IND Protocol Amendments:

IND Protocol Amendments Guidance and Template for Drug Products

ICTR Navigators

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The Johns Hopkins Institute for Clinical and Translational Research

ICTR—Where Science and People Connect

CTSA Clinical & Translational Science Awards

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1.0 Table of Contents

2.0 Abbreviations

IND	Investigational New Drug
CFR	Code of Federal Regulations
FDA	U.S. Food and Drug Administration
CDER	Center for Drug Evaluation and Research
CBER	Center for Biologics Evaluation and Research
CDRH	Center for Devices and Radiological Health
GCP	Good Clinical Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
BLA	Biologic License Application
NDA	New Drug Application
PMA	Pre-Market Application
IDE	Investigational Device Exemption

3.0 FDA Websites

Within this document, there are a number of links to various FDA forms, regulations, and/or guidance documents. The list below contains additional useful FDA websites.

FDA Title 21 Part 312 Investigational New Drug Regulations:

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=312&showFR=1

FDA Information for Sponsor-Investigators Submitting Investigational New Drug Applications:

- http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm#form1571

FDA Running Clinical Trials:

- http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm

FDA Forms:

- http://www.fda.gov/aboutfda/reportsmanualsforms/forms/default.htm

FDA – CDER Investigational New Drug (IND) Application:

- http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm

FDA – CDER Drug Guidance documents:

- http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

FDA Title 21 Regulations Search Engine (e.g., IND regulations 21CRF312):

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm

4.0 Introduction

The enclosed information is intended to provide an overview of the process for submitting an Investigational New Drug (IND) Protocol Amendment for an active IND application as per the requirements set forth in 21CRF312.30. This document is designed to be used for an active IND application for a drug in which is submitted to the FDA Center for Drug Evaluation Research (CDER).

There are three types of Protocol Amendments that can be submitted for an IND. One is a *New Protocol,* the second is *Changes in a Protocol*, and the third is a *New Investigator*. All three discussed in the section 5.0. The regulations governing Protocol Amendments, 21CRF312.30, can be found at the following website.

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.30

5.0 Guidance and Instructions:

5.1 General Information

5.1.1 Number of Copies to be submitted

One original copy and two photocopies are required.

5.1.2 Binding

IND submissions that are received loose or which are inadequately bound may be returned to the Sponsor-Investigator for proper binding and resubmission which can significantly delay the FDA review process.

If the Protocol Amendment documents can be securely held together with a standard office staple, then there is no need to place the submission in a binder. Normally, if the submission is 15 pages or less, stapling is sufficient. If the report is longer than 15 pages or it cannot be securely held together with a staple, then it will need to be bound by another means. In this

case, we suggest that the FDA Project Manager be consulted for additional instructions. Otherwise, use the binding instructions included in the "*IND Guidance and Template for FDA-CDER Products*" posted on the DDRS website (http://ictr.johnshopkins.edu/DDRS). When labeling the binders, should you use binders, indicate on the binder label that the submission is for a Protocol Amendment and the type of amendment. Each section of the amendment should begin on new page and index tabs should be used to mark each section of the submission packet.

5.1.3 Template Guidance Comments

The enclosed template guidance is a suggested format based on federal regulations, guidance documents, and previous experience. Within the template are references to applicable FDA regulations, web addresses to FDA guidance documents, comments/instructions, web addresses to FDA forms, and suggested formatting and/or language. These instructions outline what may need to be included or inserted into a particular section and may also address special considerations. As this is a basic template and each IND is unique, best judgment should be used concerning the information to be included in the submission. The sponsor-investigator may use this format or adapt it as appropriate for the particular investigational product being evaluated. As stated in introduction, there are three types of protocol amendments that can be submitted to the FDA-CDER for an IND. The primary difference in the template document is the information sheet and the types of documents submitted, which is discussed below, for each type of protocol amendment. The template contains a cover letter, placeholder for 1571, table of contents, and information sheets for each type of protocol amendment. Then at the end of the template section, each of the possible supporting documents are discussed in detail. A blank template with just the cover letter, title page, and suggested section headings and subheadings is available for download at the DDRS website.

