enters into force with the following wording:

“Art. 47. ....

.....

§ 2 The petition for substantial amendments must contain the new protocol.

....." (NR)

Art. 24. Failure to comply with the provisions contained in this resolution constitutes a sanitary infraction, under the terms of Law No. 6,437, of August 20, 1977, without prejudice to applicable civil, administrative and criminal responsibilities.

Art. 25. This Resolution enters into force in 60 (sixty) days from the date of publication.

**JARBAS BARBOSA DA SILVA JR.**