Investigational New Drug (IND) Submission checklist

Please check (✔)

☐ **1. Cover Sheet**

☐ **2. Submit completed Form FDA 1571 as instructed by FDA**

Note: If a study conduct obligations have been contracted to a CRO, indicate that a CRO is contracted rather than listing individual obligations.

Note: If an investigation involves an exception from informed consent for emergency research, state on the Cover Sheet.

☐ • 3. Table of Contents

Provide a detailed Table of Contents Page

☐ **4. Introductory Statement and General Investigational Plan**

A brief overview of the general investigational plan for the study. This information is repeated later in the IND, in a concise detail.

☐ **First section:** must include the name of drug, active ingredients, its pharmacological class, structural formula (if known), formulation of the dosage form(s) to be used, route of administration, and broad objectives and expected duration of the study.

☐ **Second section:** must include a summary of previous human experience, reference to other INDs, if relevant, and investigational and marketing experience in other countries, if applicable.

☐ **Third section:** indicate if the drug has been withdrawn from investigation or marketing for any safety or effectiveness reasons, including where and why.

☐ **Last section:** provide a summarize plans for investigating the drug within the next 12 months, including rationale for the study, indications(s) to be studied, general plan for evaluating the drug, kind of studies planned for the first year (specify if these plans are not yet complete), expected number of patients to be enrolled and anticipated risks based on animal toxicology data.

☐ **5. Investigator Brochure**

Include a copy of the Investigator's Brochure where applicable

6. Protocol(s)

☐ Submit a protocol for each planned study.

☐ Submit an Form FDA 1572 for each Investigator participating in the study

Note: Protocols not submitted with the original IND must be submitted in an IND Protocol Amendment.

☐ **7. Referencing Other Sources**

If utilizing a drug that is currently subject to a manufacturer's IND, or marketing application, refer to that IND or application or Drug Master File (if appropriate) to prevent duplicating information that are already available to FDA. Include a Letter of Authorization from the other sponsor permitting FDA to use their information for this IND. The Sponsor also must file a copy of the letter to its own FDA file.

Available information in a published scientific literature may be referenced, if appropriate. Include a copy of each of the copyrighted items with the IND submission. Material copyrighted by others must be included in a bibliography section, not in the body of the IND.

May utilize references of the current edition of the United States Pharmacopoeia – National Formulary, if appropriate, to satisfy some of the requirements in the Drug Substance and Drug Product sections.

☐ **8. Introduction**

The Introduction should state whether any information in regards to the chemistry of the drug substance, drug product, or the manufacture of either might suggest any possible human risks.

If so, document all possible human risks and indicate how these safety issues will be monitored, or why the risks can be dismissed. Ensure to describe any differences between the drug product planned for use in clinical studies and that used in animal toxicology studies. Does the differences in the drug product affect the safety profile, and how it is affected. If not, please clarify.

9. Drug Substance

Include a summary of the following elements:

☐ A brief description of the drug substance, including its physical, chemical, or biological characteristics, and some evidence to support its proposed chemical structure.

☐ The name and address of its manufacturer.

☐ A brief description of the general method of preparation of the drug substance, including a list of the reagents, solvents, and catalysts used. A detailed flow diagram is suggested as the most effective presentation. More information may be needed to assess the safety of biotechnology-derived drugs or drugs extracted from human or animal sources.

☐ The acceptable limits and analytical methods used to ensure the identity, strength, quality, and purity of the drug substance, with a brief description of the test methods used, (e.g., IR spectrum to prove the identity, and HPLC chromatograms to support the purity level and impurities). Submission of certificates of analysis is also suggested.

☐ A brief description of the stability study and the test methods used to monitor the stability of the drug substance during the toxicologic studies should be submitted. Preliminary tabular data based on representative material may be submitted. Neither detailed stability data nor the stability protocol should be submitted.

Note: Validation data and established specifications ordinarily need not be submitted at the initial stage of drug development. However, for some well-characterized, therapeutic biotechnology-derived products, preliminary specifications and additional validation data may be needed in certain circumstances to ensure safety in Phase 1.

10. Drug Product

Include a summary of the following elements:

☐ A list of all components, which may include reasonable alternatives for inactive compounds, used in the manufacture of the investigational drug product, including both those components intended to appear in the drug product and those which may not appear, but which are used in the manufacturing process. A list of one or two pages should be submitted. The quality (e.g., National Formulary, American Chemical Society) of the inactive ingredients should be cited. For novel excipients, additional manufacturing information may be necessary.

