

Instructions for investigators for completing the Planning Phase Application for IND/IDE Application Submission approval

This guidance is intended to assist clinical investigators, sponsors, and sponsor-investigators in submitting a Planning Phase Application for Investigational New Drug (IND) or an investigational device exemption (IDE) applications.

Sponsor-Investigators (IND/IDE holders) must submit a Johns Hopkins Medicine (JHM) eIRB Planning Phase Application to initiate the institutional Office of Clinical Trials review for IND/IDE submission requests in accordance with the institutional [policy](#) on Investigator-held INDs/IDEs. A Planning Phase Application must be approved by the Office of Clinical Trials (OCT) prior to submission to the FDA.

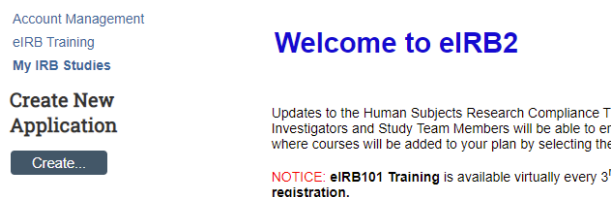
To begin this process, a Planning Phase Application should be submitted through eIRB following the step by step instructions outlined below.

Please Note: Sponsor-Investigators must complete the OCT REDCap investigator qualification process. Please use the link below to complete investigator qualification survey: <https://redcap.link/indfacultyqual> for OCT review and approval to serve as an IND/IDE holder prior to initiating a planning phase application.

IRB Website: https://www.hopkinsmedicine.org/institutional_review_board/

A link to the [eIRB Login](#) screen is located in the left navigation bar.

Select Create New Application:



The screenshot shows a navigation menu on the left with options: Account Management, eIRB Training, My IRB Studies, Create New Application, and a 'Create...' button. The main content area displays 'Welcome to eIRB2' and a notice about updates to Human Subjects Research Compliance Training for investigators and study team members.

Section 1: General Information:

Item 1: Principal Investigator:

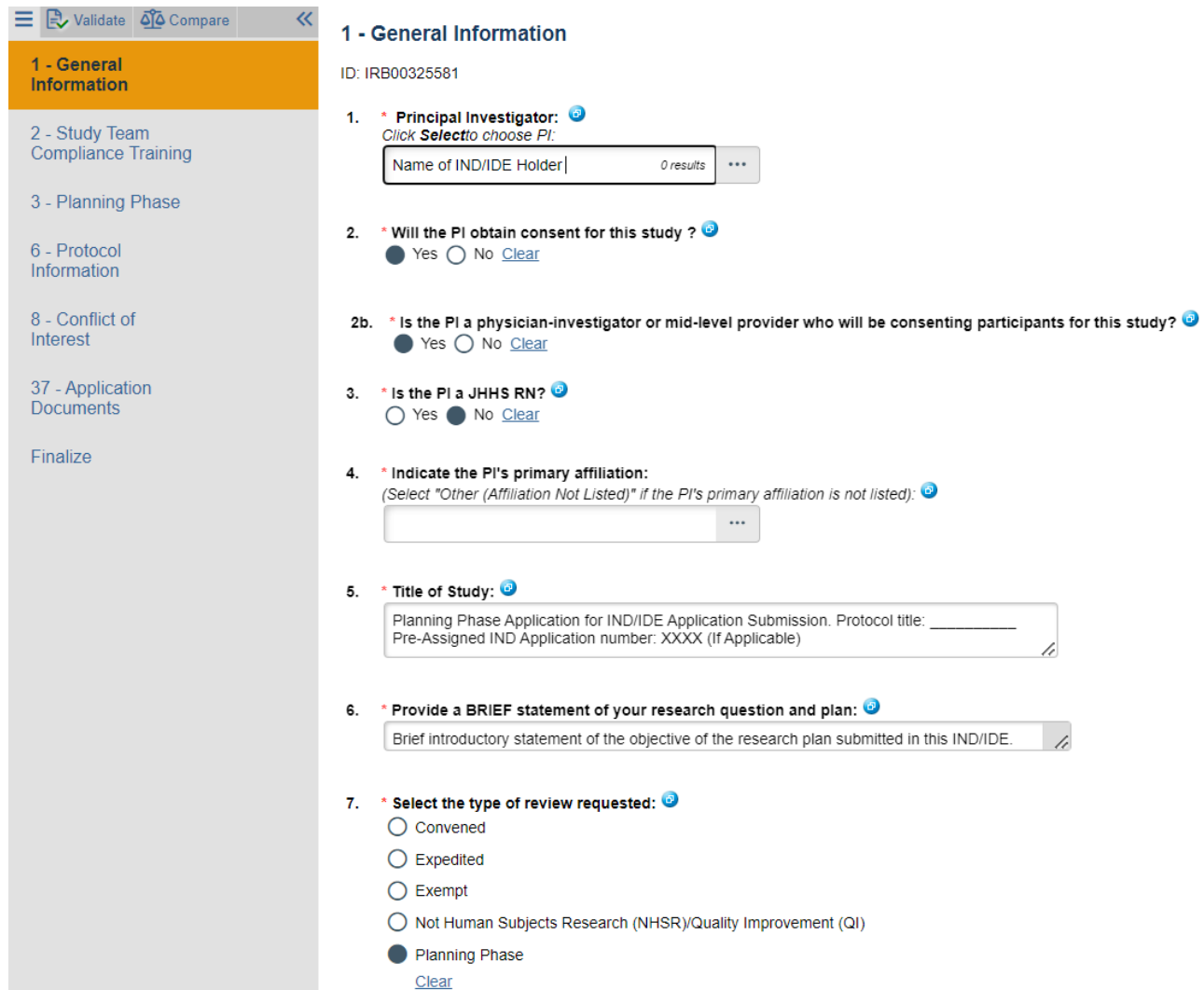
Enter the Name of the planned OCT approved IND/IDE holder in the Principal Investigator field

