Clinical Trial Regulation Guidelines

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Outline

- Brief Overview of Clinical Trial in the Philippines
- Current Guidelines and Recommendations
- Proposed Revision Regulating the Conduct of Clinical Trials
  - Objectives
  - Scope
  - General Guidelines

CLINICAL TRIAL/STUDY

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its **safety and/or efficacy.** The terms clinical trial and clinical study are synonymous.

ICH GCP E6 R2 Definition

SPONSOR

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

CONTRACT RESEARCH ORGANIZATION (CRO)

A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Clinical Trial Guidelines	Title
1. FDA Circular 2012-007	Recognition of Ethical Review Board/Committee (ERB/ERC) for Purposes of the Conduct of Clinical Trials on Investigational Medicinal Products in the Philippines for Other Purposes
2. FDA Circular 2013-003	Post Market Surveillance and Periodic Safety Update Report
3.FDA Circular No. 2013-004	Post Market Surveillance (PMS) of Authorized Drug Products
4. FDA Circular No. 2013-018	Adoption of the International Conference on Harmonization (ICH) Safety and Efficacy Guidelines
5. FDA Circular No. 2014-009	Filing and Submission of Applications for the Approval of Clinical Trial Protocol, Compassionate Special Permit (CSP), Import Permit for Investigational Drug Products, Pharmacovigilance, Adverse Events/Adverse Reaction Reports, and Other Related Documents
6. Administrative Order No. 2014-0034	Rules and Regulations on the Licensing of Establishments Engaged in the Manufacture, Conduct of Clinical Trial, Distribution, Importation, Exportation, and Retailing of Drug Products, and Issuance of Other Related Authorizations