☐ Where applicable, a brief summary of the quantitative composition of the investigational new drug product, including any reasonable variations that may be expected during the investigational stage.

☐ The name and address of the clinical study drug product manufacturer.

☐ A brief, general description of the method of manufacturing and packaging procedures as appropriate for the product. A detailed flow diagram and a brief written description of the manufacturing process should be submitted, including sterilization process for sterile products.

☐ A brief description of the acceptable limits and analytical methods used to ensure the identity, strength, quality, and purity of the drug product. For example, for sterile products, sterility and pyrogenicity tests should be submitted. Submitting a copy of the certificate of analysis of the clinical batch is suggested.

☐ A brief description of the stability study and the test methods used to monitor the stability of the drug product to be used in clinical studies (packaged in the proposed container/closure system and under expected storage conditions), should be provided. Preliminary tabular data based on representative material may be submitted, but not detailed stability data nor the stability protocol.

Note: Validation data and established specifications need not be submitted at the initial stage of drug development. For well-characterized, therapeutic, biotechnology-derived products, a detailed assessment of bioactivity and preliminary specifications should be available.

☐ **11. Placebo**

Provide a brief, general description of the composition, manufacture, and control of any placebo (if any) to be used in the proposed clinical studies.

☐ **12. Labeling**

Provide a copy of all labels and labeling for the investigational product. A mock-up or printed representation of the proposed labeling that will be provided to investigator(s) is acceptable. Investigational labels must carry a "caution" statement that reads: "Caution: New Drug - Limited by Federal (or United States) law to investigational use."

☐ **13. Environmental Impact**

If applicable, must make a claim for categorical exclusion from submission of an environmental assessment. If the product meets the exclusion requirements, state “I claim categorical exclusion under 21 CFR 25.31(e) for the study/studies under this IND. To my knowledge, no extraordinary circumstances exist.”

☐ **14. Pharmacology and Toxicology Information**

There are three parts in this section. FDA provides guidelines on conducting these assessments. The review division should be contacted or the FDA website can be searched for these documents. The first IND submission should capture all current pharmacology and toxicology information upon which the decision to proceed to study the product in humans was based, up through what is known when the IND is ready for submission. As additional information is gathered and the studies progress, submit informational amendments to keep the IND current.

☐ **15. Responsible Person(s)**

The IND must provide identification and qualifications of individual(s) who evaluated the animal safety data and have concluded as reasonably safe to begin the proposed human study. This person(s) should sign the summary attesting that the written summary accurately reflects the animal toxicology data from the various completed studies. The submission must state where the animal studies were conducted and where the records of the studies are available for inspection.

☐ **16. GLP Compliance Certification**

GLP compliance is required for in vitro and in vivo, in order to assess product safety. Regulations ensure that the data are obtained and reported to FDA appropriately. A declaration to conduct the study in full compliance with GLP must be documented. If not in compliance, a statement of reasons for noncompliance and sponsor's view on how such non-compliance might affect the interpretations of the findings must be provided.

17. Pharmacology and Drug Distribution

☐ A description of the pharmacological effects and mechanism(s) of actions of the drug in animals

☐ Information on the absorption, distribution, metabolism, and excretions of the drug.

☐ A summary report of up to 5 pages should be submitted.

18. Toxicology: Integrated Summary

An Integrated Summary is only used for drugs and well-characterized, therapeutic biotechnology-derived products. For novel biotechnology-derived products, the review division should be consulted first.

Need for studies depend on the nature of the drug and the phase of human investigation, including acute, sub-acute and chronic toxicity tests, tests on reproduction and fetal effects, any special toxicity tests unique to the product's use (e.g., dermal, inhalation, etc.) and any necessary in vitro tests. When species specificity, immunogenicity, or other considerations appear to make many or all of the toxicological models irrelevant, consult the review division.

If final quality-assured individual study reports are not available at the time of IND submission, an integrated summary report of toxicological findings based on unaudited draft reports is acceptable. Unaudited draft reports might undergo minor modifications during final review and quality assurance auditing. Full toxicology department individual study reports should be available to FDA, upon request. In addition, individual study reports should be available to FDA, upon request, as final, fully quality-assured documents within 120 days after the start of the human study for which the animal study formed part of the safety conclusion basis. These final reports should state in the introduction any changes from those reported in the integrated summary. If there are no changes, that should be also be stated clearly in the introduction of the final, fully quality-assured report.