Item 5: Title of Study:

- You must include “Planning Phase Application for IND/IDE Application Submission” in the title for the application to be routed to Office of Clinical Trials (OCT) IND/IDE Committee through eIRB.
- Please include the full study title.
- If applicable, please include the Pre-assigned IND number in the study title (see example below)

Item 6: Provide a BRIEF statement of your research question and plan:

Please include brief introductory statement of the objective of the research plan submitted in this IND/IDE.



The screenshot shows a web-based application form for IRB submission. On the left is a navigation menu with the following items: '1 - General Information' (highlighted in orange), '2 - Study Team Compliance Training', '3 - Planning Phase', '6 - Protocol Information', '8 - Conflict of Interest', '37 - Application Documents', and 'Finalize'. At the top of the form are buttons for 'Validate', 'Compare', and a back arrow. The main content area is titled '1 - General Information' and shows the ID 'IRB00325581'. The form contains several questions:

- Principal Investigator:** A dropdown menu with the text 'Name of IND/IDE Holder' and '0 results'.
- Will the PI obtain consent for this study?** Radio buttons for 'Yes' (selected) and 'No', with a 'Clear' link.
- Is the PI a physician-investigator or mid-level provider who will be consenting participants for this study?** Radio buttons for 'Yes' (selected) and 'No', with a 'Clear' link.
- Is the PI a JHHS RN?** Radio buttons for 'Yes' and 'No' (selected), with a 'Clear' link.
- Indicate the PI's primary affiliation:** A dropdown menu with the instruction '(Select "Other (Affiliation Not Listed)" if the PI's primary affiliation is not listed)'. The dropdown is currently empty.
- Title of Study:** A text area containing 'Planning Phase Application for IND/IDE Application Submission. Protocol title: _____' and 'Pre-Assigned IND Application number: XXXX (If Applicable)'. There is a small icon in the bottom right corner of the text area.
- Provide a BRIEF statement of your research question and plan:** A text area containing 'Brief introductory statement of the objective of the research plan submitted in this IND/IDE.' There is a small icon in the bottom right corner of the text area.
- Select the type of review requested:** Radio buttons for 'Convened', 'Expedited', 'Exempt', 'Not Human Subjects Research (NHSR)/Quality Improvement (QI)', and 'Planning Phase' (selected). There is a 'Clear' link below the options.

Item 25: Study Team Members:

Please include the following:

- **Regulatory staff:** A research staff experienced with research regulated by the FDA to meet the obligations of a Sponsor-Investigator.
- **Co-Investigators:** Co-investigators serving as Subinvestigators and Authorized Prescribers under whose immediate direction the Investigational Product is prescribed, dispensed and administered to a subject. For studies requiring an authorized prescriber, if the proposed Sponsor-Investigator is NOT a JHHS credentialed, U.S licensed medical provider (physician

or dentist) and cannot serve as an authorized prescriber, at least one Co-investigator must be named.

An investigator as defined in 21 CFR 312.3(b) means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team.

"Subinvestigator" includes any other individual member of that team.

- Other study team members may or may not be included in the Planning Phase applications.

