INITIAL INVESTIGATIONAL NEW DRUG APPLICATION

IND Title (if title is being used)

IND Number (if known)

Serial 0000

Name of Sponsor-Investigator, MD

X Professor, Department

DUKE UNIVERSITY

Date of Submission

# Form FDA 1571

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# Introduction

## Introductory Statement

*This section is brief; usually two to three pages should be sufficient. The information here is intended to place the use of the drug(s) with this indication into perspective for the FDA. After your introductory statement, use the headings below to ensure you fulfill all of the requirements. This is also easier for the reviewers to follow.* ***Maintain all of the headings*** *in this document and if not applicable to your IND, simply state this.*

### Name of the Drug and All Active Ingredients

### Pharmacological Class of the Drug

### Structural Formula of the Drug

*This section may not be applicable to biologics. You could describe the protein or complex of proteins instead (e.g. 341 amino acids with a molecular weight of 150 g/mol)*

### Formulation of the Dosage Forms to be Used

### Route of Administration

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

## 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.*

## Status of Drug in Other Countries

*This section is likely not applicable to you. If the drug has been withdrawn from investigation or marketing in any country for any reason related to safety or effectiveness, identification of the country(ies) where the drug was withdrawn and the reasons for the withdrawal are stated here.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.*

## References

*List any references for Section 3*

# General Investigational Plan

## Rationale

*The rationale for the drug or research study, including the dose, schedule, and patient population (the science behind why this is a good idea).*

## Indication 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

*List any references for Section 4*

# Investigator’s Brochure

*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 (also known as the package insert) and provide a URL link to the must current product label. You may find these links useful for finding current product labeling:*

* <http://dailymed.nlm.nih.gov/dailymed/about.cfm>
* <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.

A template for the information included in an IB can be found in the ICH Guideline E6: Good Clinical Practice.

*Rather than insert the IB within this document, we recommend that you assemble the IND after converting to PDF or separately printing this IND document and the IB. To ensure that the TOC on Page 3 reflects the true number of pages in the IND, format the page number on the Protocol page to reflect the additional pages in the IB.*

*To format the page number, highlight the page number in the footer, right click and choose “Format Page Numbers”. Then click “Start numbering at” and put the new number accounting for the number of inserted pages. Also note, to be able reformat page numbers, you need to insert a “section break (next page)” rather than a simple page break.*

# Protocol

## Study Protocol

*Please insert study protocol.*

*Rather than insert the protocol within this document, we recommend that you assemble the IND after converting to PDF or separately printing this IND document and the protocol. To ensure that the TOC on Page 3 reflects the true number of pages in the IND, format the page number on the Informed Consent page to reflect the additional pages in the protocol.*

*To format the page number, highlight the page number in the footer, right click and choose “Format Page Numbers”. Then click “Start numbering at” and put the new number accounting for the number of inserted pages. Also note, to be able reformat page numbers, you need to insert a “section break (next page)” rather than a simple page break.*

## Informed Consent

*Please insert study Informed Consent.*

*Rather than insert the Informed Consent within this document, we recommend that you assemble the IND after converting to PDF or separately printing this IND document and the Informed Consent. To ensure that the TOC on Page 3 reflects the true number of pages in the IND, format the page number on the Investigator and Facilities Data page to reflect the additional pages in the Informed Consent.*

*To format the page number, highlight the page number in the footer, right click and choose “Format Page Numbers”. Then click “Start numbering at” and put the new number accounting for the number of inserted pages. Also note, to be able reformat page numbers, you need to insert a “section break (next page)” rather than a simple page break.*

## Investigator and Facilities Data

*Form FDA 1572 and CV of the principal investigator(s).*

*Rather than insert the Form FDA 1572 and CV within this document, we recommend that you assemble the IND after converting to PDF or separately printing this IND document and the Form FDA 1572 and CV. To ensure that the TOC on Page 3 reflects the true number of pages in the IND, format the page number on the following CMC page to reflect the additional pages in the Form FDA 1572 and CV.*

*To format the page number, highlight the page number in the footer, right click and choose “Format Page Numbers”. Then click “Start numbering at” and put the new number accounting for the number of inserted pages. Also note, to be able reformat page numbers, you need to insert a “section break (next page)” rather than a simple page break.*

