**INITIAL INVESTIGATIONAL NEW DRUG APPLICATION**

**[Title of IND (if applicable)]**

**[Drug Name]**

**Phase # [X]**

**Serial # [XXXX]**

**[Name of Sponsor-Investigator]**

 **[Name, Department]**

**[Phone # XXX-XXX-XXXX]**

**[Mailing Address]**

**[Institution]**

**Signature of Sponsor-Investigator**

**Date of Submission: [XX Month 20XX]**

1. FORM FDA 1571 AND FORM FDA 3674[**[21 CFR 312.23(a)(1)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

[Link to form FDA 1571](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083533.pdf)

[Link to instructions for Form FDA 1571](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM182850.pdf)

[Link to Form FDA 3674](https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=0ahUKEwiV-IvIh6rNAhUQT1IKHTkrCIUQFggcMAA&url=http%3A%2F%2Fwww.fda.gov%2Fdownloads%2FAboutFDA%2FReportsManualsForms%2FForms%2FUCM048364.pdf&usg=AFQjCNGLXX1BMl8MXQnujYStV7G_d2t-qA&bvm=bv.124272578,d.aXo)

[Link to instructions for Form FDA 3674](https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=2&cad=rja&uact=8&ved=0ahUKEwiV-IvIh6rNAhUQT1IKHTkrCIUQFggiMAE&url=http%3A%2F%2Fwww.fda.gov%2Fdownloads%2FAboutFDA%2FReportsManualsForms%2FForms%2FUCM354618.pdf&usg=AFQjCNGGVKItho7YXsCp3IWpIzeIMc528A&bvm=bv.124272578,d.aXo)

*These forms should be referenced here as separate appendices.*

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1. INTRODUCTION[**[21 CFR 312.23(a)(3)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

*This section is brief; usually 2-3 pages should be sufficient. This section should contain information about the clinical indication and the reason that you think the product has a place in the treatment of these patients. The FDA is concerned primarily with the safety of the participants of your study, so the scientific merit of the study does not have to be explored in depth in this section. It is best to state briefly why you believe this study is necessary and who will benefit from the study, then go into some more detail as to how the participants in the study are to be protected.*

## 3.1. Introductory Statement

*After your introductory statement, use the headings below to ensure you fulfill all of the requirements.* ***Maintain all of the headings*** *in this document and if not applicable to your IND, simply state this.*

*(~2-3 pages in length)*

### Name of the Drug and All Active Ingredients

### Pharmacological Class of the Drug

### Structural Formula of the Drug

### Formulation of the Dosage Forms to be Used

### Route of Administration

### Objectives and Duration of the Proposed Clinical Investigation(s)

## 3.2. Summary of Previous Human Experience

*This section is a brief summary of previous human experience with the drug(s), with reference to the literature or other INDs if pertinent, and to investigational or marketing experience in other countries that may be relevant to the safety of the proposed clinical investigation(s). This topic will be written up in detail in Section 9. However, for many sponsor-investigator INDs that use commercially available drugs, Section 3.2 and 9 are often identical.*

## 3.3. Status of Drug in Other Countries

*If the drug has been withdrawn from investigation or country marketing in any country for any reason related to safety or effectiveness, identification of the stud(ies) where the drug was withdrawn and the reasons for the withdrawal are stated here. For a Sponsor-Investigator IND, you may simply state you are not aware of any withdrawals.*

## 3.4 References

1. GENERAL INVESTIGATIONAL PLAN[**[21 CFR 312.23(a)(4)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

## Rationale and Objectives

*The rationale for the drug or research study (the science behind why this is a good idea).*

## Indication(s) to be Studied

## General Approach for Evaluation of Treatment

## Description of First Year Trial(s)

## Number of Subjects to be Evaluated

## Drug Related Risks

*Any risks of particular severity or seriousness anticipated on the basis of the toxicological data in animals or prior studies in humans with the drug(s) or related drugs.*

## References

# Investigator’s BROCHURE [[21 CFR 312.23(a)(5)]](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

*For sponsor-investigator initiated INDs, there is no requirement to create an Investigator Brochure (IB) if you have a single site study. If no IB is required for your study, you may incorporate the following statement:*

In accordance with 21 CFR Part 312.55(a), an Investigator’s Brochure is not required for a sponsor-investigator IND.

*You can also state that*: All investigators will be referred to the latest version of the protocol

*If you are using the marketing approved drugs, then, it is appropriate here to refer to the product label*

[*Helpful link for finding current product labeling*](http://dailymed.nlm.nih.gov/dailymed/about.cfm)

[*Another helpful link for finding current product labeling*](http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA/)

However, if you do have a multi-site study being performed under your IND, you will need an IB.

1. PROTOCOL[**[21 CFR 312.23 (a)(6)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

## Study Protocol

*The complete clinical protocol for this clinical study can be included in the body of the IND or attached as an appendix to this IND, and referenced here*.

