Investigational New Drug (IND) Applications
PRO-008
Effective date: May 1, 2018

I. PURPOSE AND SCOPE

The purpose of this Standard Operating Procedure (SOP) is to establish procedures to determine when an Investigational New Drug (IND) Full Application or IND exemption is required as part of the IRB submission.

This SOP applies to clinical research studies conducted at Loyola University Chicago (LUC) and Loyola University Medical Center (LUMC) and covers the responsibilities of the Principal Investigator (PI) and study team members.

II. DEFINITIONS

CLINICAL INVESTIGATION: Any experiment in which a drug (or biologic or device) is administered or dispensed to, or used involving, one or more human subjects. In this context, experiment refers to any use of a drug except for the use of a marketed drug in the course of medical practice (21 CFR 312.3(b))

DRUG: A product that is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease or intended to affect the structure or function of the body and achieves its intended effect through chemical action or metabolism within or on the body.

FOOD AND DIETARY SUPPLEMENTS: Generally are not regulated as drugs. However, those that are intended or promoted to be used in the diagnosis, cure, mitigation, treatment or prevention of disease are considered drugs.

BIOLOGIC: A biological or related product derived from living sources (e.g., humans, animals, microorganisms) and regulated by the U.S. Food and Drug Administration (FDA), including blood, vaccines, allergenics, tissues and cellular and gene therapies. Studies of unlicensed biologics are generally regulated according to the IND regulations. FDA regulations related to the general use and licensing of biologics are found in 21 CFR 600 and 601.

INVESTIGATIONAL NEW DRUG APPLICATION (IND): An IND is a request for authorization from the FDA to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application. The IND exempts an investigational new drug from pre-marketing approval requirements that would otherwise be applicable and allows the drug to be lawfully shipped for the purpose of conducting clinical investigations of that drug (21 CFR 312.1(a)).

INVESTIGATIONAL NEW DRUG: An unapproved drug or biologic (or approved drug or biologic for an unapproved indication) used in an FDA-regulated clinical investigation. The term also includes biological products used in vitro for diagnostic purposes. Clinical investigations that involve FDA regulated drugs are subject to the requirements of 21 CFR 312.

SPONSOR: A person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual, pharmaceutical company, governmental agency, academic

institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator (see below).

The study sponsor is usually responsible for submitting an IND Application to the FDA and obtaining an IND number. If the study is investigator-initiated, the sponsor-investigator (i.e. the Principal Investigator) is usually responsible for submitting an IND Application or exemption confirmation to the FDA.

SPONSOR-INVESTIGATOR: An individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator include both those applicable to an investigator and a sponsor.

IND EXEMPTION: Whether an IND is needed to conduct a clinical investigation of a marketed drug primarily depends on the intent of the investigation and the degree of risk associated with the use of the drug in the investigation. According to FDA regulations 21 CFR 312.2, a clinical investigation of a *marketed* drug is exempt from the requirements to submit an IND Application to the FDA if *all* of the criteria for an exemption in 312.2(b) are met:

a. The drug product is lawfully marketed in the United States

b. The investigation is not intended to be reported to the FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;

c. If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support significant change in the advertising for the product;

d. The investigation does not involve a route of administration or dosage level or use an in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

e. The investigation is conducted in compliance with the requirements for institutional review set forth in 21 CFR part 56 and with the requirements for informed consent set forth in 21 CFR part 50; and

f. The investigation is conducted in compliance with the requirements of 21 CFR 312.7 (i.e. the investigation is not intended to promote or commercialize the drug product)

A clinical investigation involving blood grouping serum, reagent blood cells, or anti-human globulin, is exempt from ICD requirements if (a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedures and (b) it is shipped in compliance with 21 CFR 312.160. A drug intended solely for tests in vitro or in laboratory research animals is exempt from IND requirements if shipped in accordance with 21 CFR 312.160

The FDA will not accept an IND application for an investigation that is exempt under the provisions above.

A clinical investigation involving use of a placebo is exempt from IND requirements if the investigation does not otherwise require submission of an IND.

Note that IND requirements do not apply to the use in the practice of medicine for an unlabeled indication of a new drug product approved under part 21 CFR 314 or of a licensed biological product.

III. PROCEDURE

For studies involving investigational new drugs, the Loyola University Chicago Health Sciences Division Institutional Review Board (LUC HSD IRB) requires the valid IND number issued by the FDA for drug research. Valid IND numbers may be in the approval letter from the FDA, on the Sponsor's research protocol approved by the FDA, or on official correspondence from the Sponsor.