Clinical Trial Regulation

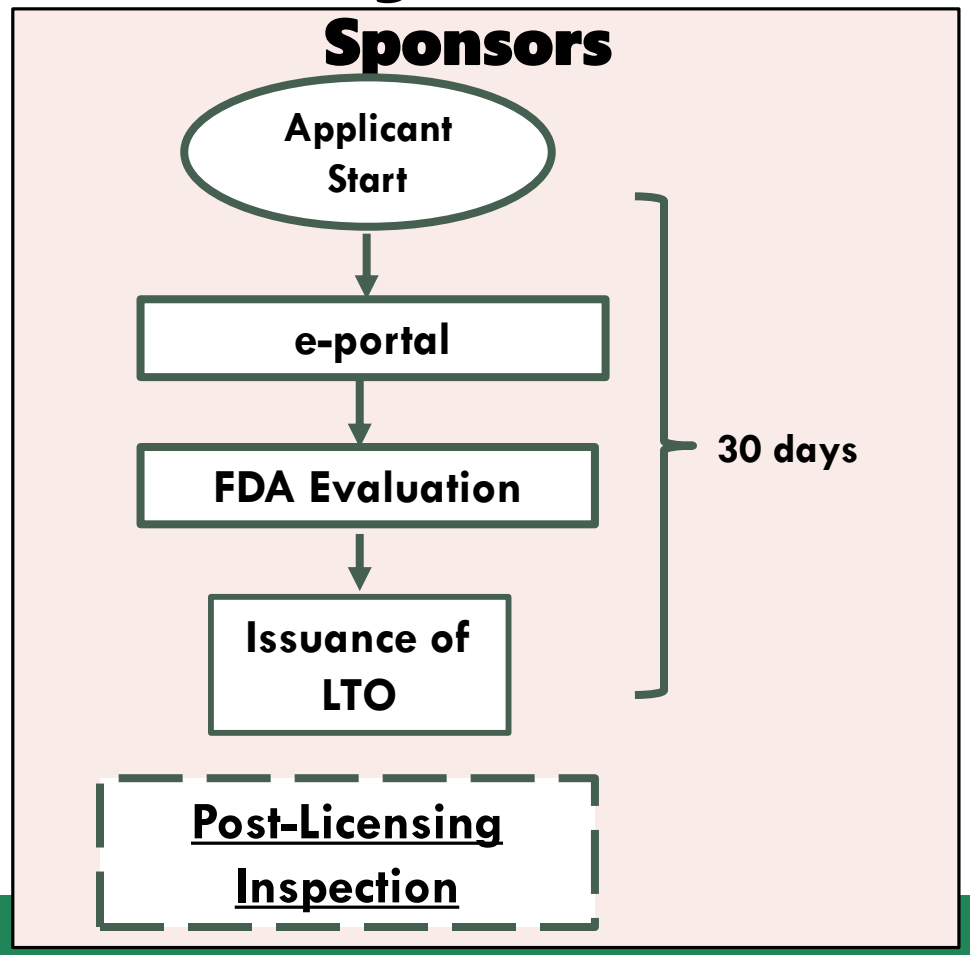
FDA Circular 2012-007

Published on June 7, 2012

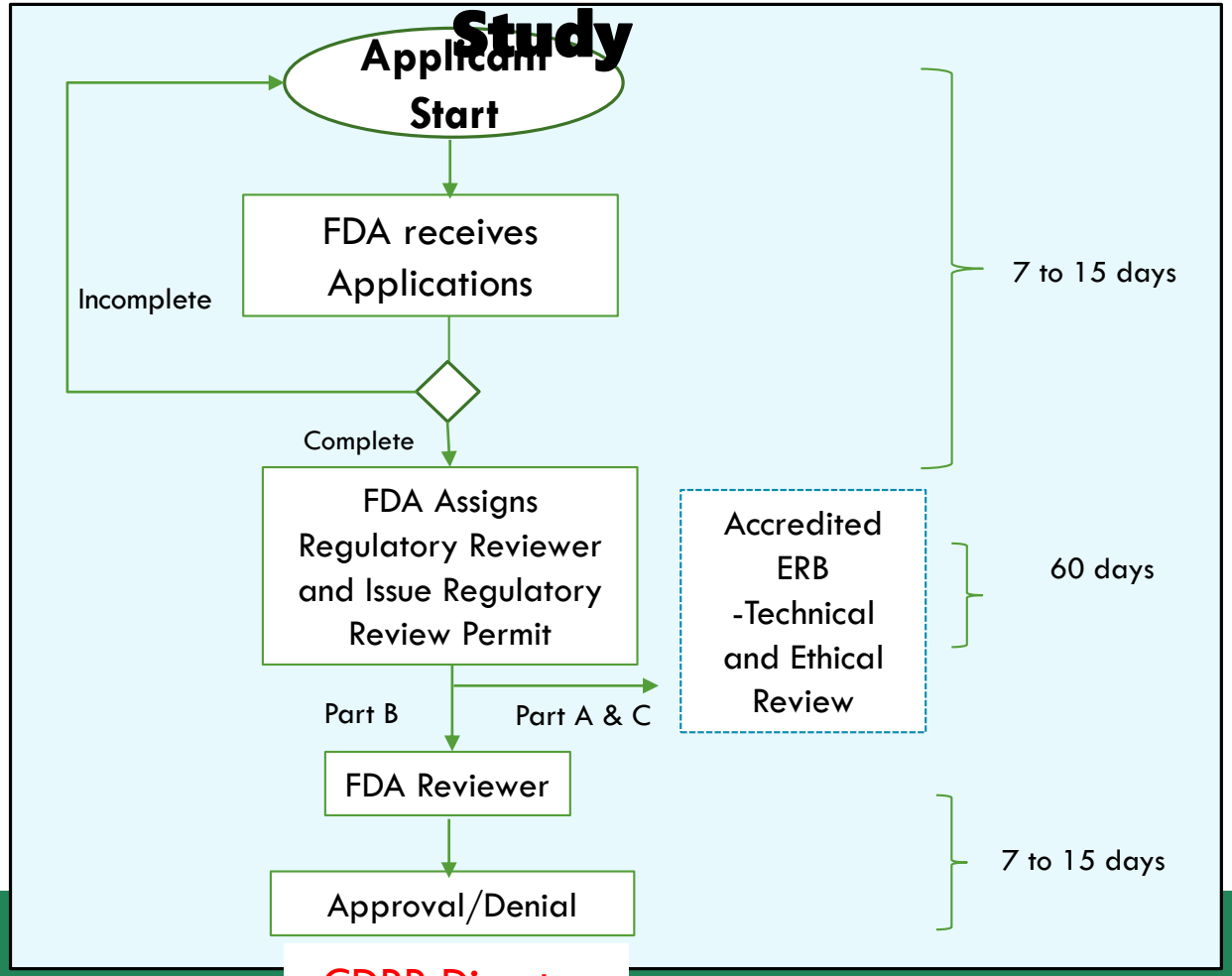
- First comprehensive guideline for the conduct of Clinical Trials on Investigational Medical Products in the Philippines
- Recognition of PHREB-Accredited IRBs to serve as Ethical and Technical Reviewers for CT Applications
- Mandatory inclusion of CT in Philippine CT Registry
- Issuance of Import Permit
- Inspection of clinical trial by FDA
- Safety reporting
- Imposition of Sanctions