Section 3: Planning Phase:

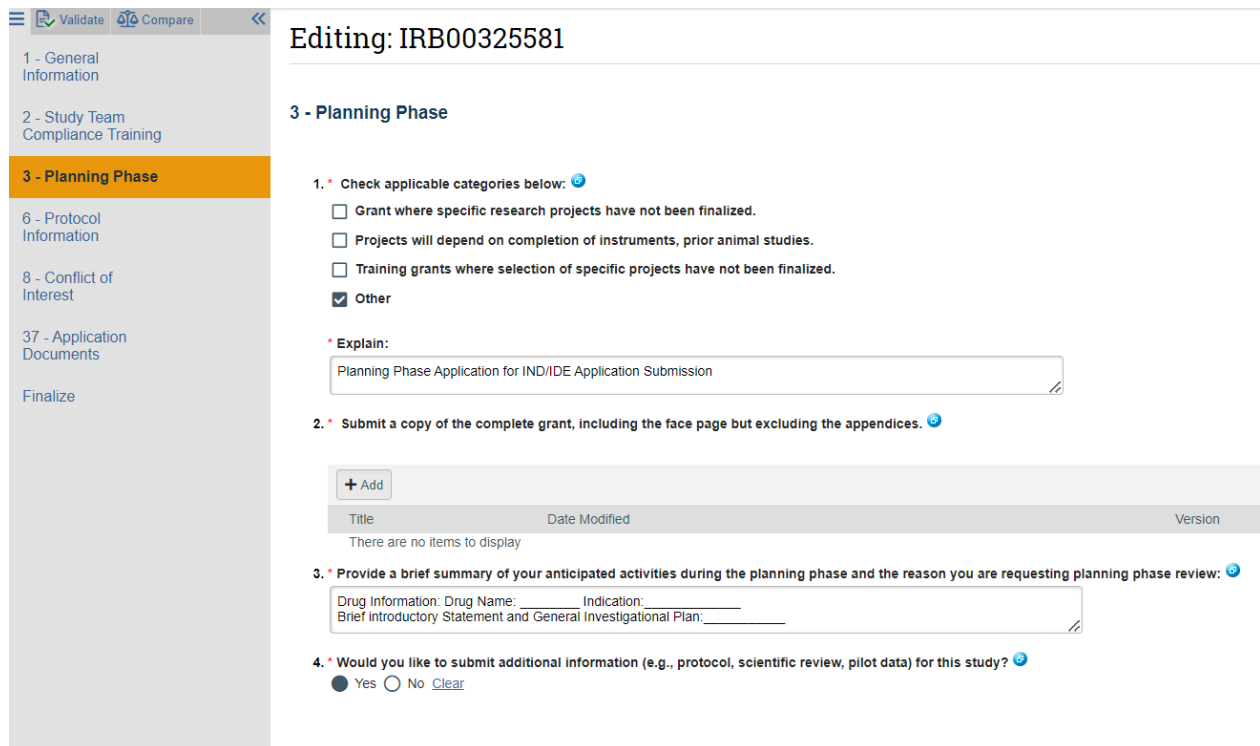
Item 1: Select: Other

Explain: Planning Phase Application for IND/IDE Application Submission

Item 2:


Please upload the following:

1. Approval from the OCT to serve as an IND/IDE holder.
2. The completed **IND/IDE Supplemental Form**. Please [click here](#) for the link to download the form.
3. IND: Investigator's Brochure (If available).



Editing: IRB00325581

3 - Planning Phase

1. * Check applicable categories below: 

Grant where specific research projects have not been finalized.


Projects will depend on completion of instruments, prior animal studies.


Training grants where selection of specific projects have not been finalized.

Other


* Explain:

Planning Phase Application for IND/IDE Application Submission


2. * Submit a copy of the complete grant, including the face page but excluding the appendices. 



Title	Date Modified	Version
There are no items to display		

3. * Provide a brief summary of your anticipated activities during the planning phase and the reason you are requesting planning phase review: 

Drug Information: Drug Name: _____ Indication: _____
Brief introductory Statement and General Investigational Plan: _____

4. * Would you like to submit additional information (e.g., protocol, scientific review, pilot data) for this study? 

Yes No [Clear](#)

Item 3:

