

BRAZILIAN HEALTH SURVEILLANCE AGENCY

COLLEGIATE BOARD

RDC RESOLUTION # 205, DECEMBER 28, 2017

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

The Collegiate Board of Brazilian Health Surveillance Agency, in the use of the assignment that confers the art. 15. III and IV together with the Art. 7, III, and IV, of Law n. 9,782, of 26 January 1999, art. 53, V, §§ 1 and 3 of internal rules adopted pursuant to Annex I of resolution of the Board - RDC n 61 of 3 February 2016, resolves to adopt the following Resolution of the Board, as discussed in the meeting held on 12 December 2017, and I, the CEO, determine its publication.

CHAPTER I – INITIAL PROVISIONS

Art.1 It is approved the special procedure to:

- I - consent of clinical trials to be conducted in Brazil for the evaluation of drugs for rare diseases;
- II - Certification for good manufacturing practices applicable to drugs for rare diseases; and
- III - health registration of new drugs for rare diseases.

Art. 2 This resolution is applied to new drugs for rare diseases.

Art. 3 For the purpose of this resolution is adopted the following definitions:

I - rare disease: one that affects up to sixty-five people in every one hundred thousand individuals, as defined by the National Policy of Integral care to people with rare diseases, based on official national data or, when absent, in data published in scientific-technical documentation;

II - new drug: one with Active Pharmaceutical Ingredient (API) unprecedented in the country for a specific rare disease;

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

IV - technical-scientific documentation: documentation based on bibliographic references, scientific publication indexed, Brazilian or international, and technical publishing, as issued by sanitary authorities and governmental.

CHAPTER II – General Provisions

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

Sole Paragraph. Will be considered drug for a rare disease that has the goal to treat, diagnose or prevent the rare disease and also:

I - to be used in serious debilitating condition; and

II – it proposes to alter into a clinically significant evolution or enable the remission of the disease.

Art. 5 At the time of the protocol of the petition of consent of clinical trials and registration of a new drug, the company must inform if the request is referred to a drug for a rare disease.

Art. 6 For clinical trials to be carried out in Brazil when the topic of petition is referring the dossier of clinical development of drug (DDCM), the analysis, according to the criteria of this resolution only applies to petitions submitted and analyzed along the initial request.

Sole Paragraph. For that specific dossiers of clinical trials and substantial alterations by the inclusion of protocol, furtherly bound to a DDCM, be assessed in accordance with this resolution, the company should inform at the time of the protocol if the request is referred to a drug for a rare disease.

Art. 7 The petitions of consent of clinical trials and registration of new drug related to drug for rare disease should be increased by the following documentation:

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

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

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

IV - an evidentiary document of appointment of drug for rare disease by another regulatory authority, when available.

Art. 8 in case it is not confirmed during the technical examination of petitions of consent of clinical trials and registration of new drug that the request refers to drug for rare disease, the petition will be rejected.

Section I – The consent of clinical trials to be carried out in Brazil.

Art.9 The dossier's submission of clinical development of drug (DDCM), a specific dossier of clinical trial, substantial modification by inclusion of protocol must be performed according to specific legislation referred to the carry out of clinical trials with drugs in Brazil, in addition to the documentation described in art. 7.

Sole Paragraph. The acquiescence of clinical trials to be carried out in Brazil with drug for rare disease may be granted without presentation of opinion embodied by the Committee on Ethics in Research (CEP).

Art.10 The following procedures should be followed for the purpose of consent of clinical trials to be conducted in Brazil with drugs for rare diseases:

I - Request by the interested party meeting of pre-submission to submission of DDCM, specific dossier of clinical trial or substantial modification by inclusion of protocol;

II – Carry out of pre-submission to submission of DDCM, specific dossier of clinical trial or substantial modification by inclusion of protocol, within sixty days after the request by the interested party;

III - Submission of DDCM, specific dossier of clinical trial or substantial modification by inclusion of protocol, by the person interested, through use of code of specific subject;

IV - Assessment of DDCM, specific dossier of clinical trial or substantial modification by Inclusion of protocol, by Anvisa, within thirty days after the submission, with the emission of the notification requirement or manifestation of completion;

V – Carry out of meeting, if the interested part sees it necessary, to discuss the requirements;

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

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

Art.11 The secondary petitions relating to DDCM, a specific dossier of clinical trial or substantial modification by inclusion of protocol assessed according to the criteria of this resolution, will have the same treatment.

Section II –Good Manufacturing Practices Certification

Art.12 The request for certification of good manufacturing practices must be performed attending to the specific legislation relating to the procedures for the granting of certification for good manufacturing practices.

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

I - request for certification of good manufacturing practices for plants in which the drug will be produced by the interested party; and

II - Publication of the decision referred to the certification of good manufacturing practices, by Anvisa, within one hundred and twenty days after the submission of the certification request.

Section III – Registry

Art.14 The request for registration of a new drug for rare disease should be performed according to specific legislation for each regulatory class, plus the documentation described in art. 7.

§ 1 in the case of drugs already registered in other countries, must be presented technical report of drug's assessment issued by the respective regulatory authorities, when available.

