

NORMATIVE INSTRUCTION # 20, DATED OCTOBER 2, 2017

Provides for the inspection procedures in Good Clinical Practices for clinical trials with medications.

The Collegial Board of Governors of the National Health Surveillance Agency (Anvisa), with the use of the attributions conferred by art.15, III and IV allied to art. 7, III and IV, of Law # 9,782 of January 26, 1999, art. 53, VI, in Paragraphs 1 and 3 of the Internal Regulation approved in accordance with Annex I of the Collegial Board of Governors' Resolution - RDC # 61, of February 3, 2016, at a meeting held on XX, XX 2016, considering that the Good Clinical Practices – GCP constitute a quality and ethical international standard for the design, conduction, record and report of clinical trials involving human participation; considering the bioethical principles of the Nuremberg Code (1947), the Declaration of Helsinki (1948), Tokyo (1975), Venice (1983) and Hong Kong (1989); considering the Document of the Americas and Manual of Good Clinical Practices of the International Conference on Harmonization (Document E6), resolves:

Art. 1. This Normative Instruction aims to establish inspection procedures to harmonize, guide and verify the compliance with the Good Clinical Practices (GCP) in clinical trials with drugs, pursuant to Resolution RDC # 09 of February 20, 2015, in order to promote the regulatory action in health surveillance capable of ensuring an unified standard of health efficacy and safety, considering the subjects and collective, observing the bioethical principles of autonomy, non-maleficence, beneficence and justice.

Art. 2. The GCP inspection will be carried out by servers of the effective staff of Anvisa, duly identified and qualified, respecting attributions and competences inherent to the said positions.

Paragraph 1. In the case of routine inspection, the site to be inspected will be notified by Anvisa, at least fifteen (15) calendar days in advance.

Paragraph 2. In the case of denunciation or suspicion of irregularities, an inspection will be carried out without prior notice.

Paragraph 3. Both the sponsor and/or the Clinical Research Organization (CRO) responsible for the study before ANVISA, and the Principal Investigator (PI) of the site to be inspected will be communicated, where applicable, about an inspection, through a Notice of the GCP Inspection Notification, sent by ANVISA.

Art. 3. The process of inspection will consist of the following steps:

- I - communication of the inspection to the sponsor/CRO and PI,
- II - opening meeting,
- III - interview with the study team,
- IV – facility visits, if applicable,

V - documentary analysis, and
VI - closing meeting.

Art. 4. The PI, where applicable, and the sponsor/CRO representative must be present at the opening and closing meetings, and one (1) staff member must be available throughout the inspection period.

Sole paragraph. The presence of other team members can be requested by ANVISA, if there is a need.

Art. 5. The inspection will have the duration specified in the letter of notification and will take place at a maximum period of 5 (five) business days, and may exceptionally be amended, with due justification.

Art. 6. After an inspection, the inspector team will elaborate the Inspection Report, which shall to be sent to the PI (if applicable) and to the Sponsor/CRO of the study within sixty (60) calendar days.

Art. 7. The Inspection Report will list and frame the observations found, according to the classification provided in art. 12 of this Normative Instruction.

Art. 8. Upon receipt of the Inspection Report, the Sponsor/CRO will have one hundred and twenty (120) calendar days for manifestation.

Art. 9. After manifestation of the Sponsor or during the term provided for in art. 8 of this Normative Instruction, Anvisa will issue the Final Inspection Opinion, which will be sent to the sponsor/CRO and PI, when applicable.

Art. 10. After observing the Inspection Report and the respective manifestation of the sponsor/CRO, Anvisa will declare, in the Final Inspection Opinion, whether the study is being conducted or not according to the GCP.

Art. 11. In cases of noncompliance with the GCP, Anvisa shall determine:

- I - the temporary interruption of the clinical trial,
- II - the definitive cancellation of the clinical trial, in the site in question,
- III - the definitive cancellation of the clinical trial in all sites in Brazil; or
- IV - the invalidation of data from sites and clinical trials that do not comply with the GCP.

Art. 12. The observations found during the inspection are defined and classified as:

- I – Critical "C": findings directly related to the research subject safety, which may result in death, risk of death or unsafe conditions; when related to study data may compromise its validity, such as unauthorized studies, tampering, lack of information or counterfeiting,
- II – Major "M": findings that may result in risk to the research subject health or data invalidation,

III – Minor "Mi": findings that do not fit into critical or major observations, but indicate deficiency and/or deviation; such findings should be cited with the purpose of implementing improvements when conducting studies,

IV - Informative "INF": descriptive and/or complementary findings, and

V – Not included/Not applicable "NI/NA": means that the item has not been checked or is not applicable.

Sole paragraph. In the hypothesis of item III of this article, such findings should be cited in the final inspection report with the purpose of implementing improvements when conducting studies,

Art. 13. Normative Instruction # 4, dated May 11, 2009, published in the Brazilian Official Gazette of May 12, 2009, is hereby revoked.

Art. 14. This Normative Instruction shall enter into force on the date of its publication.

JARBAS BARBOSA DA SILVA JÚNIOR
Chairman