



UNIVERSITY OF CALIFORNIA, SAN DIEGO
HUMAN RESEARCH PROTECTIONS PROGRAM
FACT SHEET

Investigator Initiated Clinical Trials/IND Applications

Definitions

Investigator-initiated clinical trials are those trials in which the UCSD Investigator/PI is the author or co-author of protocol. This is in contrast to clinical trials where the protocol is authored by a commercial or industry sponsor, such as a pharmaceutical company.

Clinical investigation or clinical research, as defined by the FDA, “means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA...or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.”

The FDA further defines a clinical investigation associated with an investigational drug as “an experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. Such an experiment is any use of a drug [whether approved or unapproved] except for the use of a marketed drug in the course of medical practice.”

When a drug or biological product not previously authorized for marketing in the US is intended to be used for the purposes of clinical investigation, or in certain cases, for the purposes of clinical treatment when no approved therapies are available, an Investigational New Drug (IND) Application must be submitted to the FDA.

The party who submits the IND application to the FDA is considered the sponsor of the IND application. The FDA notes, “In the absence of any other sponsor (e.g. pharmaceutical company), the investigator conducting the proposed clinical investigation is the sponsor of the IND application.”

If a UCSD Investigator authors or co-authors the protocol for a clinical trial that is associated with an investigational drug, the UCSD Investigator must submit an IND application, the Investigator would be considered the sponsor, and the Investigator must receive approval for that Investigator-held IND from the FDA before final UCSD IRB approval can be granted unless the study is found to be exempt from IND application requirements.

The FDA suggests that before submitting an IND application, the Investigator refer to the [Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications \(INDs\)—Determining Whether Human Research Studies Can Be Conducted Without an IND](#). Investigators may also review the HRPP Research Plan supplement, [IND Exemptions](#).

There are three main types of IND Applications

- IND Application for Clinical Investigations
- IND Application for Clinical Treatment - Expanded Access (including treatment of a Single Patient in a Non-emergency setting)
- IND Application for Clinical Treatment of a Single Patient in an Emergency Setting

IND Application for Clinical Investigations

The FDA provides an excellent website that includes information for the investigator about submitting an IND application to the FDA. The website is at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm343349.htm>.

The website includes what is required to be provided as part of the application including completed forms [1571](#) (IND application cover); [1572](#) (Investigator's statement); and [3674](#) (certification requirement and **mandatory registration and reporting of results for application through ClinicalTrials.gov**).

The website also outlines the responsibility of the PI/Sponsor who holds the IND. These responsibilities include "sending periodic updates and reports related to [the] application to FDA." Updates and reports include the following:

- [Protocol amendments](#)
- [Information amendments](#)
- [Safety reports](#)
- [Annual reports](#)

Please note: A "NEW" UCSD Biomedical Research application must be submitted to the UCSD IRB/HRPP for review by a convened IRB. Information about submitting an application can be found at <https://irb.ucsd.edu>.

In addition, the PI must also follow IRB/HRPP post-approval reporting requirements including review and approval of amendments before initiation except where necessary to eliminate apparent immediate hazard to the subject (see HRPP fact sheet, [Submitting an Amendment/Modification to a Research Plan \(Protocol\)](#) and reporting of adverse events and unexpected problems (see SOPP, section 3.13, [Reporting Adverse Events and Unexpected Problems](#)) as well as [Continuing Review submission](#).

IND Application for Clinical Treatment - Expanded Access (including treatment of a Single Patient in a Non-emergency setting)

The FDA defines expanded access as "the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options."

All of the following must be satisfied to be considered for expanded access:

- Patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
- The potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context of the disease or condition to be treated; and

- The expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product.

If a UCSD treating physician submits the request to open an expanded access IND application and receives FDA's authorization to use the investigational product, the UCSD treating physician is considered the sponsor and has the same responsibilities of a sponsor as for an IND application for clinical investigations (see above).

The FDA notes that FDA regulations allow access to investigational drugs for treatment purposes on a case-by-case basis for individual patients (single-patient IND application for treatment in emergency settings and non-emergency setting); intermediate-size patient populations (groups of patients, $n > 1$); and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

More information about expanded access can be found [here](#).

Specific information regarding an IND application for treatment of a single patient in a non-emergency setting can be found [here](#).

The FDA provides this additional information regarding required IRB review: "Except for emergency expanded access use...when there is not sufficient time to secure prospective IRB review, an investigator treating a patient with an investigational drug under expanded access is responsible for obtaining IRB review and approval consistent with 21 CFR part 56 before treatment with the investigational drug may begin, regardless of whether the protocol is submitted in a new IND or to an existing IND (21 CFR 312.305(c)(4)). In the case of emergency expanded access use, FDA authorization is still required (§ 312.310(d)), but it is not necessary to wait for IRB approval to begin treatment. However, the IRB must be notified of the emergency expanded access use within 5 working days of emergency use (§ 56.104(c)). Part 56 requires, among other things, that the IRB review the expanded access use at a convened IRB meeting at which a majority of the members are present (*full IRB review*) (§ 56.108(c)).

