FDA CIRCULAR
No. _____

SUBJECT : **Guidelines on the Classification of Deficiencies Observed During Inspection of the Conduct of Clinical Trials**

I. RATIONALE

Republic Act (R.A.) No. 3720, as amended R.A. No. 9711 or the Food and Drug Administration (FDA) Act of 2009, declared that it is a policy of the State to adopt, support, establish, institutionalize, improve and maintain structures, processes, mechanisms, and initiatives that are aimed, directed and designed to: (a) protect and promote the right to health of the Filipino people; (b) help establish and maintain an effective health products regulatory system and to undertake appropriate manpower development and research responsive to the country's health needs and problems.

Administrative Order (A.O.) 2020-0010 entitled, "Regulations on the Conduct of Clinical Trials for Investigational Products", directs the FDA to conduct inspections and ensure that the rights, safety, and well-being of study subjects have been protected, to ensure integrity of the scientific data collected and to assess adherence to the International Council on Harmonization of Good Clinical Practices (ICH-GCP) Principles and other applicable FDA regulations.

Consequently, in order to achieve the objectives of R.A. No. 9711 of ensuring the FDA's monitoring and regulatory coverage over establishments and products under its jurisdiction; with its duty to conduct, supervise, monitor and audit research studies on health and safety issues of health products undertaken by entities duly approved by the FDA, it is vital that a classification of deficiencies observed during GCP inspection of clinical trials are coherent, and all stakeholders are guided by FDA-implemented rules and regulations in the conduct of clinical trials for investigational products.

Finally, in compliance with the declared policy of the State laid down in R.A. No. 11032 or the Ease of Doing Business and Efficient Government Service Delivery Act of 2018 to promote integrity, accountability, establish effective practices, aimed at efficient turnaround of the delivery of government services and the prevention of graft and corruption in government, the FDA is committed to take appropriate measures to promote transparency.

II. OBJECTIVES

This Circular aims to provide a uniform understanding and implementation of the classification of deficiencies/non-conformances observed in the conduct of inspection of the different phases of a clinical trial for investigational products. And to establish a consistent understanding of the compliance requirements for all stakeholders, as prescribed by R.A. No. 3720, as amended by R.A. No. 9711, R.A. No. 11032, A.O. 2020-0010, and pertinent national and international standards and policies.

III. SCOPE OF APPLICATION

These guidelines shall apply to Sponsors, Clinical Research Organizations (CROs), Investigators, Research Ethics Committees (RECs), FDA GCP Inspectors, and other stakeholders involved in the approval, conduct, monitoring and inspection, in all phases of clinical trials for Investigational Products intended for eventual product registration and marketing.

IV. GUIDELINES

A. For uniformity, efficiency, and transparency, non-conformances observed during inspections are classified based on the following criteria with reference to R.A. No. 3720, as amended by R.A. No. 9711, R.A. No. 11032, A.O. 2020-0010, and pertinent national and international standards and policies:

1. **Critical deficiency** - practices or processes that have been observed to adversely affect the rights, safety and/or well-being of the trial subjects, or the quality and integrity of data, or that represents a serious violation of applicable laws and guidelines that would result in regulatory action.

2. **Major deficiency** - practices or processes that have been observed that could potentially adversely affect the rights, safety and/or well-being of the trial subjects, or the quality and integrity of data, or that could represent a violation of laws and guidelines.

3. **Minor deficiency** - practices or processes that have been observed that would not be expected to adversely affect the rights, safety, and/or well-being of the trial subjects or the quality and integrity of data. This may also include deficiencies that would not fall under critical or major deficiencies.

Note: deficiencies may be reclassified into a higher classification if a pattern/ recurrence is observed and/or numerous observations are noted.

B. In case of findings classified as critical deficiency(ies), the organization, institution, or entities is directed to initiate outright any or all of the following:

1. Suspension or termination of the clinical trial as deemed necessary, except for trial-related procedures intended for safety and well-being of participants.
2. Rejection of collected data from the final clinical trial report.
3. Cease administration of investigational product and/or recruitment, as applicable.

C. In addition to the above, critical findings may result in the FDA imposing subsequent regulatory action, including disapproval of clinical trial related applications, or, after notice and hearing, suspension, or revocation of the issued authorization.

D. The organization, institution, or entities shall address all deficiencies (whether critical, major, or minor) by submitting a Corrective Action and Preventive Action (CAPA) plan and objective evidence of compliance, not later than fifteen (15) working days reckoned on the day following the receipt of the inspection report.

If there are significant issues on compliance with International Council for Harmonisation-Good Clinical Practice (ICH-GCP), current National Ethical Guidelines, FDA Rules and Regulations, and other existing laws, coordination with the stakeholders (e.g., Clinical Research Section, Research Ethics Committee/s, Philippine Health Research Ethics Board) shall be done as necessary.

A list of all inspection observations shall be classified according to the definitions and will be included in the attached reference as **Annex A**. The list is non-exhaustive and other observations may be added, removed, or re-classified as appropriate, subject to prior notice to the concerned stakeholders and amendment of such list.

V. MONITORING AND EVALUATION (M&E) CLAUSE

Within three (3) years of its implementation, this Circular shall be reviewed and evaluated to determine whether the policy's objectives, impact, and effectiveness are achieved.

VI. PENALTY CLAUSE

Violation of any of the provisions of this Order shall be subject to the penalties/sanctions provided for under Book II, Article I, Section 4 of the Rules and Regulations of R.A. 9711 or the Food and Drug Administration Act of 2009.

VII. REPEALING CLAUSE

Any provisions of existing FDA-issued Circulars or Memoranda that are inconsistent with the provisions of this Circular are hereby repealed, withdrawn and/or revoked accordingly.

VIII. SEPARABILITY CLAUSE

If any provision of this Circular or application of such provision to any circumstances is held invalid, the validity of the remainder of the provisions hereof not affected shall continue to be in effect.

IX. EFFECTIVITY

This Circular shall take effect after fifteen (15) days following its publication in any newspaper of general circulation and upon filing of three (3) certified copies with the University of the Philippines Law Center-Office of the National Administrative Register (UP-ONAR).