*Use this link to access Form FDA 1572:*

[*http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf*](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf)

*Use this link to access instructions for completing Form FDA 1572:*

[*http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM223432.pdf*](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM223432.pdf)

# Chemistry, Manufacturing and Control Information

*If you have Letter of Authorization referencing an IND regarding information that would normally be included in this section, place a copy of the LOA here.*

## Introduction

*Provide general information about the investigational drug and the study that is proposed under this IND.*

### Mitigation of Potential Human Risk

*What are the potential human risks relating to the method of manufacture or an inherent risk associated with the drug substance (e.g., you have an attenuated viral vector) and what measures were taken to mitigate the potential human risk?*

## Drug Substance

### Description of Drug Substance

*Description of the drug substance including physical, chemical and biological characteristic of the compound. If there is a conformational picture of the drug substance, please paste it in this section.*

### Manufacturer

*Name and address of the manufacturer*

### Control of Raw Materials

The raw materials used in the manufacture of XY dug substance is listed below

| **Item Description/Name** | **Manufacturer** | **Cat#** | **Grade** | **Acceptance Criteria** |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

### Control of the Starting Material

*What are the acceptance criteria for each raw material to be used in the production (if differs from the information in the table). For example if plasmid is used in the manufacturing, do you sequence it before use? If yes, please describe the process and acceptance criteria. If raw material is commercially purchased and accepted based on the CoA or package insert, you can just state it in the table and skip this part.*

### Manufacturing of the Drug Substance

*Please make a general manufacturing diagram describing how the manufacturing flow looks like. Two* ***examples*** *are shown below (flow diagram or table).*

General manufacturing flow diagram:



### Manufacturing Process and In-Process Testing

|  |  |  |  |
| --- | --- | --- | --- |
| Step | Description | In-process testing | Release testing |
| 1. |  |  |  |
|  | ↓ |  |  |
| 2. |  |  |  |
|  | ↓ |  |  |
| 3. |  |  |  |
|  | ↓ |  |  |
| 4. |  |  |  |
|  | ↓ |  |  |
| 5. |  |  |  |

### Production Specifics

*Every step of the drug substance manufacturing should be described here pointing out if there are any in process testing that will be performed and what are the acceptance criteria of those*

**1. Process XY 1**

*Please describe the process No. 1.*

**2. Process XY 2**

*Please describe the process No. 2.*

**3 Process XY 3**

*Please describe the process No. 3.*

**4. Process XY 4**

*Please describe the process No. 4.*

### Analytical Testing of In-Process Products

*Please describe the analytical testing performed on the intermediate drug substance products during the manufacturing*.

### Analysis of the Drug Substance

*Please describe the analytical testing performed on drug substance*

## Drug Product

### Description and Composition

*Please note the difference between drug substance and drug product. Drug substance is the active ingredient. Drug product is the final product configuration that contains drug substance, and it might also contain diluents, vialed in the certain volume etc*.

### Manufacturer

*Name and address of the manufacturer of the final drug product*

### Manufacturing of the Drug Product

#### General Manufacturing Flow Diagram

*This is just an example, how one diagram that would for example represent the filling and vialing scheme of the final product. You should modify to reflect you manufacturing process. Again, this can be presented as a process flow diagram or cells in a table.*

### Dosage Preparation and Storage Scheme

### Tests and Specifications

*As for the manufacturing of drug substance, please list all the in-process testing that might be done during the manufacturing of drug product (if you have any)*

### Proposed Release Criteria

*As for the drug substance, please list what are the released criteria for your final product*

### Container Closure System

*Describe the container closure system*

### Stability Testing

*What is your plan for stability testing? How frequently they will be performed and what are the tests that you will use to evaluate stability? What is the acceptance criteria? Typically, stability testing is performed according to ICH Guidelines Q1A (R2): “STABILITY TESTING OF NEW DRUG SUBSTANCES AND PRODUCTS”. Testing is performed at 0, 3, 6, 9, 12, 18, 24, 36, 48, etc, where the 0 month is data from release testing.*

## Placebo

*If you are using placebo in your trial, please describe what it is and how do you manufacture it.*

*As for the drug substance, you need to list the manufacturer of placebo, source of the material, controls used as an acceptance and release criteria etc. Please look through the previous sections.*

## Labeling

*Include the information in the label as indicated below, listing the font size and the dimensions of the label.*

Product Name

Date of Manufacture, Lot Number

Concentration, Volume, Total units

Caution: New Drug – Limited by

Federal law to investigational use

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

## Description of the Manufacturing Facility

## Environmental Assessment

*Include the following statement:*

An Environmental Assessment is not required because the action requested qualifies for a categorical exclusion per 21 CFR 25.31(e). To the applicant’s knowledge, no extraordinary circumstances exist per 21 CFR 25.15(d).