Overview of Regulatory Procedure

Licensing of CROs and Sponsors



Conduct of Clinical Trial Study



CT Licensed Establishments

Type	
Sponsor	24
Contract Research Organization (CRO)	27

Data as of 31 July 2018,
Valid and with Pending Renewal

Clinical Trial Applications

Phase	2012	2013	2014	2015	2016	2017	Total
Phase 1	1	7	3	4	2	0	17
Phase 1/2	0	3	0	1	0	2	6
Phase 2	9	3	9	12	6	9	48
Phase 2/3	2	3	0	1	2	1	9
Phase 3	60	74	69	36	42	33	314
Phase 3/4	0	0	1	0	0	2	3
Phase 4	9	9	7	4	4	2	35

Gaps in Implementation

2012-2017 (5 Years)

FDA Circular 2012-007

Concerns and weaknesses were expressed after implementation…

Moving forward

2018

FDA Review of CT Policies, Systems and Procedures

Creation of Clinical Trial Regulatory Roadmap for the Philippines

Improve CT regulatory framework and guidelines

FDA REVIEW OF CLINICAL TRIAL REGULATIONS

March 2018	FDA Internal Review of CT Policies, Systems and Procedures
May 2018	Initial Consultation with Stakeholders (CROs, Sponsors, IRBs)

FDA Clinical Trial Regulatory Management Plan

FDA REVIEW OF CLINICAL TRIAL REGULATIONS

8 Elements:

- ❑ Legal Basis
- ❑ Guidelines
- ❑ Ethical Oversight
- ❑ Organization and Structure
- ❑ Assessment Procedures
- ❑ Human and Other Resources
- ❑ Records and Outputs
- ❑ Availability of Information

Clinical Trial Regulation: Implementation gaps

1 **Legal Basis**	**Already mandated by Law** **RA 3720**-Food Drug and Cosmetics Act and its amendments **RA 9711-** Food and Drug Administration Act of 2009
2 **Guidelines**	**Revision of the Current Guidelines (FDA Circular 2012-007) to cover:** • Scope of Regulation • Registration of Investigational New Drugs • Pharmacovigilance system to manage the collection, verification, presentation and evaluation of all reported Adverse Events/Reactions (including SUSARs) • Inspection Guidelines for the Inspectorate • Phase I to Phase IV approval

Clinical Trial Regulation: Implementation gaps

3	**Ethical Oversight**	There is a need for an established system to provide oversight to Ethical Reviewers
4	**Organization and structure**	Technical and Scientific Review Process is not fully in line with what is promoted by World Health Organization Scientific and Technical experts should be **within** FDA

Clinical Trial Regulation: Implementation gaps

5	**Assessment Procedures**	GCP Inspection is not conducted Unpredictability of the release of Import Permits
6	**Human and Other Resources**	The FDA is currently understaffed and there is a lack of expertise internally to review protocols

Clinical Trial Regulation: Implementation gaps

7	**Records and Outputs**	Paper based transfer of information is inefficient No single database for all applications
8	**Availability of Information**	Not all studies are posted 30 days after approval There is no monitoring/audit mechanism Coordination with PCHRD is needed

THE CLINICAL TRIAL REGULATORY MANAGEMENT PLAN

Clinical Trial Regulatory Management Plan

Phase I:

1. Revised Policies on Clinical Trial
2. Guidance Document for Stakeholders
3. Review Tools
4. Training Module for Scientific and Technical Reviewers

Phase II:

Training for Regulatory Reviewers

Implementation

Phase III:

Regulatory Impact Assessment

CALENDAR (PHASE 1)

Activities or Workplan	Expected Output	M1	M2	M3	M4	M5	M6	M7
		Aug 2018	Sep 2018	Oct 2018	Nov 2018	Dec 2018	Jan 2018	Feb 2018
Initial Policy Review	Revised Policies Dissemination of revised policies							
Consultative Meetings								
Analysis and Revision of Policies								
Policy Dissemination								
Creation of Review Tools								
Creation of Guidance Document for Stakeholders	Guidance Document for Stakeholders							
Creation Training Module for Reviewers and Inspectors	Training Module for Reviewers and Inspectors							