*State here where the study is to take place and give the name and address of the Institutional Review Board responsible for the initial and continuing review and approval of the study.*

## Informed Consent

*If the investigation involves an exception from informed consent under 21 CFR 50.24, the sponsor shall prominently identify on Form FDA 1571 and here that the investigation is subject to the requirements in 21 CFR 50.24.*

*Otherwise it must be stated here that informed consent will be obtained by the participants of the study in accordance with 21 CFR Part 50 Protection of Human Subjects.*

## Investigator and Facilities Data

*Attach* [*FDA Form 1572*](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf) *as appendix (*[*instructions*](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM223432.pdf)*)*

*Form is not required, but is the easiest way to include all information in this section that is required under 21 CFR 312.23(a)(6)(iii)(b).*

*Attach CV (credentials) of the principal investigator(s) and co-investigators as appendices*

*Reference these appendices here*

# CHEMISTRY, MANUFACTURING AND CONTROL INFORMATION

[**[21 CFR 312.23(a)(7)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

*Include Letter of Cross-Reference Authorization here if one is available that references an IND that would cover the information that would be included in this section.*

*If the investigational drug has already been marketed, this section may be covered by referring to the product labeling*

## Introduction

*Describe general information about the drug that this IND will be using.*

### Mitigation of Potential Human Risk

*Describe potential human risks which can be related to the method of manufacture or an inherent risk associated with the drug.*

*Include what measures you will take to mitigate these potential risks.*

## Drug Substance

### Description of Drug Substance

*Physically, chemically, and biologically describe the drug substance characteristics.*

### Manufacturer

*State the name, address, and other information of the manufacturer of the drug.*

### Control of Raw Materials (Components) and Criteria [[21 CFR 210.3(b)(3)]](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=210.3)

*List the raw materials that are used to manufacture the drug. The example table may be used or altered to fit the needs of the drug.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Material** | **Manufacturer** | **Category #** | **Grade** | **Acceptance Criteria** |
|  |  |  |  |  |
|  |  |  |  |  |

### Manufacturing of the Drug Substance

*Describe the process in which the drug is manufactured. This can be by narrative, comprehensive diagram, or a step-by-step procedure.*

### Production Specifics and Analysis of In-Process Material

[**[21 CFR 210.3(b)(9)]**](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=210.3)

*Describe each step of the drug substance manufacturing.*

*If there are in-process tests, indicate them along with the acceptance criteria for those tests.*

*Describe the analytical tests that are performed on intermediate drug substance processes that are created throughout the complete drug manufacturing process.*

### Analysis of the Drug Substance

*Describe the analytical test that is performed on the final drug substance that is created.*

* 1. Drug product[**[21 CRF 210.3(b)(4)]**](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=210.3)

*Drug product is different from drug components or drug substance. Each is linked to their respective definition as defined by the FDA in “Code of Federal Regulations Title 21”.*

### Description and Composition

*Describe the drug product, which is the drug substance (active ingredient) plus any diluents.*

### Manufacturer

*State the name, address, etc. of the manufacturer of the final drug product.*

### Manufacturing of the Drug Product

*Use a diagram to represent, describe, or tabulate, the filling and vialing scheme that is used to reach the final drug product.*

### Dosage Preparation and Storage Scheme

### Proposed Release Criteria

*List what the proposed acceptance criteria will be for the final drug product.*

### Container Closure System

*Describe the container and the closure system*

### Stability Testing

*Describe your plan for stability testing, including frequency, types of tests, and the acceptance criteria for the tests.*

*Refer to ICH Guidelines Q1A (R2): “STABILITY TESTING OF NEW DRUG SUBSTANCES AND PRODUCTS” for general stability testing information.*

## Placebo

*IF a placebo will be used in the study, describe what it is and the manufacturing process.*

*Refer to previous sections regarding the manufacturing, acceptance criteria/tests, and raw materials and repeat them for the placebo.*

## Labeling

*Include the information that will be displayed on the label. List the font size and dimensions of the label. An example is provided below.*

*Note: Labels must contain the phrase: “Caution: New Drug – Limited by Federal law to investigational use”.*

Product Name

Date of Manufacture, Lot Number

Concentration, Volume, Total units

Caution: New Drug – Limited by

Federal law to investigational use

## Description of the Manufacturing Facility

## Environmental Assessment

*Include the following statement (unless there is reason to believe the distribution and use of the drug could have environmental impact):*

“We request a claim for categorical exclusion for preparation of an environmental assessment for the drug used in this proposed clinical trial as provided for in 21 CFR Part 25.31(e), action on an IND.”