5.1.4 Protocol Amendment Header and Footer

The following are the suggested format of the headers and footers to be used with the annual report. Note that headers and footers are not included in the template and must be inserted manually and may be modified as necessary.

Header:
[Left Hand Side]
Protocol Amendment: *[New Protocol OR Changes in a Protocol OR New Investigator]*
[INSERT Date of Submission]

[Right Hand Side]
IND # *[INSERT Number]*,
Serial Number: *[INSERT 1571 Serial number]*

Footer:
[Left Hand Side]
John Hopkins University
[INSERT: Sponsor-Investigator Name]
Confidential and Proprietary

[Right Hand Side]
Page *[##]*

5.1.5 FDA, CDER Mailing Address

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

5.1.6 Website Address Hyperlinks

All hyperlinks to websites included are operational as of the date of this document. Please contact the ICTR Research Navigators via the contact information below if any non-functional hyperlinks are identified so that they may be updated.

5.1.7 Questions and Additional Contact Information

For questions regarding any of the information presented or use of the template, please contact the ICTR Research Navigators at ICTR_Navigators@jhmi.edu or via telephone at 410-614-5383 or 410-955-8120.

5.2 Protocol Amendment: New Protocol

If a sponsor-investigator wants to open a new protocol under an existing IND, then sponsor-investigator must submit the new protocol to the FDA for review. A new protocol is one that is not covered by a protocol already contained in the IND. The sponsor-investigator may initiate the new protocol once the following two conditions are met: (1) The sponsor-investigator has submitted the protocol to FDA for its review; and (2) the protocol has been approved by the Institutional Review Board (IRB) with responsibility for review and approval of the protocol in accordance with the requirements of 21CFR56. The sponsor-investigator may comply with these two conditions in either order. Please note that the FDA regulations do not specify the amount of time a sponsor-investigator must allow for the FDA to review the new protocol.

The following is a list of documents and information that may be required to submit with the Protocol Amendment: New Protocol submission packet.

- Cover letter
- Form FDA 1571
- Protocol Amendment: New Protocol Information Sheet
    - The information sheet must provide (1) a brief description of the most clinically significant differences between the new protocol and previous protocol(s) and (2) an outline the requested information per box 8 of the form FDA 1572.
- Protocol
- Consent form
- IRB approval (if applicable)
- IRB application (if applicable)
    - If the protocol, consent form, and other documentation does not provide all pertinent information (design, risks, monitoring, etc…) that the FDA needs to review, then it is suggested that the IRB application be submitted.
- Form FDA 1572
- Sponsor-Investigator curriculum vitae (CV) and medical license per box 2 of the Form FDA 1572 (if applicable)
- Sub-investigator(s) curriculum vitae (CV) and medical license per box 6 of the Form FDA 1572 (optional)

  - A sponsor-investigator is not required to submit sub-investigators' curriculum vitae and medical license, but must maintain copies of this documentation is the regulatory binder.
- Disclosure of Financial Interests (21CFR54)
  - Form FDA 3454 (if applicable)
    - If there are any new investigators or sub-investigators listed on the 1572 (box 1 and box 6) that who were not previous reported to the FDA and they do not have any financial interests in the development of the product, then a revised FDA 3454 should be submited
  - Form FDA 3455 (if applicable)
- Form FDA 3674
- Other supporting documentation (if applicable)
  - Submit any additional documentation that is pertinent to the FDA review of the new protocol.

5.3 Protocol Amendment: Changes in a Protocol

A sponsor-investigator is required to submit a protocol amendment, change in protocol, that describes any changes in a Phase 1 protocol that significantly affects the safety of subjects or any changes in a Phase 2 or 3 protocol that significantly affects the safety of subjects, the scope of the investigation, or the scientific quality of the study per 21CFR312.30. However, even if the protocol in question is not a phase 1, 2, or 3, sponsor-investigators are advised to submit protocol amendments to the FDA when the changes significantly affects the safety of subjects, the scope of the investigation, or the scientific quality of the study.