If the integrated summary is based upon unaudited draft reports, sponsors should submit an update to their integrated summary by 120 days after the start of the human study (s) identifying any differences found in the preparation of the final fully quality-assured study reports and the information submitted in the initial integrated summary. If there were no differences found, that should be stated in the integrated summary update.

FDA believes 10 to 15 pages of text with additional tables (as needed) should suffice for the integrated summary. FDA also encourages the use of visual data displays (e.g., box plots, stem and leaf displays, histograms or distributions of lab results over time). The integrated summary should contain the following:

☐ Describe the design of the studies and any deviations from that design that occurred. Include the dates when the studies were performed. Reference to the study protocol and protocol amendments may suffice for some of this information.

☐ Present the animal toxicology and toxicokinetic findings systematically (a "systems review" perspective, e.g., CNS, cardiovascular, pulmonary, etc.). Those findings that an informed and

	experienced expert would reasonably consider as possible signals of human risk should be highlighted. If a product's effects on a particular body system have not been assessed, that should be noted. If any well-documented toxicological "signal" is not considered evidence of human risk, the reason should be given. In addition, the sponsor should note whether these findings are discussed in the investigator's brochure.
	19. Toxicology - Full Data Tabulation Submit for each animal toxicology study that support the safety of the proposed clinical investigation (a full tabulation of data suitable for detailed review). This should consist of line listings of the individual data points, including laboratory data points for each animal in these trials, along with summary tabulations of these data points. To allow interpretation of the line listings, ensure the line listings should be either:
☐	A brief (usually a few pages) description (i.e., a technical report or abstract including a methods description section) of the study **Or**
☐	A copy of the study protocol and amendments.
☐	**20. Previous Human Experience** Include relevant information about previous investigations or marketing in the United States and other countries, including published material relevant to the product's safety and/or effectiveness. List other countries where the product has been marketed and whether it was withdrawn from any of those markets (and why), or state that there has been no previous human experience. Previous human experience may be presented in an integrated summary report.
☐	**21. Additional Information** When referencing any previously submitted information, refer to it by name, reference number, and volume and page number to assist FDA in finding the reference(s). Examples of other information that can be included: discussion about drug dependency or abuse potential and radioactive dissymmetry information.
☐	**22. Other FDA-Requested Information** FDA may require other additional information be included in the IND
☐	**23. Material in a Foreign Language** Material in a language other than English (including scientific literature published in a foreign journal) must be included in the IND with a certified accurate and complete English translation.
	24. Format
☐	**Jackets:** FDA has detailed specifications about the binders, called Jackets, which must be used for the IND. Refer to www.fda.gov/cder/ddms/binders.htm and follow the specifications. Specific Jacket colors are required: • **Red**: Original (for the FDA archive) • **Green**: Copy (for the FDA CMC reviewer) • **Orange:** Copy (for other applicable FDA reviewers)
☐	**Tabs:** tab and clearly label each part within a Jacket, including sub-sections.
☐	Submit original and two copies of the IND to the appropriate FDA Center (Refer to Form FDA 1571)

IND ANNUAL REPORT CHECKLIST

Submitted 60 days of the date IND went into effect

INDIVIDUAL STUDY INFORMATION: a brief summary of the status of each study in progress and each study completed during the previous year. The summary is required to include the following information for each study:

ELEMENT	**INCLUDED**
Title of the study (with protocol number)	
Purpose of the study	
Brief statement identifying the patient population	
Statement whether the study is completed	
Total number of subjects initially planned for inclusion	
Number enrolled to date: tabulated by age, gender, race	
Number who completed the study	
Number who dropped out of the study	
Brief description of any available study results	

SUMMARY INFORMATION: Information obtained during the previous year's clinical and nonclinical investigations, including:

ELEMENT	**INCLUDED**
A narrative or tabular summary showing most frequent and SAEs by body system	
Summary of all IND Safety Reports submitted during the past year	
List of subjects who died during participation and reasons for deaths	
List of subjects dropped during the study due to AE whether drug related or not	
Brief description of what was learned of drug's action, including, dose response, information from controlled trials, bioavailability	
List of preclinical studies (including animal studies)completed or in progress and summary of major preclinical findings	
Summary of any significant manufacturing or microbiological changes made during the past year	

PLAN FOR UPCOMING YEAR: The general investigational plan should contain information required under 312.23 (a)(3)(iv):