"A physician submitting an individual patient expanded access IND using Form FDA 3926 may select the appropriate box on that form to request a waiver under § 56.105 of the requirements in § 56.108(c), which relate to full IRB review. FDA concludes that such a waiver is appropriate for individual patient expanded access INDs when the physician obtains concurrence by the IRB chairperson or another designated IRB member before treatment use begins. A physician submitting an individual patient expanded access IND using Form FDA 1571 may include a separate waiver request with the application."

Please note: A "NEW" UCSD Biomedical Research application must be submitted to the UCSD IRB/HRPP for review by a convened IRB. Information about submitting an application can be found at <https://irb.ucsd.edu>.

A sample treatment consent document for adults can be found [here for UCSD](#) and [here for RCHSD/UCSD](#). A sample treatment parent permission document can be found [here for UCSD](#) and [here for RCHSD/UCSD](#). A sample treatment adolescent assent document can be found [here for UCSD](#) and [here for RCHSD/UCSD](#).

Note: It is the treating physician's responsibility to ensure the information included in the consent is accurate including the costs associated with the treatment such as the cost of the drug. Consultation with the Office of Coverage Administration (OCA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. It also the treating physician's responsibility to ensure any appropriate agreements are in place. Consultation with the Office of Contracts and Grants (OCGA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. Consultation with RCHSD Research Administration for RCHSD studies is also recommended.

In addition, the PI must also follow IRB/HRPP post-approval reporting requirements including review and approval of amendments before initiation except where necessary to eliminate apparent immediate hazard to the subject (see HRPP fact sheet, [Submitting an Amendment/Modification to a Research Plan \(Protocol\)](#) and reporting of adverse events and unexpected problems (see SOPP, section 3.13, [Reporting Adverse Events and Unexpected Problems](#) as well as [Continuing Review submission](#)).

IND Application for Clinical Treatment of a Single Patient in an Emergency Setting

If a UCSD treating physician wishes to treat a single patient in an emergency setting, an emergency investigational new drug (EIND) application must be opened with the FDA. Once the UCSD treating physician receives the FDA's authorization to use the investigational product, the UCSD treating physician is considered the sponsor.

The FDA defines emergency use of a test article, in association with an IND, as "...the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval." (21 CFR 56.102(d))

The FDA also states, "In the case of emergency expanded access use, FDA authorization is still required (§ 312.310(d)), but it is not necessary to wait for IRB approval to begin treatment. However, the IRB must be notified of the emergency expanded access use within 5 working days of emergency use (§ 56.104(c))."

The criteria for an emergency use of a test article include the following:

- The patient has a condition that is life-threatening or severely debilitating.
- No standard acceptable treatment is available.
- There is not sufficient time to obtain IRB approval in advance of the use of the test article. In most cases, a minimum of two working days before a Biomedical IRB meeting is required for a convened IRB to review an emergency use application. Thus, there is sufficient time to obtain IRB approval if the physician decides the test article is not needed prior to the next scheduled Biomedical IRB meeting and the complete emergency use application can be submitted at least two days prior to that meeting. If there is insufficient time to prepare the application and submit the application for review by a convened IRB, the exemption from IRB review is met. **The physician should not delay treatment if waiting for convened IRB review would jeopardize a patient's health and safety.**
- There is no known available IRB-approved protocol using the same test article or the patient does not qualify for an existing protocol.
- A test article is available that in the opinion of the physician might be beneficial.

- A test article is available from a sponsor or elsewhere.
- The emergency use of the test article is not part of a systematic investigation designed to develop or contribute to generalizable knowledge.
- The emergency use will be reported to the UCSD HRPP within five working days after test article use.
- Consent will be sought and documented from the prospective participant or participant's legally authorized representative, unless the criteria for exception to the requirement for consent are met.

The FDA provides many excellent documents to help the physician with submitting the EIND at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm343022.htm>. These documents include the following:

- [A physician's checklist for an IND Application for Emergency Treatment](#)
- [EIND timeline](#)
- [EIND eligibility tool](#)

FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

The Treating Physician should notify the Director of the HRPP at 858-246-4777 and complete and upload the [Biomedical Emergency Use Facesheets](#) to allow the HRPP Office to track the emergency use. Additional information will also need to be submitted including a completed [Emergency Use Notification Form](#) and [Emergency Use Notification, 5-day Post Use form](#).

A sample treatment consent document for adults can be found [here for UCSD](#) and [here for RCHSD/UCSD](#). A sample treatment parent permission document can be found [here for UCSD](#) and [here for RCHSD/UCSD](#). A sample treatment adolescent assent document can be found [here for UCSD](#) and [here for RCHSD/UCSD](#).

Note: It is the treating physician's responsibility to ensure the information included in the consent is accurate including the costs associated with the treatment such as the cost of the drug. Consultation with the Office of Coverage Administration (OCA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. It also the treating physician's responsibility to ensure any appropriate agreements are in place. Consultation with the Office of Contracts and Grants (OCGA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. Consultation with RCHSD Research Administration for RCHSD studies is also recommended.

As noted above, an emergency use of a test article is exempt from prior IRB review and approval. However, the emergency use of a test article must be reported to the IRB within 5 working days of date of the emergency use. The determination to use a test article in an emergency setting is made by the treating physician in concert with the FDA and should not be dependent on the submission of information to the UCSD IRB/HRPP. If possible, the IRB should be notified prior to an emergency use of a test article.

Version date: 4/27/2018