The changes to the protocol may be implemented once the sponsor-investigator submits the changes for FDA review and receives IRB approval in accordance with the requirements of 21CFR56. The sponsor-investigator may comply with these two conditions in either order. The only exception to implementation of changes to a protocol is in the case of eliminating a hazard to the participants, which may occur immediately with the understanding that the FDA and IRB must notify as soon as possible of the changes. Please note that the FDA regulations do not specify the amount of time a sponsor-investigator must allow for the FDA to review the changes to the protocol.

The following is a list of documents and information that may be required to submit with the Protocol Amendment: Change in a Protocol submission packet.

- Cover letter
- Form FDA 1571
- Protocol Amendment: Change in a Protocol Information Sheet
  - The information sheet must provide (1) a brief description a brief description of the change and (2) reference (date and 1571 serial number) to the submission that contained the original protocol.
- Amended Protocol
- Amended Consent form (if applicable)
- IRB approval (if applicable)
- Form FDA 1572 (if applicable)
  - If any of the changes affect the information provided on the 1572, then a revised 1572 should be submitted with the submission package.
- Sponsor-Investigator CV and medical license per box 2 of the Form FDA 1572 (if applicable)

    - If a revised 1572 is being submitted, then the sponsor-investigator's curriculum vitae and medical license should be submitted.
- Sub-investigator(s) CV and medical license per box 6 of the Form FDA 1572 (if applicable)
    - If a revised 1572 is being submitted and there are changes to the sub-investigators, then the sub-investigators' CV and medical license can be submitted. Note, that a sponsor-investigator is not required to submit sub-investigators' CV and medical license, but must maintain copies of this documentation is the regulatory binder.
- Disclosure of Financial Interests (21CFR54)
    - Form FDA 3454 (if applicable)
        - If there are any new investigators or sub-investigators listed on the 1572 (box 1 and box 6) that who were not previous reported to the FDA and they do not have any financial interests in the development of the product, then a revised FDA 3454 should be submitted.
    - Form FDA 3455 (if applicable)
- Other supporting documentation (if applicable)
    - Submit any additional documentation that is pertinent to the FDA review of the changes to the protocol.

5.4 Protocol Amendment: New Investigator

A sponsor-investigator must submit a Protocol Amendment: New Investigator when a new investigator is added to a previously submitted protocol, except that a protocol amendment is not required when a licensed practitioner is added in the case of a treatment protocol under 312.34. Once the investigator is added to the study, the investigational drug may be shipped to the investigator and the investigator may begin participating in the study. The sponsor shall notify FDA of the new investigator within 30 days of the investigator being added.

The following is a list of documents and information that may be required to submit with the Protocol Amendment: New Investigator submission packet.

- Cover letter
- Form FDA 1571
- Protocol Amendment: New Investigator Information Sheet
    - The information sheet a brief description of the new investigator and new site as well as it must reference (date and 1571 serial number) to the submission that contained the original protocol that the new investigator is being added.
- Form FDA 1572
    - The 1572 must be completed by the new investigator listing all of the new investigator's information per the requirements of the 1572.
- Investigator CV and medical license per box 2 of the Form FDA 1572
- Sub-investigator(s) CV and medical license per box 6 of the Form FDA 1572
    - A sponsor-investigator is not required to submit sub-investigators' curriculum vitae and medical license, but must maintain copies of this documentation is the regulatory binder.
- Disclosure of Financial Interests (21CFR54)
    - Form FDA 3454
    - Form FDA 3455
- IRB approval (if applicable)
- Other supporting documentation (if applicable)
    - Submit any additional documentation that is pertinent to the FDA review of the addition of the new investigator and new site.