ELEMENT	**INCLUDED**
Description of general investigational plan for the coming year to replace the submitted 1 year earlier	
If the Investigator's brochure has been revised, a description of the revision and a copy of the new brochure	
Description of any significant Phase I protocol modifications made during the previous year and not previously reported to the IND in a protocol amendment	
Brief summary of significant foreign marketing developments with the drug during the past year, i.e. marketing in any country or withdrawal or suspension from marketing in any country	
If desired by the Sponsor, a log of any outstanding business with respect to the IND for which the sponsor requests or expects a reply, comment or meeting	

Checklist completed by: _____

Date: _____

IND APPLICATION EXEMPTION CHECKIST

The following checklist is intended to assist the investigator in determining whether an IND application needs to be submitted to the FDA for studies involving FDA-approved drugs. Answer each question below. If any question is answered “yes”, an IND application must be submitted to the FDA. If the answer to All questions are “no”, then the study may meet the criteria for an exemption from an IND.

For Research Studies Involving the use of an FDA approved Drug:

1. Does the study involve a different route of administration of the marketed drug than already FDA-approved that significantly increases the risk (or decreases the acceptability of the risks) to study subjects? □ Yes □ No

2. Does the study involve the administration of different drug dosage levels that significantly increase risk or decrease the acceptability of the risk to study subjects? □ Yes □ No

3. Does the study involve the administration of the drug to a different patient population for whom there may be increased risk or decreased acceptability of risk? □ Yes □ No

4. Does the study entail any other factor that significantly increases the risk or decreases the acceptability of risk to study subjects? □ Yes □ No

5. Are the results of the study intended to be reported to the FDA in support of any significant change in labeling or advertising for the drug? □ Yes □ No

6. Name of drug (generic and brand name):

7. If there is any uncertainty regarding the answer to any of the above questions, contact the FDA consumer safety officer for confirmation and document:
    a. Name of consumer safety officer:
    b. Telephone number:
    c. Date of Discussion:

KUMC Research Institute
Investigational New Drug (IND) Application Submission Checklist

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☐ Cover Letter

☐ Introductory Statement: Brief explanation of drug, all active ingredients, structural formula of drug, formulation and dosage(s) to be used, route of administration, and the broad objections. This information is usually provided in the investigator's brochure or package insert.

☐ General Investigational Plan: Brief description of the overall plan for investigating the drug and product for the following year. Should include:

a. rationale for the drug/research study
b. indication
c. general approach to be followed in evaluating the drug
d. the kind of clinical trials to be conducted in the first year
e. estimated number of patients to be given the drug
f. risks anticipated, toxicological data in animals in prior studies and humans of drug and related drugs

☐ Form FDA 1571

☐ Study Protocol

☐ Form FDA 1572

☐ IRB approval letter and approved consent form: If not yet approved by IRB, include IRB submission cover letter, provisos if available and consent submitted

☐ Environmental Exclusion Request
When claiming an exclusion from the requirement to submit an environmental assessment, include the statement referenced in the FDA/CDER Information for Sponsor-Investigators Submitting IND applications, "I claim categorical exclusion (under 21 CFR 25.31[e]) for the study under this IND. To my knowledge, no extraordinary circumstances exist."

☐ Letter Authorizing the Cross-Reference

☐ Submission Package
Submit three copies (one original and two copies) as a single package to the FDA at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center/HFM-99, Room 200N
1401 Rockville Pike
Rockville, MD 20852

☐ Sponsor Files: When applicable, forward one copy to the funding source

University of Cincinnati
Investigational New Drug (IND) Application Submission Checklist

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- □ Cover Letter
- □ Introductory Statement: Brief explanation of drug, all active ingredients, structural formula of drug, formulation and dosage(s) to be used, route of administration, and the broad objections. This information is usually provided in the investigator's brochure or package insert.
- □ General Investigational Plan: Brief description of the overall plan for investigating the drug and product for the following year. Should include:
    a. rationale for the drug/research study
    b. indication
    c. general approach to be followed in evaluating the drug
    d. the kind of clinical trials to be conducted in the first year
    e. estimated number of patients to be given the drug
    f. risks anticipated, toxicological data in animals in prior studies and humans of drug and related drugs
- □ Form FDA 1571
- □ Study Protocol
- □ Form FDA 1572
- □ IRB approval letter and approved consent form: If not yet approved by IRB, include IRB submission cover letter, provisos if available and consent submitted
- □ Environmental Exclusion Request
  When claming an exclusion from the requirement to submit an environmental assessment, include the statement referenced in the FDA/CDER Information for Sponsor-Investigators Submitting IND applications, "I claim categorical exclusion (under 21 CFR 25.31[e]) for the study under this IND. To my knowledge, no extraordinary circumstances exist."
- □ Letter Authorizing the Cross-Reference
- □ Submission Package
  Submit three copies (one original and two copies) as a single package to the FDA at the following address:

