Public Consultation No. 255, dated June 19, 2017
D.O.U of 06/20/2017

The Board of the National Health Surveillance Agency, in the use of the powers provided for by article 15, III and IV combined with article 7, III and IV, of Law No. 9782, of January 26, 1999, and article 53, III, §§ 1 and 3 of the Internal Regulation approved pursuant to Annex I of the Board Resolution – RDC No. 61, of February 3, 2016, decides to submit to public consultation, for comments and suggestions from the general public, the Attached normative act proposal, as decided at a meeting held on June 6, 2017, and I, Deputy President, determine its publishing.

Art. 1 The time limit of 30 (thirty) days is established for the submission of the comments and suggestions to the regulation proposed text of the special procedures for the consent of clinical trials, certification of good manufacturing practices and registration of new drugs for the treatment, diagnosis or prevention of rare disease, according to the Annex.

Sole paragraph. The time limit referred to in this article will begin 7 (seven) days after the publishing date of this Public Consultation in the Official Gazette of Brazil.

Art. 2 The normative act proposal will be available in full text on the website of Anvisa and the suggestions shall be electronically submitted through the filling of a specific form, available on the address: http://formsus.datasus.gov.br/site/formulario.php?id_aplicacao=32378.

§1 The received contributions are considered public and will be available to any concerned party through the tools available in the electronic form, on the “result” menu, and also during the consultation process.

§2 At the electronic form filling completion a protocol number will be available to the concerned party registering his/her participation, and the mail submission or the in person protocol of physical documents at the Agency are dismissed.

§3 In case of the citizen access limitation to computerized resources it will be allowed to send and receive suggestions in writing, in physical medium, during the consultation period, to the following address: Agência Nacional de Vigilância Sanitária/ Gerência-Geral de Medicamentos e Produtos Biológicos - GGMED, SIA trecho 5, Área Especial 57, Brasília-DF, CEP 71.205-050.

§4 Exceptionally, international contributions may be submitted in physical medium, to the following address: Agência Nacional de Vigilância Sanitária/Assessoria de Assuntos Internacionais – AINTE, SIA trecho 5, Área Especial 57, Brasília-DF, CEP 71.205- 050.

Art. 3 After the deadline settled in article 1, the National Health Surveillance Agency will conduct the analysis of the contributions and, at the end, will publish the public consultation results on the Agency website.

Sole paragraph. The Agency may, as needed and for convenience and opportunity reasons, discuss it with the bodies and entities involved with the subject, and also with those who have expressed an interest in the matter, in order to subsidize further technical discussions and the final decision of the Board.

PROPOSAL ON PUBLIC CONSULTATION

Procedure No. 25351.447401/2016-40
Subject: Regulation proposal of special procedure for the consent of clinical trials, certification of good manufacturing practices and registration of new drugs for the treatment, diagnosis or prevention of rare diseases.
Regulatory Agenda 2015-2016: Not a subject of the Agenda
Procedure Regime: Common
Responsible area: General Management of Drugs and Biological Products – GGMED
Relator: Fernando Mendes Garcia Neto

Board Resolution No. XX, of [Month] [day], 2017

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

The Board of the National Health Surveillance Agency, in the use of its powers as provided for in the item V of article 53 of Annex I of Resolution-RDC No. 61, of February 3, 2016, decides:

CHAPTER I
Initial Provisions

Art. 1 The special procedure is approved for the:

I - consent of clinical trials to be carried out in Brazil for the assessment of drugs intended to rare diseases;

II – certification of good manufacturing practices applicable to drugs intended to rare diseases; and

III – registration of new drugs intended for rare diseases.

Art. 2 This resolution is not applicable to new drugs assigned by Anvisa to rare diseases.

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

I - rare disease: which affects up to 65 people in every 100,000 individuals, as defined by the National Policy of Extensive Care to People with Rare Diseases;

II - new drug: the active pharmaceutical input unknown in the country for specific rare disease; and

III – debilitating critical condition: disease or condition associated with irreversible morbidity or high probability of death, unless the disease course is interrupted.

CHAPTER II
General Provisions

Section I
The drug assignment for rare disease

Art. 4 The drug assignment for rare disease consists in the step prior to the consent of clinical trials to be held in Brazil, the register of new drugs and the certification of good manufacturing practices.

Sole paragraph. The assignment referred to in the *caput* is mandatory so that the criteria provided for in this resolution can be applied.

Art. 5 The drug assignment for rare disease will be granted provided that the drug has the purpose of treating, diagnosing or preventing the disease that:
I – is used in debilitating critical condition; and
II – significantly changes the evolution or enables the disease remission.

Art. 6 The request for the drug assignment for rare disease must be submitted to Anvisa through specific topic code, with the following documentation:

I. application forms duly completed and signed;

II. description of the rare disease for which the drug will be indicated to;

III. drug relevance for the patient treatment;

IV. global and national data on the prevalence and incidence of the rare disease for which the drug will be indicated to; and

V. document evidencing the drug assignment for the rare disease by another regulatory authority, when available.

Sole paragraph. Anvisa may also, regardless of a request, assign drugs for rare diseases.

Art. 7 The conclusive declaration of Anvisa regarding the assignment will occur within 30 days after the request application.

Art. 8 Anvisa will publish, by means of Resolution (RE), the list of drugs assigned for rare diseases, and their relevant indications.