6.0 Template Guidance

6.1 Cover Letter

[Sponsor-Investigator letterhead or address]

[DATE]

[Recipient Address – FDA Project Manager Responsible for IND]

RE: Protocol Amendment: ***[Insert type of amendment: New Protocol OR Change in a Protocol OR New Investigator]*** for IND Number ***[Insert: ######]***, for ***[Insert: PRODUCT NAME]***

Dear ***[Insert: FDA Project Manager Name]***,

Please find enclosed a Protocol Amendment ***[Insert type of amendment: New Protocol OR Change in a Protocol OR New Investigator]*** for IND Number ***[Insert: ######]***, for ***[Insert: PRODUCT NAME]***.

[NOTE: If the amendment is not yet approved by the IRB, insert statement explaining status of IRB review. Statement such as "This amendment has been submitted to the IRB and is scheduled to be reviewed on ##/##/##."]

Sincerely,

[Sponsor-Investigator Name]
[Title]

Enclosure:

6.2 Cover Page

INVESTIGATIONAL NEW DRUG

PROTOCOL AMENDMENT: *[INSERT TYPE OF AMENDMENT]*

Date: *[INSERT: Month Day, Year]*

IND Number: *[INSERT: IND Number "###,###"]*

Drug Name: *[INSERT: Drug Name]*

Sponsor-Investigator: *[INSERT: Name]*
[INSERT: Title]
[INSERT: Address]
[INSERT: Phone Number]
[INSERT: Fax Number]
[INSERT: Email Address]

6.3 Form FDA 1571

[INSERT signed and dated FDA Form 1571 here]

- *FDA Form 1571*
http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083533.pdf

- *1571 Instructions*
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm#form1571

6.4 Table of Contents

Table of Contents

[Instructions: List all documents being submitted with the amendment.]

6.5 Protocol Amendment Information Sheets

6.5.1 Protocol Amendment: New Protocol Information Sheet

Protocol Amendment: New Protocol Information Sheet

IND Number:	***[Instructions: Insert IND number]***
Serial Number:	***[Instructions: Insert serial number of 1571 being submitted with this amendment.]***
Date:	***[Instructions: Insert date of submission]***
Sponsor-Investigator:	***[Instructions: Insert sponsor-investigator name.]***
Protocol Title:	***[Instructions: Insert title of protocol.]***
[Chose: Protocol Number OR IRB Number]:	***[Instructions: Insert either the protocol identification number or the IRB application number if a protocol identification number has not been assigned. Please choose appropriate identifier in the left hand column.]***

Most clinically significant differences between it and the previous protocol:

This study is designed to ***[Instructions: Insert brief descriptions of objectives and hypothesis, as applicable, for New Protocol.]***

The previous protocol ***[Instructions: Insert brief descriptions of objectives and hypothesis, as applicable, of all previous protocols submitted under this IND.]***

The differences between are ***[Instructions: Insert summary of differences.]***

Information to address Question 8 on the 1572:

[Instructions: Provide the information requested in question 8 of 1572 as per the phase of the study the amendment is referencing.]

Protocol Amendment: New Protocol Supporting Documents

[Instructions: Briefly describe the documents being submitted with the amendment for the FDA to review. Each document should be listed in the table of contents.]

6.5.2 Protocol Amendment: Changes in a Protocol Information Sheet

Protocol Amendment: Changes in a Protocol Information Sheet

IND Number:	***[Instructions: Insert IND number]***
Serial Number:	***[Instructions: Insert serial number of 1571 being submitted with this amendment.]***
Date:	***[Instructions: Insert date of submission]***
Sponsor-Investigator:	***[Instructions: Insert sponsor-investigator name.]***
Protocol Title:	***[Instructions: Insert title of protocol.]***
[Chose: Protocol Number OR IRB Number]:	***[Instructions: Insert either the protocol identification number or the IRB application number if a protocol identification number has not been assigned. Please choose appropriate identifier in the left hand column.]***

Original submission of protocol reference:

> ***[Instructions: Insert date the original protocol was submitted to the FDA along with the serial number of the 1571 that was submitted with the protocol.]***