  Food and Drug Administration
  Center for Biologics Evaluation and Research
  Document Control Center/HFM-99
  Room 200N
  1401 Rockville Pike
  Rockville, MD 20852
- □ Sponsor Files: When applicable, forward one copy to the funding source

SPONSOR-INVESTIGATOR RESPONSIBILITY CHECKLIST
For holders of an IND

Principal Investigator	
Department/Division	
IRB Protocol Number	
IND holder	
IND number	
Date checklist completed	
Person completing checklist	

According to FDA Regulations:

21 CFR 312.50: GENERAL RESPONSIBILITIES AS A SPONSOR
Selecting qualified investigators and providing them with the information they need to conduct an investigation properly.
Ensuring proper monitoring of the investigation.
Ensuring the investigation is conducted in accordance with the protocol.
Maintaining an effective IND with respect to the investigation.
Ensuring the FDA and all participating investigators are promptly informed of significant adverse events or risks with respect to the drug.

21 CFR 312.60: GENERAL RESPONSIBILITIES AS AN INVESTIGATOR
Ensuring that an investigation is conducted according to the signed investigator statement, investigational plan, and applicable regulations.
Protecting the rights, safety, and welfare of the investigator's subjects.
Controlling the drugs under investigation.
Obtaining the informed consent of each human subject to whom the drug is administered.

CHECKLIST

Regulation	Documentation in Sponsor-Investigator's Files
312.50: (As a Sponsor) **Maintain an effective IND with respect to the investigation**	
Original IND application	□ Form FDA-1571 and accompanying documentation for the initial investigational new drug (IND) application, including: □ Cover letter □ Protocol(s) □ chemistry, manufacturing, and controls data □ FDA letter of no objection □ Documentation of IND#
Notify the FDA of new protocols using the same IND, change in protocol, new investigator, new information, safety reports, and	□ Form FDA-1571 and accompanying documentation for each correspondence with the FDA □ New (additional) protocol □ Change in protocol

Developed by Kathleen Gifford, Human Subjects Protection Office

changes in financial disclosure.	□ New investigator □ New information □ Safety report □ Annual report (within 60 days of IND anniversary date □ Response to FDA request for information □ Change in financial disclosure □ General correspondence □ Updated Form FDA-1572 when there is a new investigator
312.52: (As a Sponsor) **Transfer of obligations to a contract research organization (CRO)**	
Describe in writing the obligations that have been transferred to a CRO	If obligations are transferred to a CRO: □ Contract with the CRO
312.53: (As a Sponsor) **Selecting investigators and monitors**	
Select investigators qualified by training and experience as appropriate experts to investigate the drug. Select monitors qualified by training and experience to monitor the progress of the investigation.	□ Form FDA-1572 for each site □ Curriculum Vitae for each principal investigator showing the experience that qualifies the investigator for the specific trial □ Financial disclosure information for each investigator □ Protocol for each site, if they differ □ Curriculum Vitae for each monitor showing the experience that qualifies the monitor for the specific trial
312.55: (As a Sponsor) **Informing investigators**	
Keep investigators informed of new observations on the drug, particularly with respect to adverse effects and safe use.	□ Documentation of communications with investigators with respect to new observations □ Documentation of communications with investigators with respect to adverse events and safety reports □ Current Investigator Brochure, if applicable □ all pertinent correspondence between sponsor-investigator and investigators at other sites
312.56: (As a Sponsor) **Review of ongoing investigations** **312.64:** (As an Investigator) **Investigator reports**	
Monitor the progress of <u>all</u> investigations being conducted under the IND. Assure the compliance of all investigators with the signed agreement (Form FDA-1572), the general investigational plan, and the IND regulations.	□ Monitor reports and monitoring log for the investigation titled: _____ □ Monitor reports and monitoring log for the investigation titled: _____ □ Monitor reports and monitoring log for the investigation titled: _____ □ All correspondence with monitor(s)