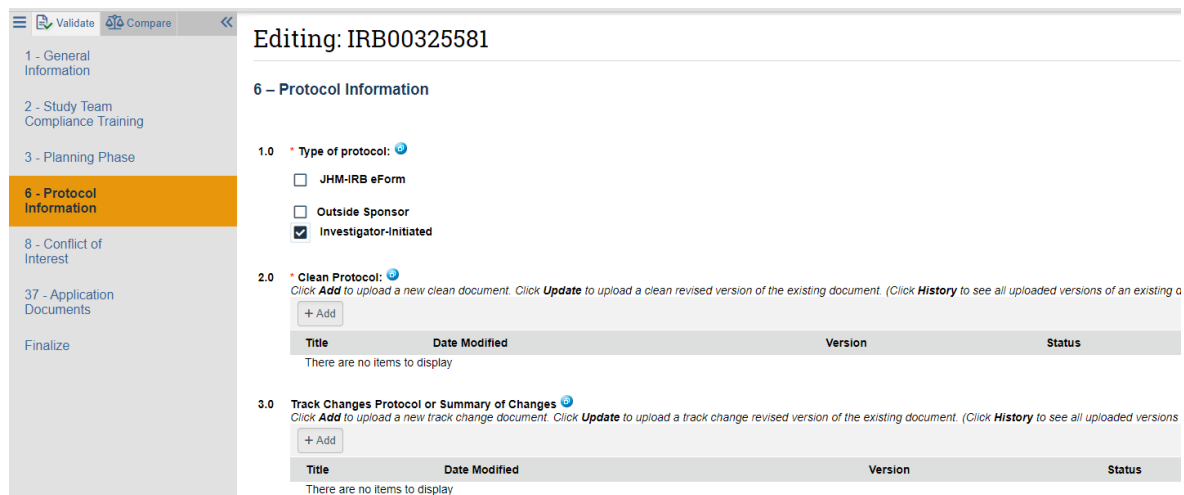
Please include:

- For IND: Please include Drug Information: “Drug Name & Indication”
- For IDE: Please include purpose (the name and intended use of the device and the objectives and duration of the investigation)
- Brief introductory Statement and General Investigational Plan

Section 6: Protocol Information:

Item 2.0 Clean Protocol:

Please upload the protocol for the planned study to be submitted to the FDA. You may include a draft version of the protocol. Please refer to the Appendix 2 for regulatory guidance on protocol development.



The screenshot shows a web interface for editing IRB00325581. The left sidebar contains a navigation menu with items: 1 - General Information, 2 - Study Team Compliance Training, 3 - Planning Phase, 6 - Protocol Information (highlighted), 8 - Conflict of Interest, 37 - Application Documents, and Finalize. The main content area is titled 'Editing: IRB00325581' and shows the '6 - Protocol Information' section. Under '1.0 * Type of protocol:', there are three options: 'JHM-IRB eForm' (unchecked), 'Outside Sponsor' (unchecked), and 'Investigator-initiated' (checked). Under '2.0 * Clean Protocol:', there is a '+ Add' button and a table with columns 'Title', 'Date Modified', 'Version', and 'Status'. Below the table, it says 'There are no items to display'. Under '3.0 Track Changes Protocol or Summary of Changes', there is another '+ Add' button and a similar table with the same columns and 'There are no items to display' below it.

Section 8: Conflict of Interest:

If the application involves a conflict of interest (COI), the application will be reviewed by the Office of Outside Interests (OOI). Please indicate individual and/or institutional conflict(s) of interest.

For Planning Phase Application for IND/IDE Application Submission approval, the OOI’s review will be limited to determining whether the individual submitting the application may serve as the IND or IDE holder under Johns Hopkins University (JHU)’s [COI policy](#).



8 - Conflict of Interest

1.0 * Does the Johns Hopkins PI or any Johns Hopkins study team member (or their spouse, domestic partner, or dependent children) have a financial interest that 1) could be affected by the research, or 2) is in an entity that could be affected by the research?

* This applies to current interests/relationships and those within the past 12 months.
 Yes No [Clear](#)

All conflicted individuals must disclose potential conflicts of interest to the Office of Policy Coordination (OPC) before this application can be submitted.

2.0 * Indicate whether the PI has a conflict of interest or will serve as a non-conflicted designee:

Principal Investigator

First	Last	* Conflict	* Non-Conflicted Designee	Management Plans
		Yes ▼	No ▼	There are no items to display

3.0 View each study team member, conflict status and non conflict designee as noted from their agree to participate as well as any management plans.

First Name	Last Name	Conflict	Non Conflict Designee	Management Plan
Martin	Pomper			

5.0 * Enter the non-conflicted designee's contact number (to be included on the consent form):

6.0 * To the best of your knowledge, does Johns Hopkins have a financial interest that 1) could be affected by the research or 2) is in an entity who could be affected by the research?
 Yes No [Clear](#)

Item. 1: If the answer is yes:

- All conflicted individuals must disclose potential conflicts of interest to Office of Outside Interests (OOI) before this application can be approved.
- Please use this link to [Disclose Your Outside Activities in eDisclose](#). Please update your eDisclose disclosure to include the Planning Phase Application for IND/IDE Application number.

Item. 6: If the answer is yes.

IND/IDE Supplemental Form will include JHTV disclosure number (e.g., C12345) of all University proprietary information and/or intellectual property supporting the Investigational drug or Investigation device.

Appendix 1

Regulatory guidance on IND/IDE Application Submission to the FDA

What is Investigational New Drug Application (IND)?

An Investigational New Drug Application (IND) is a request from a clinical study sponsor to obtain authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. Clinical studies are often conducted to collect safety and effectiveness information in support of marketing applications for biologic and drug products. Unless exempted, the sponsor for a clinical study must obtain authorization from FDA for conducting the study by submitting an IND Application. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics Product License Application.

Research Investigational New Drug Applications:

A research IND (also called a non-commercial IND) is one for which the sponsor (generally an individual investigator, academic institution or non-profit entity) does not intend to later commercialize the product. These studies are strictly for research, are usually shorter in duration and may result in publications in peer-reviewed journals.

- IND Applications for Clinical Investigations: Regulatory and Administrative Components are listed [under this link](#).
- Investigator-Initiated Investigational New Drug (IND) Applications webpage: The resources for application reporting and applications procedures for IND applications for both clinical research and clinical treatment are [under this link](#).
- The following [link](#) includes resources for the legal requirements of an IND application, IND review principles, policies and procedures.
- Investigator's Checklist for IND Application Submission is [under this link](#).
 - Sponsor-investigators may address the requirements for nonclinical and CMC information by providing a Letter of Authorization, also known as an "LOA" from the commercial manufacturer of the investigational product. The LOA allows FDA to reference the nonclinical and CMC information in the commercial manufacturer's IND on behalf of the sponsor-investigator.
 - Please review details for IND Applications for Clinical Investigations: Chemistry, Manufacturing, and Control (CMC) Information [under this link](#).
 - Please include details for any drugs, substances, or biologicals used in the protocol that is prepared or manipulated by JHM pharmacy and/or anyone outside of a JHM pharmacy after initial product manufacturing.

- Please review Manufacturing Requirements if JHU will be have a role in manufacturing of the investigational product/device that is subject of this IND/IDE application.
 - Manufacturing Requirements for IND Applications:
 - If applicable, for any Phase 1 clinical investigations conducted under the IND application, drug has to be prepared in accordance with the principles of cGMP and the manufacturing processes outlined in the corresponding IND.
 - If applicable, for any Phase 2 or 3 clinical investigations conducted under the IND application, drug has to demonstrate strict compliance with the FDA’s current Good Manufacturing Practice (cGMP) regulations at 21 CFR Parts 210 and 211 (or 21 CFR Part 212 for Positron Emission Tomography radiopharmaceuticals).
 - Please includes details of the drug manufacturing plan in the protocol and/or Investigator’s Brochure.
 - Manufacturing Requirements for IDE Applications:
 - If applicable, the JHU facility/laboratory that will be engaged in manufacturing of investigational devices for the IDE application has to operate in strict compliance with the FDA regulations related to device manufacturing establishment registration, as set forth in 21 CFR Part 807.
 - If applicable, the JHU facility/laboratory that will be engaged in manufacturing of investigational devices for the IDE application has to operate in strict compliance with all FDA regulations and guidance applicable to the specific type of device, including both physical devices and regulated software
 - Please includes details of the device manufacturing plan in the protocol and/or Investigator’s Brochure.
- Environmental Assessment of Human Drug and Biologics Applications: Please review the FDA [guidance under this link](#).
Please review 21 CFR 25.20. You may submit a request for categorical exclusion from environmental assessment for investigational drug use in human clinical trials in an IND, in accordance with 21 CFR 25.31(e), with a statement that (1) all wastes from the investigational drugs will be properly controlled, (2) the amount of waste expected to enter the environment is extremely small and expect to be non-toxic, and (3) to the best of your knowledge, no extraordinary circumstances exist where you would need to complete an Environmental Assessment.
Please see an example of statement:
In accordance with 21 CFR 25.31(e), we claim for categorical exclusion from the environmental assessment requirements of 21 CFR 25.20 for approval of Investigational drug on the basis that this drug product is the subject of an Investigational New Drug Application. All wastes from the investigational drugs

will be properly controlled, the amount of waste expected to enter the environment is extremely small and expect to be non-toxic. Additionally, to the best of our knowledge, no extraordinary circumstances exist.

- Please review details for IND Applications for Clinical Investigations: Pharmacology and Toxicology (PT) Information [under this link](#).
- Please review details for IND Applications for Clinical Investigations: Previous Human Experience with the Investigational Drug [under this link](#).
- IND for commercially distributed product which the investigator will purchase from the pharmacy. In situations where, the drug will be used “as is” (without any further “manufacturing steps”) and the FDA agrees that the existing preclinical testing is sufficient for the new indication, then submission of the approved product label, can satisfy the requirement for preclinical pharmacology/toxicology testing and providing manufacturing information.

Center for Drug Evaluation and Research (CDER) Research IND submissions:

As part of the U.S. Food and Drug Administration (FDA), CDER regulates over-the-counter and prescription drugs, including biological therapeutics and generic drugs. CDER Offices and Divisions are [under this link](#).

Please note, FDA transferred some of the therapeutic biological products that had been reviewed and regulated by the Center for Biologics Evaluation and Research (CBER) to the Center for Drug Evaluation and Research (CDER). CDER now has regulatory responsibility, including premarket review and continuing oversight, over the transferred products. In regulating the products assigned to them, CBER and CDER will consult with each other regularly and whenever necessary. Please review Transfer of Therapeutic Products to the Center for Drug Evaluation and Research (CDER) [under this link](#).

FDA/CDER accepts electronic submission via CDER NextGen Portal.

Visit CDER’s Next Gen Portal <https://edm.fda.gov> and the [NextGen Portal Video Tutorials](#) for instructions on the enrollment process, as your future submission may be a great candidate to submit electronically.

Requesting a Pre-Assigned Application number:

FDA guidance for Requesting a Pre-Assigned Application number is [under this link](#):

1. For submitting via CDER NextGen Portal, please follow the instructions below:

Pre-assigned **IND** number requests can now be submitted via the CDER NextGen Portal

How to Gain Access

- **New Users**

To register for an account with the CDER NextGen Portal, navigate to <https://edm.fda.gov> and follow the signup instructions.

- **Existing Portal Users**

Pre-Assignment tab was added to your account automatically – click on it when you are ready to submit a request.

Note: If you submitted a request via portal, *do not* re-submit via e-mail. Portal is the preferred way of submitting requests.

2. For submitting via e-mail, please follow the instructions below:

Send one email per application number request to cderappnumrequest@fda.hhs.gov.

Subject: Request for a Pre-Assigned Number

Text:

- Name of Applicant that will be on form (FDA 1571)
- Applicant Address (street, city, state, zip code)
- Name of US Contact, Phone Number, Fax Number, Email Address
- Name of drug or Subject of Master File
- Drug Trade Name (if applicable)
- Indication
- Review Division, if known

If requesting for an IND, please include one of the following:

- "Commercial IND" if the product under investigation is intended to be commercialized at a later date
- "Research IND" if the product under investigation is not intended to be commercialized at a later date. Research INDs are generally sponsored by individual investigators, academic institutions and non-profit entities. May include INDs for emergency use or other expanded access.

Sample e-mail

To: cderappnumrequest@fda.hhs.gov

Subject: Request for a Pre-Assigned <insert Application Type> Number

Application information:

Name of Applicant

Address line 1

Address line 2

Name of U.S. Contact

Phone number

Fax number

Email address

Drug Information:

Drug Name:

Trade Name:

Dosage Form:

Indication:

A pre-assigned number will be issued within 3 business days.

Notes:

- CDER Offices and Divisions are listed [under this link](#).
- A planning phase application for IND submission is not required for Exemptions from IND Requirements.

Please review FDA guidance for Application Procedures: Exemptions from IND Requirements [under this link](#).

Please submit IND exemption request in writing to the reviewing division at FDA to obtain a formal “Acknowledge/Exempt IND” letter. IND exemption request includes a summary of the proposed investigation for FDA. In certain cases, FDA staff may advise the sponsor to submit a full IND application for the proposed investigation for FDA review. If during that review FDA concludes the IND application meets the criteria for exemption, the sponsor will be so notified.

IND exemption request usually include the following:

- Form FDA 1571: Under Box 11: Please select Other (Specify): IND exemption request
- Cover letter

Note: investigators that for studies involving approved drugs, if a company gives them the product they must confirm whether or not it is commercially distributed material (same as the pharmacy would receive) or is from an investigational batch. If the latter then an IND will be required regardless of any other consideration about the trial because an “unapproved” or investigational manufacturing process is being used for the drug.

- Protocol

The Center for Biologics Evaluation and Research (CBER) Research IND submission:

Center for Biologics Evaluation and Research (CBER) is the Center within FDA that regulates biological products for human use under applicable federal laws, including the Public Health Service Act and the Federal Food, Drug and Cosmetic Act. CBER protects and advances the public health by ensuring that biological products are safe and effective and available to those who need them. CBER also provides the public with information to promote the safe and appropriate use of biological products.

This [link](#) provides information for submission of an Investigational New Drug Application (IND) to Center for Biologics Evaluation and Research (CBER).

Please note, FDA transferred some of the therapeutic biological products that had been reviewed and regulated by the Center for Biologics Evaluation and Research (CBER) to the Center for Drug Evaluation and Research (CDER). Please review Transfer of Therapeutic Products to the Center for Drug Evaluation and Research (CDER) [under this link](#).

Investigational New Drug Applications (INDs) for CBER-Regulated Products resources under [this link](#).

Contacts in the Center for Biologics Evaluation & Research (CBER) are under [this link](#).

What is an Investigational Device Exemption (IDE)?

An IDE is issued by the FDA to allow the use investigational devices in human subjects. The IDE permits use of the device in a clinical investigation to evaluate the safety and/or efficacy of the investigational medical device. An IDE may be held either by a commercial sponsor or by a physician-investigator.

Please review JHM IRB guidelines for Investigational Medical Devices [under this link](#).

There are two possible classifications for investigational medical devices:

- a) Significant Risk (**SR**) or
- b) Non-Significant Risk (**NSR**).

The distinctions between the two device risk categories are:

- a) A SR device poses a “potential for serious risk to the health, safety, or welfare of a subject.” Such devices may only be studied under an Investigational Device Exemption (IDE) granted by the FDA. A device is SR (and requires an IDE) if it:
 - is intended as an implant, or
 - is purported or represented to be for a use in supporting or sustaining human life, or
 - is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health; or

- otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
- b) Non-significant risk devices do not meet the above definition. The assessment of whether or not a device study represents a NSR is initially made by the sponsor/investigator. The IRB will then determine if the NSR designation is appropriate. If the IRB disagrees with the NSR claim, it will require the sponsor/investigator to submit an IDE application to the FDA

A sponsor of a clinical trial that meets the criteria for a significant risk device study must submit a complete IDE application to FDA. There are no preprinted forms for an IDE application; however, an IDE application must include certain required information. The sponsor must demonstrate in the application that there is reason to believe that the risks to human subjects from the proposed investigation are outweighed by the anticipated benefits to subjects and the importance of the knowledge to be gained, that the investigation is scientifically sound, and that there is reason to believe that the device as proposed for use will be effective.

FDA IDE Application Required Elements are listed [under this link](#).

Center for Devices and Radiological Health (CDRH):

Regarding IDE submission method including IDE reports: There is no Electronic Submissions Gateway (ESG) or email method for submitting IDE submissions such as IDE reports, etc.

You should prepare the IDE report in the form of only one valid eCopy on CD, DVD, or flash drive, along with a printed paper cover letter, no paper copy is required and accepted.

Please refer to the [eCopy guidance document](#), section V, Table 1. page 6-7.

You should **send** the valid eCopy with the printed cover letter to the CDRH Document Control Center (DCC):

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center (DCC) – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Your cover letter is a document on your letterhead that typically includes the purpose of your submission and contact information (including phone number and email address), along with the required signature. It must include a signature (may be a wet (i.e., ink) signature or a valid digital signature). For detailed on eCopy over letter requirements, please refer to the eCopy guidance document, Section A-attachment 1, page 18: <https://www.fda.gov/media/83522/download>



Please refer to the “eCopy Program for Medical Device Submissions: Frequently Asked Questions”: <https://www.fda.gov/medical-devices/how-study-and-market-your-device/ecopy-program-medical-device-submissions-frequently-asked-questions>

The “eCopy Program for Medical Device Submissions” webpage provides information on eCopy, e-submitter-eCopy tools. <https://www.fda.gov/medical-devices/how-study-and-market-your-device/ecopy-program-medical-device-submissions>

You may find it useful to review the following resources for e-Copy:

- [Device Advice: eCopy Program for Medical Device Submissions](#)
- [eCopy Program for Medical Device Submissions: Guidance for Industry and Food and Drug Administration Staff](#)

JHM Office of Human Subjects Research - Institutional Review Board guidelines for Investigational Medical Devices are [under this link](#).

Appendix 2

Regulatory Guidance on Protocol Development

Please refer to FDA protocol guidance under [this link](#). Sec. 312.22 General principles of the IND submission.

IDE Application protocol guidance is [under this link](#).

Please review suggested Templates:

- NIH Protocol Templates for Clinical Trials are [under this link](#).
- Cancer Therapy Evaluation Program (CTEP) Protocol Templates and Guidelines are [under this link](#).

A protocol is required to contain the following elements:

- Protocol title: Please indicate phase of an investigation, and if it's a multisite study (Any study that has phases conducted at more than one site).
- Protocol title page will include:
 - Principal Investigator (PI): The name and address
 - IND # or IDE #: Please enter "TBD" if an IND # or IDE # is not yet available.
 - IND/IDE holder
 - Multisite studies will include the following:
 - The Coordinating Center must be designated on the title page.
 - Sites: The name and address of each participating institution.
 - The name and address of each reviewing Institutional Review Board.
 - The name and address of each responsible investigator at each participating institution (Site PI).
- Study Objective (s) and Endpoints: A statement of the objectives and purpose of the study.
- Patient Selection:
 - Eligibility Criteria: The criteria for patient selection and for exclusion of patients and an estimate of the number of patients to be studied.
- Study Design: A description of the design of the study, including the kind of control group to be used, if any, and a description of methods to be used to minimize bias on the part of subjects, investigators, and analysts.
- Analytical Methods:
 - The method for determining the dose(s) to be administered, the planned maximum dosage, and the duration of individual patient exposure to the drug.
 - A description of the observations and measurements to be made to fulfill the objectives of the study.

- Study Schedule:
 - Study Procedures & Schedule of events:
A description of clinical procedures, laboratory tests, or other measures to be taken to monitor the effects of the drug in human subjects and to minimize risk.
- Statistical Considerations and Analytical Plan: Description of statistical methods, case report forms if applicable, an analysis of the protocol demonstrating its scientific soundness.
- Adverse Events Reporting Requirements.
- Data and Safety Monitoring plan.
- Investigational Drug or Investigational Device Information
 - For Investigational Drug Studies:
 - Investigators may obtain Investigator’s Brochure (IB) from IND product’s manufacturer to be uploaded under Section 3: Planning Phase. item 2.
 - Investigators will include the following information in the draft protocol: IND study agent(s), including information to support safety issues and the rationale for the proposed starting dose, dose escalation scheme, and regimen chosen. Please also provide information on the mechanism of action, summaries of nonclinical and clinical studies, nonclinical and clinical pharmacokinetics, and major route of elimination. If available, please include information on the metabolism of the study agent in humans and its potential for drug interactions, if any interactions.
 - Brief description of the drug substance and the formulation, including the structural formula, if known
 - Summary of the pharmacological and toxicological effects of the drug in animals and, to the extent known, in humans
 - Summary of the pharmacokinetics and biological disposition of the drug in animals and, if known, in humans
 - Summary of information relating to safety and effectiveness in humans obtained from prior clinical studies
 - Description of possible risks and side effects to be anticipated on the basis of prior experience with the drug under investigation or with related drugs, and of precautions or special monitoring to be done as part of the investigational use of the drug. Adverse Events (AEs) described in the IB help determine whether an AE that occurs during a clinical trial is “expected” and, if so, how it will be reported to FDA.
 - The sponsor-investigator may request a waiver from the requirement of an investigator’s brochure for this application when their study that is being conducted at a single site where they are affiliated. Please review the FDA CFR - Code of Federal Regulations 21CFR312.55 [under this link](#). 21CFR312.55(a) states, in part, that “Before the investigation begins, a sponsor (other than a sponsor-investigator) shall give each participating clinical

investigator an investigator brochure containing the information described in 312.23(a)(5)” If the sponsor is also the investigator, we believe a waiver from the requirements of 21CFR312.55(a) is justifiable.

- Please refer to the FDA Investigator’s Brochure guidance [under this link](#).
- For IDE Studies: Please include the following in the protocol.
 - description of this device (a description of each important component, ingredient, property, and principle of operation of the device and any anticipated changes in the device during the investigation)
 - monitoring procedures (the sponsor's written procedures for monitoring the investigation and the name and address of each monitor.
 - additional records and reports (a description of any records or reports of the investigation other than those required in Subpart G of the IDE regulations).
- Description of the manufacturing if JHU will be have a role in manufacturing of the investigational product/device that is subject of this IND/IDE application.
- Description for any drugs, substances, or biologicals used in the protocol that is prepared or manipulated by JHM pharmacy and/or anyone outside of a JHM pharmacy after initial product manufacturing.
- Description of the Accountability, Handling and Storage of Investigational Products.
- Accountability for all investigational product should be sufficient to show:
 - Subjects received proper dose/device
 - Which dose/vial/device was provided to which subject and when
 - Accountability for all investigational product
 - Product was shipped, received, and stored at the proper temperature and conditions
- Multicenter Guidelines: multi-site studies protocols will include:
 - Responsibilities of the coordinating centers.
 - Plan for the monitoring of ALL sites where the study will be conducted.
 - The frequency and timing of data submission forms to the Coordinating Center should be stated.
 - Patient registration procedures must be stated in the protocol.
 - Adverse event reporting instructions for the participating institutions.
 - Investigational Product management plan at each participating institution.