Summary of changes to protocol:

> ***[Instructions: Briefly describe a summary of the changes to the protocol. If there is a separate document describing the changes to the protocol, then reference it here and place as the first document of the supporting documents.]***

Protocol Amendment: Changes in a Protocol Supporting Documents

> ***[Instructions: Briefly describe the documents being submitted with the amendment for the FDA to review. Each document should be listed in the table of contents.]***

6.5.3 Protocol Amendment: New Investigator Information Sheet

Protocol Amendment: New Investigator Protocol Information Sheet

IND Number:	***[Instructions: Insert IND number]***
Serial Number:	***[Instructions: Insert serial number of 1571 being submitted with this amendment]***
Date:	***[Instructions: Insert date of submission]***
Sponsor-Investigator:	***[Instructions: Insert sponsor-investigator name]***
Protocol Title:	***[Instructions: Insert title of protocol]***
[Chose: Protocol Number OR IRB Number]:	***[Instructions: Insert either the protocol identification number or the IRB application number if a protocol identification number has not been assigned. Please choose appropriate identifier in the left hand column.]***

Original submission of protocol reference:

> ***[Instructions: Insert date the protocol the new investigator will be participating in was submitted to the FDA along with the serial number of the 1571 that was submitted with the protocol.]***

New Investigator:

> ***[Instructions: Provide a brief summary of new investigator and site along with any amendment supporting documents being submitted.]***

6.6 Protocol Amendment Supporting Documents

Below is a list of possible supporting documents that may be submitted with the amendment and the required documents depends on the type of amendment. It is strongly suggested that a cover page be placed on top of each supporting document listing the document and then the cover page number can be used in the table of contents.

The below list of documents are not listed in a specific order and they should be ordered based on information listed above in section 5. General information concerning the documents is provided below but if more information is needed, the "*Sponsor-Investigator IND Guidance and Template for FDA-CDER Products*" posted on the DDRS website (http://ictr.johnshopkins.edu/DDRS) should be reviewed.

6.6.1 Protocol:

If applicable, submit the new or amendment protocol.

If you are submitting an eFormA for New Protocol submission, it is suggested that you submit the eIRB application with the submission as the eFormA may not provide all the pertinent information the FDA needs to review.

6.6.2 Consent Form:

If applicable, submit a copy of the consent form. If there are multiple consent forms, submit a copy of each consent form.

6.6.3 IRB Application:

When using an eFormA, it is recommended that a copy of the eIRB application be submitted because the eFormA does not convey all necessary information to the FDA (e.g., Data Safety Monitoring Plan, Recruitment, Consenting, etc…). If you are not using an eFormA, then only submit the eIRB application if it contains information not contained elsewhere the FDA should review.

6.6.4 IRB Approval Letter:

Include a copy of the IRB approval letter with the submission. If the amendment has not been approved by the IRB, then it is strongly suggested that in the cover letter or in the information sheet a statement is included explaining when IRB approval is expected.

6.6.5 Form FDA 1572:

If applicable, submit a completed 1572 with the amendment. To determine if a 1572 is required, please refer to section 5 above or the FDA 1572 guidance document. Below are web addresses for the form and the FDA guidance (FAQs) for the 1572.

- Form FDA 1572:
  http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf

- FDA Guidance - 1572 FAQs:
  http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf

6.6.6 Sponsor-Investigator OR Investigator curriculum vitae (CV):

If a 1572 is being submitted, then a CV should be submitted as documentation of the box 2 of the 1572. If the amendment is a New Protocol or Change in a Protocol, then the sponsor-investigator CV should be submitted. If the amendment is for a New Investigator, then the investigator CV should be submitted.

6.6.7 Sub-investigators CVs listed in box 6 of 1572:
Sub-investigators' curriculum vitae and medical license are not required to be submitted with an amendment that includes a 1572. However, copies of this documentation must be maintained in the regulatory binder. Please note that while this is not a requirement industry requires that this documentation be submitted as a best practice.