Clinical investigations that are exempt from IND requirements still require review and approval by the LUC IRB.

Investigators are responsible for supplying sufficient information to the IRB to make a final decision.

1.1. Complete the Application for IRB Review in the Loyola Wired Portal.

1.1.1. Upload the research protocol, investigator brochure, informed consent document, recruitment materials, and any other required study documents.

1.1.2. If this is a sponsored trial, upload the letter from the FDA indicating the IND status of the project (the sponsor should provide this letter to the site), or ensure that the IND number appears on the protocol.

1.1.3. If this is an Investigator-initiated trial using an investigational new drug, complete the "IND Decision Worksheet" and upload the worksheet as part of the IRB submission.

1.2. If the Investigator has indicated in the IND Decision Worksheet that their project meets IND exemption criteria, the LUC HSD IRB will review the submission and make one of the following determinations:

1.2.1 Confirm that the IND status is exempt and no further FDA confirmation is needed.

1.2.2 Determine that the project does not appear to be exempt and request that a full IND application be submitted to the FDA.

1.2.3 Require the Investigator to confirm exemption by submitting an IND exemption confirmation request to the FDA.

The Clinical Research Office can assist investigators with submitting IND exemption confirmation requests and full IND applications to the FDA.

The investigator will be informed in writing of the IRB's final determination.

IV. REFERENCES

1) IND Decision Worksheet

2) *Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs)—Determining Whether Human Research Studies Can Be Conducted Without an IND* **U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, FOOD AND DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH (CDER), CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER), CENTER FOR FOOD SAFETY AND APPLIED NUTRITION (CFSAN) SEPT 2013**

3) CODE OF FEDERAL REGULATIONS, TITLE 21, PART 312: INVESTIGATIONAL NEW DRUG APPLICATION: *https://www.ecfr.gov*

V. APPROVALS

Colleen Fitzgerald, MD, MS — 4/25/18 Date
Medical Director, Loyola University Chicago Clinical Research Office

David Hecht, MD — 5/2/18 Date
Executive Vice President of Clinical Affairs, Loyola University Medical Center

INVESTIGATIONAL NEW DRUG (IND) DECISION WORKSHEET
For Investigator-Initiated Clinical Investigations

Does Your Study Require an IND Submittal to the FDA?

Note: The following worksheet is intended only to help determine whether an IND is required prior to initiating your Investigator-Initiated Clinical Trial. Please complete this worksheet and upload it with your IRB submission. The Loyola University Chicago Health Sciences Division Institutional Review Board will review and determine if your study meets exemption criteria, or if further confirmation is needed from the FDA.

Does your study meet ALL of the following criteria for IND exemption?

Investigation of a drug product that is *lawfully marketed* in The United States may be exempt from IND requirements provided **ALL** of the following statements are **true** (per 21 CFR Part 312.2) [https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.2]:

Exemption Criterion	TRUE	FALSE
1 (a) The investigation **IS NOT** intended to be reported to the FDA as a well-controlled study in support of a new indication for use.		
1 (b) The investigation **IS NOT** intended to be used to support any other significant change in the labeling for the drug.		
2 (a) The drug being used in your investigation **IS** lawfully marketed as a prescription drug product.		
2 (b) The investigation **IS NOT** intended to support a significant change in the advertising for the product.		
3 (a) The investigation **DOES NOT** involve a **ROUTE OF ADMINISTRATION** that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.		
3 (b) The investigation **DOES NOT** involve a **DOSAGE LEVEL** that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.		
3 (c) The investigation **DOES NOT** involve **USE IN A PATIENT POPULATION** that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.		
3 (d) The investigation **DOES NOT** involve **ANY OTHER FACTOR** that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.		
4 (a) The investigation **IS** conducted in compliance with the requirements for Institutional Review (IRB) per 21 CFR Part 56 and the requirements for Informed Consent, per 21 CFR Part 50.		
5 (a) The investigation is conducted in compliance with 21 CFR Part 312.7 which means you are **NOT PROMOTING** the drug being studied as safe or effective.		
6 (a) The investigation **DOES NOT** provide for exception for Informed Consent (21 CFR Part 50.24).		

Name of drug product: _____

LU Number: _____

Principal Investigator (type or print name): _____

Principal Investigator Signature: _____ **Date:** _____