Discontinue the participation of non-complying investigators, secure unused drug, and notify the FDA. Review and evaluate the evidence relating to the safety and effectiveness of the drug. Submit reports regarding safety to the FDA. Submit annual reports to the FDA on the progress of the investigation. <u>When investigations are determined to present an unreasonable and significant risk</u> to subjects, discontinue investigations within 5 working days of the determination, and a) notify the FDA, all IRBs, and all investigators, b) assure the disposition of all stocks of the drug outstanding as required by 21 CFR 312.59, and c) furnish the FDA with a full report of these actions.	See Addendum to Checklist: Monitoring of Sites □ Documentation of a safety monitoring plan □ Documentation of a data monitoring plan □ Documentation of review of safety and data as outlined in the data safety monitoring plan □ Form FDA-1571 and accompanying documentation for each annual report
312.57: (As a Sponsor) **Record keeping and record retention** **312.62:** (As an Investigator) **Investigator record keeping and record retention** **312.64:** (As an Investigator) **Investigator reports**	
(As a Sponsor) Maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug (to include, as appropriate, the name of the investigator to whom the drug is shipped, and the date, quantity, and batch or code mark of each such shipment) (As an Investigator) Maintain	□ Drug Accountability Log (if received from outside) □ receipt date □ quantity □ lot # □ return/disposition □ method of disposal □ Drug Accountability Log (if shipped by sponsor-investigator to other sites) □ date □ destination □ who shipped □ quantity □ lot # □ return/disposition □ method of disposal □ Enrollment log/Randomization log

adequate records of the disposition of the drug, including dates, quantity, and use by subjects	□ Drug Dispensing Record □ date □ lot # □ quantity □ ID of subject □ ID of person dispensing □ record of return/disposition
(As an Investigator) Prepare and maintain adequate and accurate case histories that record all observations and other pertinent data to the investigation (including documentation that informed consent was obtained prior to participation in the study) on each individual administered the investigational drug or employed as a control in the investigation.	□ Source data □ Case report forms □ Subject eligibility documented □ Concomitant medications recorded □ Original signed consent forms □ Documentation that informed consent was obtained prior to study procedures □ Documentation that subject was given a copy of signed and dated consent form □ Date/signature of staff recording data onto forms □ Staff signature log
Maintain complete and accurate records showing any financial interests of the investigators as related to the investigational study. Retain the records and reports for 2 years after a marketing application is approved for the drug or, if an application is not approved for the drug, for 2 years after the shipment and delivery of the drug for investigational use is discontinued and the FDA has been so notified.	□ Financial disclosure information for each investigator
312.58: (As a Sponsor) **Inspection of sponsor's record and reports** **312.68:** (As an Investigator) **Inspection of investigator's records and reports**	
Permit an authorized employee of the FDA to have access to and copy records and reports relating to IND clinical investigations. Permit an authorized employee of the Drug Enforcement Administration or the Department of Justice to have access to and copy records concerning shipment, delivery,	

receipt, and disposition of a drug that is a controlled substance.	
312.58(b): (As a Sponsor) **Controlled Substances** **312.69:** (As an Investigator) **Handling of controlled substances**	
If the investigational drug is listed as a controlled substance, assure that adequate precautions are taken, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance to into illegal channels of distribution.	□ Temperature monitoring log □ Humidity monitoring log
312.59: (As a Sponsor) **Disposition of unused supply of investigational drug**	
Assure the return or alternative disposition of all unused supplies of the investigational drug from all investigators. Maintain written records of any disposition of the drug in accordance with 312.57.	□ Drug Accountability Log(s) □ Drug Dispensing Records
312.61: (As an Investigator) **Control of the investigational drug**	
Administer the drug only to subjects under the personal supervision of the investigator or a sub-investigator responsible to the investigator.	□ Delegation of Responsibility Log
312.66: (As an Investigator) **Assurance of IRB review**	
Assure that an IRB will be responsible for the initial and continuing review and approval of the proposed clinical study. Assure prompt reporting to the IRB of all changes in the research activity and all unanticipated problems involving risk to human subjects. Assure that no changes are made in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.	Copies of IRB correspondence at sponsor-investigator site, including copies of the documents that were reviewed by the IRB: □ Initial review □ Clinical protocol □ Informed consent form □ Recruitment □ Continuing review □ Amendments □ Reports of unanticipated problems □ Protocol deviations involving risk □ Current investigators brochure/device manual □ Other IRB correspondence □ From each site in a multi-site study, copies of the IRB

	approval documents (initial and continuing)