6.6.8 Disclosure of Financial Interests:
The Sponsor-Investigator must have documentation on file for himself/herself and each investigator and subinvestigator who is involved in the clinical trial(s) being conducted under an IND that states whether or not the individual has any type of financial interest that could be perceived as potentially influencing the outcome per the requirements of 21CFR54. As such, there are two FDA forms that should be submitted to the FDA and maintained in the regulatory binder to document this requirement. The forms are the Form FDA 3454 and Form FDA 3455, discussed below. If the amendment includes the addition of new site investigator or new subinvestigators listed in box 6 of the 1572, then the required documentation must be submitted to the FDA.

For information concerning disclosure requirements and conflict of interests, please review the information on the following websites or the Sponsor-Investigator IND Guidance and Template for FDA-CDER Products" posted on the DDRS website (http://ictr.johnshopkins.edu/DDRS).

- Federal regulation 21CFR54:
  http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=54&showFR=1
- FDA Guidances:
  - Current Guidance dated 2001
    http://www.fda.gov/RegulatoryInformation/Guidances/ucm126832.htm
  - Draft Guidance Dated May 2011
    http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM256525.pdf
- HHS-OHRP Guidance:
  http://www.hhs.gov/ohrp/policy/fguid.pdf
- JHM IRB Guidance:
  http://www.hopkinsmedicine.org/institutional_review_board/guidelines_policies/organization_policies/103_11.html
- JHU Conflict of Interest Policy:
  http://jhuresearch.jhu.edu/Policy_onConflict_of_Interest.pdf
- JHU Research Administration – Conflict of Interest website:
  http://jhuresearch.jhu.edu/compliance-conflict.htm

6.6.8.1 Form FDA 3454 (Disclosure: Financial Interest and Arrangements of Clinical Investigators):
The Form FDA 3454 provides documentation to the FDA that the Sponsor-Investigator, other clinical investigator(s), and/or subinvestigator(s) **DO NOT** have any financial interests that may influence the outcome of the study as required per federal regulation 21CFR54.

- FDA Form 3454:
  http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048304.pdf

6.6.8.2 Form FDA 3455 (Disclosure: Financial Interest and Arrangements of Clinical Investigators):
Reportable Disclosures: If the Sponsor-Investigator, other clinical investigator(s), and/or subinvestigator(s) have any financial conflict of interest(s) that must be disclosed to the FDA per 21CFR54 and/or is/are being managed per JHU policies, each conflicted individual must complete and submit a Form FDA 3455 with a copy of the conflict management plan attached to the form.

No Reportable Disclosures: The DDRS has been informed that during FDA inspections/audits, the FDA has cited investigators for not having a completed Form FDA 3455 as part of the IND's regulatory documentation. Therefore, even if there are no reportable disclosures, any time a Form FDA 3454 is being submitted a Form FDA 3455 should also be submitted. When completing the Form FDA 3455, all sections of the form should be completed except you do not check off any of the boxes describing reportable financial disclosures.

- FDA Form 3455: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048310.pdf

6.6.9 Form FDA 3674:

If the amendment is a New Protocol, then the Form FDA 3674, entitled 'Certification of Compliance, under 42 U.S.C § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C § 282(j))', must be submitted. Per Title VIII of the Food and Drug Administration Amendments Act of 2007 or FDAAA (U.S. Public Law 110-85) clinical trial registration and reporting requirements, all applicable trials must be registered at clinicaltrials.gov, and results reported as required. As part of this requirement, the FDA created the Form FDA 3674 to certify compliance with registration of trials.

- FDA Guidance Document on registering trials on ClinicalTrials.gov: http://www.fda.gov/RegulatoryInformation/Guidances/ucm125335.htm

- FORM FDA 3674 website to download PDF fillable form**:** http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf

- Form FDA 3674 instructions website: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm#form3674

6.6.10 Other Supporting Documents:

Include any additional supporting documents that may be necessary for the FDA to review the amendment. Please include the document in the table of contents.