§ 2 The submission of a registration request can be accepted with presentation of protocol inspection request for emission of the certificate of good manufacturing practices.

§ 3 in the submission of a registration request can be accepted study of long-term stability in progress, conducted in accordance with the conditions of temperature and humidity required by a specific legislation, with the outcome that are available until the date of the protocol.

§ 4 can be accepted reports of safety and effectiveness with the presentation of studies phase II completed and phase III studies in progress, or without the presentation of phase III clinical studies, when the realization of these studies is not feasible.

§ 5 in the case of imported drugs, it is permitted the suppression of quality control in Brazil, since it is performed quality control by the manufacturer of the drug and presented summary report of qualification of operation of the transport system.

§ 6 The registration request can be instructed in accordance with the format Common Technical Document (CTD), defined in the guide M4 of the International Conference on Harmonization (ICH).

Art.15. May be accepted for presentation of complementation of data and additional evidence subsequent to the granting of the registration, by means of signing of term of commitment between the Anvisa and the requesting company registry.

Sole Paragraph. The non-fulfilment of the commitments may imply the cancellation of the registration of drugs.

Art.16. In cases in which the requesting company of the record does not have the full clinical development of the drug for a rare disease with active pharmaceutical ingredient (API) new in the country, it may be presented clinical report containing:

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

II - studies of comparability in vitro or in vivo using drug international comparator;

III - Bioequivalence/bioavailability studies on using drug international comparator, when applicable;

IV – Package leaflet and assessment of public opinion of international comparator drug issued by the regulatory authority;

V - the Pharmacovigilance Plan or risk minimization plan, where applicable, in accordance with the specific legislation; and

VI - updated pharmacovigilance report of the drug, in the case of drugs commercialized in other countries.

§ 1 For the purposes of registration in the condition described in the caput, the Anvisa may allow the use of international comparator drug registered in another regulatory authority when:

I - there is agreement or agreement concluded with Anvisa, and there is a similarity of sanitary measures between the regulatory authority and Anvisa; and

II - the registration of comparator drug is valid for at least ten years in regulatory authority and the drug is being commercialized.

§ 2 prior to submission of registration, the company must consult the Anvisa regarding to proposed international comparator drug to be used.

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

§ 4 The registered drug in accordance with the caput cannot be elected as the reference drug.

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

Art.17. The Anvisa may allow the use of international comparator drug registered in another regulatory authority, in accordance with the provisions described in § 1 of art.16 in case of a request for registration of drug for rare disease with same APIs of drug already registered.

Sole Paragraph. The drugs that fall into the situation described in the caput, only follow the criteria of this resolution with regard to the possibility of use of international comparator drug, not applying the other special procedures.

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

I - meeting request for pre-submission by the interested party for presentation of the product;

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

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

IV - assessment of the request for registration of drug by Anvisa within sixty days after submission, with the emission of the notification requirement or conclusive opinion;

V – Carry out of meeting, if the interested individual finds it necessary, to discuss the requirements;

VI – Compliance of the requirements, by the interested party, within thirty days after reading the notification; and

VII - assessment of requirements' compliance, by Anvisa within forty-five days after the submission of the agency.

§ 1 The absence of meeting request for pre-submission, under the terms of section I of the caput, prevent the analysis of registration request under this resolution.

§ 2 in the case of drugs for national development, the meeting request for pre-submission may be held at any time, provided it has not been requested record in another regulatory authority.

§ 3 In the case of imported drug the meeting request for pre-submission must be held within 60 days after the first registration request in another regulatory authority, except if it is attributable to the company interested.

§ 4 in cases in which the records of drugs for rare diseases have been requested or if the drugs are already registered in other authorities prior to the publication of this resolution, will be accepted requests for pre-submission meetings provided for in Subsection I of the heading at any time.

CHAPTER II – Final and Transitory Provisions

Art.19. The companies that submit request for registration of new drugs according to the criteria of this resolution shall submit dossier of definition of maximum price concomitantly to the protocol of the registration request.

Art.20. The drugs registered by means of the criteria of this resolution will have a period of up to three hundred and sixty-five days to be commercialized, counted from the date of publication of the registry.

Art.21. For the registration requests for new drugs for rare diseases shall not apply the provisions described in the art. 2 of the Resolution of the Collegiate Board - RDC N 20, of 10 April of 2013.

Art. 22. Are Repealed:

the point "e" of section IV of art. 3, and the point "e" of Section VIII of art. 38 of the Resolution of the Collegiate Board - RDC N. 9, 20 of February of 2015.

Art. 23. The § 2 of art. 47 of the Resolution of the Collegiate Board - RDC N. 9, of 2015 is effective with the following wording:

"Art. 47.

.....

§2 the petition of substantial amendments must contain the new protocol.

....." (NR)

Art. 24 The noncompliance with the provisions contained in this resolution constitutes violation of sanitary ware, in terms of Law n. 6,437, of 20 August 1977, without prejudice to the responsibilities of civil, administrative and criminal sanctions.

Art. 25. This resolution comes into effect in 60 (sixty) days from the date of its publication.

JARBAS BARBOSA DA SILVA JR.