# PHARMACOLOGY AND TOXICOLOGY INFORMATION

[**[21 CFR 312.239(a)(8)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

*In this section, list all of the pharmacology and toxicology information that you have about the drug.*

*Include Letter of Cross-Reference Authorization here if one is available that references an IND that would cover the information that would be included in this section.*

*If this IND will include nonclinical studies that were performed in support of this IND, then the following headings in Section 8 should be used.* ***Otherwise, they can be deleted.***

## Introduction

### Structural Formula of the Drug

### Formulation of the Dosage Forms

### Route of Administration

### Comparison of Toxicology and Clinical Lots

## Pharmacology

### Pharmacological Effects

### Mechanism of Action

### Absorption, Distribution, Metabolism, and Excretion

## Toxicology

### Introduction

### Integrated Summary of Toxicity Studies

### Qualifications of Individuals performing Toxicity Study

### Testing Facility for the Nonclinical Toxicity Study

### Declaration of GLP Compliance

## Other Nonclinical Studies

## References for Section 8

1. PREVIOUS HUMAN EXPERIENCE[**[21 CFR 312.23(a)(9)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

*The following sections regarding previous human experiences are only required if they are applicable to the drug and may be deleted if not.*

## Marketed Experience

*Summarize any FDA-approved marketed indications for the drug. Provide FDA drug labels for the indications.*

## 9.2. Prior Clinical Research Experience

*Summarize prior clinical studies that have used the investigational drug.*

## 9.3. Clinical care Experience

*Describe any “off-label” uses of the marketed drug in clinical settings.*

## 9.4. References

*Any references for section 9*

1. ADDITIONAL INFORMATION[**[21 CFR 312.23(a)(10)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

*Certain applications may require information on “special” topics that are listed below. This section may not be applicable in which you should include “10. ADDITIONAL INFORMATION” is “Not Applicable’.*

## 11.1. Drug Dependence, Abuse Potential

*If the drug is a psychotropic substance or otherwise has abuse potential, a section describing the relevant clinical studies and experience and studies in test animals.*

## 11.2. Radioactive Drugs

*If the drug is a radioactive drug, sufficient data from animal or human studies to allow a reasonable calculation of radiation-absorbed does to the whole body and critical organs upon administration to a human subject. Phase 1 studies of radioactive drugs must include studies which will obtain sufficient data for dosimetry calculations.*

## 11.3. Pediatric Studies

*Plans for assessing pediatric safety and effectiveness.*

## 11.4. Other Studies

*A brief statement of any other information that would aid evaluation of the proposed clinical investigations with respect to their safety or their design and potential as controlled clinical trials to support marketing of the drug.*

## 11.5. References

# RELEVANT INFORMATION

*If requested by the FDA, any other relevant information needed for review of the application.*

* 1. **Information Previously Submitted**

*The sponsor ordinarily is not required to resubmit information previously submitted, but may incorporate the information by reference. A reference to information submitted previously must identify the file by name, reference number, volume, and page number where the information can be found. A Reference to information submitted to the agency by a person other than the sponsor is required to contain a written statement that authorizes the reference and that is signed by the person who submitted the information.*

* 1. **Material in a Foreign language**

*The sponsor shall submit an accurate and complete English translation of each part of the IND that is not in English. The sponsor shall also submit a copy of each original literature publication for which and English translation is submitted.*

* 1. **Number of Copies**

*The sponsor shall submit an original and two copies of all submissions to the IND file, including the original submission and all amendments and reports.*

*Note: PI should make and retain an additional copy for reference before sending the original plus two copies to the FDA.*

* 1. **Numbering of IND Submissions**

*Each submission relating to an IND is required to be numbered serially using a single, three-digit serial number. The initial IND is required to be numbered 000; each subsequent submission is required to be numbered chronologically in sequence.*

* 1. **Identification of Exemption from Informed Consent**

*If the investigation involves an exception from informed consent under 50.24 of “Code of Regulations Title 21, the sponsor shall prominently identify on the cover sheet that the investigation is subject to the requirements in 50.24.*

**General/Formatting Information:**

*Delete all instructional text*

*Format page numbers to match the Table of Contents based on your specific IND application, the numbers indicated on the TOC are not uniform and are included to help format.*

*If sections are not applicable to your study, state “Not Applicable” under the main section.*

 *Ex: “10. ADDITIONAL INFORMATION” is “Not Applicable’.*

*In the headings, the FDA “Code of Federal Regulations Title 21” is hyperlinked into the specific section of the IND Application that the section covers. Use this if extra information is wanted regarding the details about that section of the application.*

 *Ex:* [**[21 CFR 312.23(a)(10)]**](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.23)

*This indicator refers to the “Code of Regulations Title 21” and specifically the 10th piece under section 312.23 (a), “Additional Information”.*

*Also, some definitions are linked, such as “drug substance” and “drug” product for sections that are applicable as they are commonly mixed-up.*

 *Ex:* **[21 CFR 210.3(b)(9)]**

*This indicator refers to the “Code of Regulations Title 21” and specifically the 9th piece under section b of 210.3(b) (definitions) and describes an “active ingredient”.*