# Pharmacology and Toxicology Information

*Please list all the pharmacology & Toxicology information that you might have. If drug product is marketed in the US just refer to its label.*

*If you have a Letter of Authorization (LOA) referencing an IND regarding information that would normally be included in this section, place a copy of the LOA here.*

*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 the Toxicity Studies

*Include each toxicology report summary taken from the completed tox study reports*.

*List the volumes that will contain the full toxicology reports for each summary provided*.

### Qualification of Individuals Performing Toxicity Study

### Testing Facility for the Nonclinical Toxicity Study

### Declaration of GLP Compliance

## Other Nonclinical Studies

## References for Item 8

# Previous Human Experience

*A summary of previous human experience with the investigational drug, if any, known to the applicant. Simply citing Authorization letters may be appropriate to fulfill this section. If the drug(s) is already marketed in the US, then you may be able to simply refer to the product labeling. If not, the following information is required:*

1. *If the drug has been investigated or marketed previously, either in the United States or other countries, detailed information about such experience that is relevant to the safety of the proposed investigation or to the investigation’s rationale.*
2. *If the drug has been the subject of controlled trials, detailed information on such trials that is relevant to an assessment of the drug’s effectiveness for the proposed investigational use(s) should also be provided. Any published material that is relevant to the safety of the proposed investigation or to an assessment of the drug’s effectiveness for its proposed investigational use should be provided in full. Published material that is less directly relevant may be supplied by a bibliography.*
3. *If the drug is a combination of drugs previously investigated or marketed, the information should be provided for each active drug component. However, if any component in such combination is subject to an approved marketing application or is otherwise lawfully marketed in the United States, the sponsor is not required to submit published material concerning that active drug component unless such material relates directly to the proposed investigational use (including publications relevant to component- component interaction).*
4. *If the drug(s) has been marketed outside the United States, a list of the countries in which the drug has been marketed and a list of the countries in which the drug has been withdrawn from marketing for reasons potentially related to safety or effectiveness.*

## References

*List any references for Section 9*

# Additional Information

*For certain applications, as described below, information on special topics may be needed. Such information shall be submitted in this section as outlined below. If these subsections are not relevant, just delete them, but keep the header “10. ADDITIONAL INFORMATION” and state “Not Applicable”*

## Drug Dependence and Abuse Potential

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

## Radioactive Drugs

*If the drug is a radioactive drug, sufficient data from animal or human studies should be provided, to allow a reasonable calculation of radiation-absorbed dose 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.*

## Pediatric Studies

*If the investigational drug will be studied in pediatric setting, plans for assessing pediatric safety and effectiveness should be provided.*

## Other Information

*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.*

## Selected References

*If you are including reprints with your submission, list them in this section.*

# Biosimilar User Fee Cover Sheet (Form FDA 3792)

*Biosimilar biological products are products that are demonstrated to be interchangeable with an FDA-licensed biological product. For sponsor-investigator initiated INDs, this section is probably not applicable due to the fact that the majority of sponsor-investigator initiated INDs are not developing biosimilars. If you are a sponsor-investigator developing a biosimilar biological product, please complete Form FDA 3792 and include it here in section 11.*

*State* Not Applicable *if appropriate, but leave this header in*.

# Clinical Trials Certification of Compliance (Form FDA 3674)

*Include a signed and dated Form FDA 3674.*

*Use this link to access the Form FDA 3674:*

[*http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf*](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf)

*Use this link to access instructions for completing Form FDA 3674:*

[*http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM354618.pdf*](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM354618.pdf)

*Use this link to access the Checklist for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT) Under 42 CFR 11.22(b):*

[*https://prsinfo.clinicaltrials.gov/ACT\_Checklist.pdf*](https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf)