STEP BY STEP GUIDANCE FOR SPONSORS-INVESTIGATORS TO A SUCCESSFUL IND SUBMISSION

IND DEVELOPMENT PROCESS

An academic researcher may be required to submit an IND application to the FDA in order to study a marketed medical product in a new (i.e. unapproved) clinical indication. An investigator is always required to hold an IND to study an un-marketed (i.e. unapproved) medical product. In both cases, the products are considered "investigational" by FDA. The vast majority of INDs on file with the FDA are for noncommercial research.

An IND Handbook with detail information has been created for any additional information that you may need. Please refer to the following link to use this Handbook as a resource for clarifications.

Handbook for Investigational New Drug (IND) and New Drug Application (NDA) Regulatory Process

The following information and template models for the IND process have been prepared from multiple resources including the FDA web site/Guidance documents in order to assist Sponsors/Investigators at UNM HSC.

UNM HEALTH SCIENCES CENTER | Clinical & Translational Science Center CTSC

ADMINISTRATIVE STEPS FOR SPONSORS-INVESTIGATORS TO PREPARE THE INTITAL IND SUBMISSION

Pre-IND Process: Review the requirements in 21 CFR 312.2 to determine if your study qualifies for exemption from an IND. Pay specific attention to requirement #3. *The FDA Draft Guidance Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted without an IND* provides more detail on a range of issues, including the process for consulting with FDA.

Start with **IND Decision Tool.** Determine if IND is required.

If no IND is required, use the following template for An IND Exemption Letter :

IND Exemption Letter Template

If you are uncertain and think a pre-IND meeting is required , use the following information and the templates for a meeting request letter and pre-IND briefing packet :

1. **IND Decision Tool**

   Pre-IND Consultation Contact List

   Request for Pre-IND Meeting

   Pre-IND Briefing Packet

   Types of Meetings with the FDA

2. **IND Required:** Review the **IND Protocol Template** for required content. A completed protocol must be included in the IND application.

   Start with a protocol synopsis (page 7 and 8 of the protocol template). The protocol synopsis will be valuable if you are planning a pre-IND meeting. Compile a reference list - include all published articles and unpublished reports or manuscripts cited.

3. **Prepare the Initial IND Submission**

   Compile information in the following areas :

   Animal Pharmacology and Toxicology Studies - Preclinical data used to assess whether the product is reasonably safe for studies in humans. For studies of marketed drugs io new indications, this section might contain data from animal models supporting the utility of the drug in the new indication.

	Manufacturing Information - The composition, stability, and controls used for manufacturing the drug substance and the drug product. For marketed drugs, the FDA already has this information on file in the manufacturer's Drug Master File (DMF). An Investigator-Sponsor can request a Letter of Authorization (LOA) from the manufacturer to refer to the information, although it is not required. For legally marketed drugs, the information in the product label or package insert might suffice for the manufacturing information. **Clinical Protocols and Investigator Brochures** - A detailed clinical study protocol, and Investigator Brochure are required sections of an IND application. (***The Investigator Brochure is primarily needed for multi-center studies and is a summary of information needed by participating investigators to assess the safety of the investigational product).***
4.	**Write the IND in the format of IND Application Template** - The IND investigator writes the IND in the following template format: **IND Application Template** The initial IND submission should be accompanied by a Cover Letter, IND application Form 1571 and Certification of Compliance Form 3674. The IND Sponsor-Investigator must also submit form 1572 that is a formal contract with FDA to adhere to IC, IRB review, and general IND regulations. Refer to Steps 5 and 6 to Cover Letter Template and FDA Forms.
5.	**Prepare a Cover letter** – Accompany your cover letter using the following template: **IND Cover Letter Template**
6.	**Fill out FDA IND Applications:** Form FDA 1571 (PDF - 221KB): Investigational New Drug Application (IND) Form FDA 1571 Instructions Form FDA 1572 (PDF - 208KB): Statement of Investigator Form FDA 1572 Instructions FDA Form 1572 (Box 8) - Protocol Summary Template Form FDA 3674 (PDF - 411KB): Certification of Compliance Form FDA 3674 Instructions Form FDA 3455 (PDF - 56KB): Disclosure: Financial Interest and Arrangements of Clinical Investigators

7. Assemble all completed forms in triplicate as well as one PDF of the original documents.

8. Send the original and two copies to the appropriate address via overnight courier.

For a Drug:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Rd.
Beltsville, Md. 20705-1266

For a Therapeutic Biological Product:

Food and Drug Administration
Center for Drug Evaluation and Research
Therapeutic Biological Products Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

NOTE Keep one copy of the submission packet as well as a photocopy of the courier air bill.

9. On the delivery date, track the shipment on the courier website for confirmation of delivery. Print the delivery confirmation (select *Adobe* from the print menu) and file it with the PDF and third copy of the submission packet, which is kept in an IND Binder.

10. The FDA responds to the initial submission of a new IND with a letter, acknowledging receipt of the submission and assigning the IND number. The sponsor must wait 30 calendar days before initiating any clinical trials. During this time, FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk. If there are no issues, the IND generally goes into effect 30 days after the *Date of Receipt* shown in this letter.

The IND Acknowledgement letter also provides the mailing address for all subsequent submissions to the IND.

ADMINISTRATIVE STEPS FOR SPONSOR-INVESTIGATORS TO MAINTAINE THE IND

To maintain an IND, the Sponsor-Investigator has three reporting responsibilities. Each type of report is time-sensitive and has a specific structure. The first two, Protocol Amendments and Safety Reports, are submitted when needed to report updated or unforeseen circumstances. The third type, the Annual Report, is submitted every year, even when no studies are in progress under the IND. Send all submissions to the address provided in the IND Acknowledgement letter received in response to the initial submission.

1. **IND PROTOCAL AMENDMENTS -**

   Template: IND Protocol Amendment, Cover Letter

2. **IND Annual Reports** - requires a **cover letter** and is a brief report of the progress of studies conducted under an IND, due annually to the FDA within 60 days of the anniversary of the date that the IND went into effect.

   Templates: **Annual Report, Cover Letter for Annual Report**

3. **IND Safety Report** - is expedited, written notification to the FDA of an adverse experience associated with the use of a study drug that is both serious and unexpected. "Associated with the use of the drug" is a Code of Federal Regulations term meaning "There is a reasonable possibility that the experience may have been caused by the drug. An **IND Safety Report** is due to the FDA within **15 calendar days** of initial receipt of the **Serious Adverse Event (SAE)** Report. The **safety report** consists of a **cover letter** and MedWatch Forms:

These forms are fillable on your computer using the free Adobe Acrobat Reader. You can also choose to just print the blank form, and fill it out by hand. The Voluntary Form FDA 3500 features a postage-paid pre-addressed mailer.

Form FDA 3500 - Voluntary Reporting

For use by healthcare professionals, consumers, and patients. Submit the completed form using supplied postage-paid mailer or fax to 1-800-332-0178. **(Send only page 1 plus any continuation pages - do not send instruction pages) Instructions for Completing Form FDA 3500**

Form FDA 3500A - Mandatory Reporting
For use by IND reporters, manufacturers, distributors, importers, user facilities personnel **Instructions for Completing Form FDA 3500A**

4. **Federal Requirements for Record Retention -** For Investigational New Drug (IND) research, the FDA requires that sponsors and investigators retain "records and reports required by this part for 2 years after a marketing application is approved for the drug; or if an application is not approved for drug, until 2 years after shipment and delivery of the drug for investigational use is discontinued and the FDA so notified."