PROPOSED ADMINISTRATIVE ORDER ON THE CONDUCT OF CLINICAL TRIALS FOR PHARMACEUTICAL PRODUCTS AND BIOLOGICS

OBJECTIVES (Draft)

This Administrative Order aims to achieve the following objectives:

1. Ensure the full protection of rights and safety of human subjects and the integrity of clinical trial data through the adoption and implementation of international standards on Good Clinical Practice (GCP) and maintenance of a Clinical Trial Database;
2. Streamline the process and requirements for the approval of Phase I to Phase III clinical trial protocols;
3. Provide standards and requirements for the regulation and importation of Investigational New Drugs;
4. Creation of Regulatory Review Board and Scientific Advisory Committee as recommending bodies to the FDA in the review of Clinical Trial Protocols;

OBJECTIVES (Draft)

This Administrative Order aims to achieve the following objectives:

5. Establishment of Clinical Research Section (CRS) to act as Secretariat to the Scientific, Technical and Ethical Review of Clinical Trials;
6. Establishment of Pharmacovigilance system to manage the collection, verification, presentation and evaluation of all reported Adverse Events/Reactions; and
7. Strengthen the monitoring of compliance of all organizations, institutions and entities to GCP and other related FDA regulations through regulatory inspections

SCOPE (Draft)

This Administrative Order (AO) shall apply to Sponsors, Contract Research Organizations (CROs), Investigators, and Ethical Review Committees (ERCs) in the approval, conduct, monitoring and inspection of clinical trials, in all phases, for product registration or marketing purposes.

This will not cover products with issued Marketing Authorization. Also, locally manufactured Herbal Drug Products are **excluded** from this AO.

GENERAL GUIDELINES (Draft)

1. Only Study Sponsor and/or CROs, as defined by ICH-GCP, including those government-owned institutions, with FDA license, can conduct Clinical Trials in the Philippines.
2. All establishments involved in the conduct of Clinical Trials shall be under the supervision of a qualified person(s) as required by pertinent rules and regulations.
3. All Clinical Trials on investigational new drug for human use, from Phase I to Phase III, including amendment/s thereto, are required to undergo mandatory approval from FDA.

PHASE IV

Phase IV begins after **drug approval**. Therapeutic use studies go beyond the prior demonstration of the drug's safety, efficacy and dose definition.

Studies in Phase IV are all studies (other than routine surveillance) performed after drug approval and related to the approved indication.

They are studies that were not considered necessary for approval but are often important for optimising the drug's use.

They may be of any type but should have valid scientific objectives.

Commonly conducted studies include additional drug-drug interaction, dose-response or safety studies and studies designed to support use under the approved indication, e.g. mortality/morbidity studies, epidemiological studies.

GENERAL GUIDELINES (Draft)

4. Evaluation of the clinical trial protocol, including scientific, technical and ethical review, shall be conducted by FDA Regulatory Reviewers and Scientific Advisory Committee (SAC). The composition of FDA Regulatory Reviewers and SAC, as well as the method of evaluating application shall be identified by the FDA.
5. A clinical trial can only commence once the FDA has issued the approval.
6. Imported Investigational Drug to be used in the conduct of clinical trials shall be issued an "Import Permit." The responsibility of ensuring the quality of products used in the conduct of clinical trials shall rest upon the Sponsor/s and CRO/s involved in the conduct of the studies.

GENERAL GUIDELINES (Draft)

7. All Serious Adverse Events (SAE) of products used in the conduct of CT shall be reported to the FDA.
8. All Clinical Trials shall be uploaded in the registry which shall be made available to the public for transparency. The registry for Clinical Trials conducted in the country shall be monitored by the FDA.

GENERAL GUIDELINES (Draft)

9. FDA shall have the authority to enter any establishment for inspection of compliance and/or verification of submitted documents in relation to any application.

10. Only FDA will give the final decision to approve or deny an application. Likewise, FDA shall give sanctions, as appropriate, to any violation which undermines the rights and safety of human subjects.

11. Disapproved application(s) may be appealed to for reconsideration.

Now we would like to hear your thoughts…

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FOR FEEDBACK AND COMMENTS