# [ FDA Circular No. 2015-003, March 06, 2015 ]

## GUIDELINES ON THE IMPLEMENTATION OF NEW RULES AND REGULATIONS ON THE LICENSING OF SPONSORS AND CONTRACT RESEARCH ORGANIZATIONS (CROS) FOLLOWING ADMINISTRATIVE ORDER NO. 2014-0034, DATED 13 OCTOBER, 2014

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### I. RATIONALE

The conduct of clinical trial is one of the most critical and complex components in the drug development process. The management of clinical trials in all phases should take into account two important aspects: the protection of the rights, safety and well-being of the subjects or patients, and the credibility and integrity of the clinical trial data obtained.

With a steady and substantial increase in the number of establishments involved in clinical trials, there is a need for appropriate monitoring and regulation to ensure that these two aspects are met. It is in this context that the Food and Drug Administration (FDA) has required the licensing of these establishments.

On 13 October 2014, Administrative Order No. 2014-0034 was issued to (a) update and streamline regulatory approaches in licensing of drug establishments, (b) provide faster access of drug products to the public; and (c) promote transparency through the universal use of electronic transaction.

In line with the new rules and regulations on the licensing of establishments classified as sponsors or CROs, FDA hereby prescribes the requirements for the applications for initial and renewal issuance of License to Operate (LTO), variations, as well as other guidelines relevant to these establishments.

### II. DEFINITION OF TERMS

Definition of terms shall follow the definitions provided for under Administrative Order No. 2014-0034. In addition, the following terms are hereby defined:

1) Clinical Trial Protocol - a document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.
2) Good Clinical Practice (GCP) - a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of

clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

3) Investigator - a person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

   An investigator may also refer to an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to or used involving a subject.

## III. GENERAL GUIDELINES

A. All local sponsors and CROs conducting local clinical trials for purposes of drug registration must secure an LTO from the FDA.

B. No clinical trial of a foreign sponsor may be conducted in the country unless an FDA-licensed CRO takes up the responsibility for the foreign sponsor.

C. Other licensed drug establishments (e. g. manufacturer, importer, or distributor) desiring to engage in clinical trials as either a sponsor or CRO must secure the appropriate LTO.

D. Entities engaged in the following trial-related duties and functions delegated by a sponsor are required to secure an LTO as CRO:

   1) Oversight (e.g. ensuring quality assurance and/or quality control systems are in place to ensure clinical trials are conducted, data is gathered, and subsequently reported)
   2) Management of clinical trials
      (a) development of protocols and/or trial design;
      (b) selection of investigator(s) and/or site(s);
      (c) screening and/or recruitment of subjects;
      (d) data handling (e.g. collection, analysis/evaluation, and record keeping)

   Entities involved in the procurement/importation, storage, and/or distribution of investigational product(s) are not required to secure an LTO as CRO, unless they are involved in other activities mentioned above. These entities must follow other existing licensing requirements.

E. Accredited bioequivalence testing centers need not apply for LTO as Sponsor or CRO.

## IV. LICENSE TO OPERATE (LTO) APPLICATIONS

A. *Documentary Requirements*

   1) Application Form

A completely filled-out and notarized application form signed by the owner/authorized representative must be submitted.

2) Proof of Business Name Registration

   A valid proof of business name registration must be submitted:

   (a) For single proprietorship - Certificate of Business Registration issued by the Department of Trade and Industry (DTI)
   (b) For corporation, partnership and other juridical person – Certificate of Registration issued by the Securities and Exchange Commission (SEC) and Articles of Incorporation
   (c) For government-owned or controlled corporation - the law highlighting the provision creating such establishment

   The proof of business name registration must specify the exact and complete address, e.g., unit number, floor, building, lot, block, phase, street, barangay, city/municipality, province, where applicable.

3) Credentials of Qualified Person

   The Certificate of Attendance to basic and advanced GCP courses of the identified qualified person must be submitted.

   Other credentials of the qualified person as proof of qualification will not be submitted during application but may be verified during inspection.

4) Risk Management Plan

   A general risk management plan (RMP) for the establishment must be submitted. The RMP shall contain details on how to identify, characterize, prevent or minimize risk relating to the IP they engage with. These shall include pharmacovigilance activities and interventions of the establishment to manage the risks.

5) Location Plan

   A sketch of the location of the establishment must be submitted which shall be used for inspection purposes. This sketch must indicate clear directions with identified landmarks to locate the establishment.

   In addition, the Global Positioning System (GPS) Coordinates in decimal degrees (DD) [Latitude and Longitude] must be indicated in the submission.

6) Proof of Payment

   Proof of payment (e.g, official receipt or authorized bank payment slip) must be included as proof of filing of application.

7) Self-assessment Toolkit