Section II

The consent of clinical trials to be held in Brazil

Art. 9 The submission of a Drug Clinical Development Dossier (DDCM), specific dossier of clinical trial, substantial modification by inclusion of protocol to be carried out in compliance with the specific legislation, adding the declaration of Anvisa regarding the assignment of the drug indicated for the rare disease.

Art. 10. For the purposes of consent of clinical trials to be held in Brazil, after the favorable declaration of Anvisa regarding the assignment of drug for rare disease, the following procedures must be followed:

I. request for a pre-submission meeting by the concerned party to present the DDCM, specific dossier of critical trial or substantial modification by protocol inclusion;

II. request for a pre-submission meeting to present the DDCM, specific dossier of critical trial or substantial modification by protocol inclusion;

III. submission of DDCM, specific dossier of clinical trial or substantial modification by protocol inclusion, by the concerned party, using the specific topic code;

IV. assessment of DDCM, specific dossier of clinical trial or substantial modification by means of protocol inclusion, by Anvisa, within 30 days after the submission, with the issue of requirement notification or conclusion declaration;

V. meeting, if the concerned party finds it necessary, in order to discuss the requirements;

VI. compliance with the requirements by the concerned party within 30 days after the notification reading; and

VII. assessment of the requirements compliance, by Anvisa, within 30 days after its submission to the agency, with the possibility of submitting new requirements or issue the conclusion declaration.

Art. 11. For the clinical trials to be held in Brazil, the granting of the drug assignment for rare disease is applied to the initial request of consent in the DDCM process.

Sole paragraph. The new request for drug assignment for rare disease should be performed for each new application of clinical trial specific dossier and for substantial modifications by the inclusion of a protocol subsequently linked to a DDCM previously authorized pursuant to this Resolution.

Section III
The certification of good manufacturing practices

Art. 12. The request for the certification of good manufacturing practices should be made in view of the specific legislation, in addition to the declaration of Anvisa regarding the drug assignment for rare disease.

Art. 13. For the purposes of the certification of good manufacturing practices, after Anvisa favorable declaration regarding the drug assignment for rare disease, the procedures below must be followed:

I. request for the certification of good manufacturing practices of the plant(s) where the drug will be produced by the concerned party; and

II. issue of a conclusive opinion regarding the certification of good manufacturing practices, by Anvisa, within 120 days after the submission of the certification request.

Sole paragraph. If the certification request has been made after the granting of the drug assignment for rare disease, the same deadline provided for by item II is applied, counted from Anvisa declaration regarding the drug assignment for rare disease.

Section IV
The registration

Art. 14. The request for the drug registration must be performed compliant with the specific legislation for each regulatory category, adding Anvisa declaration regarding the drug assignment for rare disease.

Art. 15. For the purposes of the drug registration, after Anvisa favorable declaration regarding the drug assignment for rare disease, the procedures below must be followed:

I. request for a pre-submission meeting by the concerned party to present the product within 60 days after the first registration application in another regulatory agency;

II. pre-submission meeting to present the product, after the request by the concerned party.

III. submission of the registration request by the concerned party, by means of the specific topic code, within 30 days after the pre-submission meeting;

IV. Assessment of the drug registration request by Anvisa within 60 days after the submission, with the issue of the requirement notification or conclusive opinion;

V. meeting, if the concerned party finds it necessary, in order to discuss the requirements;

VI. compliance with the requirements, by the concerned party, within 30 after the notification reading; and

VII. assessment of the requirements compliance, by Anvisa, within 45 days after its submission to the agency, with the possibility of submitting new requirements or issue of conclusive opinion.

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

§ 2 In the case of national development drug, the pre-submission meeting request can be performed at any time.

§ 3 In the cases when the registration has been requested or the drugs are already registered in other agencies prior to the publishing of this resolution, the pre-submission meetings requests will be accepted as provided for in the item I of the *caput* at any time.

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

§ 5 The submission of the drug registration request can be accepted without the submission of the registration evidence in the country of origin.

§ 6 In the registration request submission, the long-term stability study in progress can be accepted, when conducted according to the temperature and humidity conditions required by specific laws, with the results that are available until the protocol date.

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

§ 8 In the case of imported drugs, the suppression of quality control in Brazil is allowed, since the quality control is performed by the drug manufacturer and the summary report with the transport system operation qualification summary is submitted.

§ 9 The registration request can be instructed according to the *Common Technical Document* (CTD) format, as provided for in the M4 guide of the *International Conference on Harmonization* (ICH).

Art. 16. In the case of drugs already registered in other countries, the drug assessment technical report issued by the relevant regulatory authorities should be submitted, when available.

Art. 17. The presentation of complementary data and additional evidences can be accepted after the registration granting, by means of the signature of a commitment statement between Anvisa and the company requesting the registration.

§ 1 The complementary data and additional evidences after the registration granting cannot impair the safety and effectiveness analysis of the drugs at the time of granting the registration.

§ 2 The non-compliance with the assumed commitments may cause the drug registration cancelation.

CHAPTER II
Final Provisions

Art. 18. The drugs registered by means of the criteria of this resolution will have a deadline of 365 days to be sold, counted from the registration publication date.

Sole paragraph. Drugs not sold within the deadline established in the *caput* will have its registration cancelled by Anvisa.

Art. 19. The non-compliance with the provisions in this resolution is a health infraction, pursuant to Law No. 6437, of August 20, 1977, without prejudice to the civil, administrative and criminal responsibilities applicable.

Art. 20. This resolution will be effective on the date of its publishing.

JARBAS BARBOSA DA SILVA JR.