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SERVICE GUIDANCE No. 104/DIRE2/ANVISA, OF JUNE 17, 2021

Provides for the detailing of the procedures for analyzing the documents required for submission of the Clinical Drug Development Dossier (DDCM) and the changes that potentially impact the quality or safety of the investigational drug, active comparator or placebo.

The Director of the National Health Surveillance Agency, in the use of the attribution conferred on her by art. 44, IV, allied to art. 54, II of the Internal Regulations approved by the Resolution of the Collegiate Board of Directors RDC No. 255, of December 10, 2018,

considering the Resolution of the Collegiate Board of Directors - RDC No. 9, of February 20, 2015, which provides for the Regulation for conducting clinical trials with drugs in Brazil; and

considering the need to speed up the evaluation of the development of clinical drug research in Brazil without compromising the technical quality of the analysis, resolves:

Art. 1st Establish, within the scope of the Coordination of Clinical Research in Medicines and Biological Products (COPEC), the procedures for analyzing the documents required in item VII, art. 38 for submission of the Clinical Drug Development Dossier (DDCM) and in item III, art. 43, of the Collegiate Board Resolution - RDC No. 9, of 2015, for submission of changes that potentially impact the quality or safety of the experimental drug, active comparator or placebo.

Single paragraph. For the purposes of the caput, changes that potentially impact the quality or safety of the investigational drug, active comparator or placebo are the same as substantial changes in quality.

Art. 2 This Service Guidance applies to:

I - DDCMs that have at least one clinical trial, at any stage of development, approved by at least one regulatory authority from at least one founding Regulatory Members or Standing Regulatory Members
Members) of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) or by the UK regulatory authority (MHRA);

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II - DDCMs of experimental drugs registered in at least one country that meets the criteria described in item I; and

III - Substantial quality modifications approved by at least one regulatory authority from any of the countries that meet the criteria described in Item I.

§ 1 There is no obligation for the clinical trial mentioned in item I to be the same submitted for approval in Brazil.

§ 2 The experimental DDCM drug submitted to Anvisa must be identical to the one approved by the regulatory authorities of any of the countries that meet the criteria described in Item I, with the exception of models of labels and secondary packaging.

§ 3 The manufacturing process of the experimental drug must meet the criteria and recommendations described in the current ICH guides, where applicable, according to the clinical development phase.

Art. 3rd DDCM petitions and substantial quality changes that meet the criteria described in art. 2 must be accompanied by all the documents required in item VII, art. 38 and item III, art. 43, of the Resolution of the Collegiate Board of Directors - RDC No. 9, of 2015, of which the following will be analyzed by COPEC:

I - Results of stability studies under accelerated and long-term conditions that support the proposed shelf life for the experimental drug and, when applicable, for the placebo and modified comparator, when the storage recommendation is at room temperature (between 15 and 30°C);

II - Model of experimental drug label, for DDCM petitions;

III - Dossier of placebo quality, when the petition to be evaluated was framed in this SO only by item II of art. 2nd.

Art. 4 For the purpose of proving compliance with the criteria described in art. 2, must be presented:

I - Official document issued by at least one of the regulatory authorities of any of the countries mentioned in item I of art. 2, which proves the authorization to conduct the clinical trial or the substantial change in quality; and

II - Declaration of compliance with the criteria described in art. 2, according to Annex.

Single paragraph. In the absence of the document described in item I, justification must be presented demonstrating that the conduction of the clinical trial or the substantial modification of quality was authorized.

Art. 5 The documents described in art. 4 must be submitted by means of a secondary petition before the start of the technical analysis of the petition to be framed in the criteria of this Service Guidance (OS). For subject code 11634 - CLINICAL TRIALS - Simplified Quality Dossier Analysis, the petition must be linked to the corresponding DDCM case number.

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§ 1 For the purposes described in the caput, the status of the petition of the aforementioned subject code will be updated to "Agreed" if all the criteria of this SO are met for carrying out a simplified analysis.

§ 2 In the event of non-compliance with all the criteria of this SO, the status of the petition of the aforementioned subject code will be updated to "Non-Annuated" and a letter will be sent to the company with the respective justification and COPEC will proceed with the non-simplified analysis, as the Resolution of the Collegiate Board of Directors - RDC No. 9, of 2015.

Art. 6 The provisions of this SO may be applied to petitions for DDCMs and substantial quality changes submitted before their publication, upon request through subject code 11634 - CLINICAL TRIALS - Simplified Quality Dossier Analysis, provided that the interest is still in the queue awaiting the start of the technical analysis.

Art. 7th The provisions of this SO do not presuppose prioritization of the analysis of petitions.

Art. 8 Anvisa may at any time analyze all documents required in item VII, art. 38 and item III, art. 43, of the Collegiate Board Resolution - RDC No. 9, of 2015, based on the risk analysis related to the investigational drug.

Art. 9th Service Guidance No. 88, of July 31, 2020, republished in Service Bulletin No. 42, of August 17, 2020, p. 22.

Art. 10. This Service Guidance is effective on the date of its publication.

MEIRUZE SOUSA FREITAS

ATTACHMENT

Service Guidance Form - OS No. XX, of XX of XXXX, 2021.

I. (__) Analysis of the Clinical Drug Development Dossier (DDCM) petition or,

II. (___) Substantial change in the quality of the investigational drug, modified active comparator or placebo, File No. _____ (inform the change file number).

Pursuant to the provisions of OS No. XX, of XX of XXXXX of 2021, I DECLARE that:

1- The clinical trial(s)_____[inform the code(s) of the protocol(s) described in the DDCM Development Plan for the investigational drug] was(ram)) authorized in the following country(ies): _____[at least one

country listed must be Founding Regulatory Members or Standing Regulatory Members of the ICH or the United Kingdom].

2- The investigational drug_____ [insert drug name/code] to be administered in the clinical trial(s) to be conducted in Brazil is identical to the one administered in the clinical trials listed in item 1.

3- The investigational drug to be administered in the clinical trial(s) to be conducted in Brazil is registered in: _____ [at least one listed country must be a Founding Regulatory Member or Standing Regulatory Members) of the ICH or the UK].

4- Substantial quality modifications of the investigational drug, active comparator or placebo, if applicable, are the same as those approved in the following country(ies): _____ [at least one listed country must be a Founding Regulatory Member Members) or Standing Regulatory Members of the ICH or the UK].

5- The manufacture of the investigational drug _____ [inform the name/code of the drug] follows the ICH guidelines, as applicable, for the clinical development phase.

6- I assume civilly and criminally, full responsibility for the information provided here.

_____

Sponsor's Legal Representative