



Human Subject Protection Program
Investigator Guidance
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CLINICAL INVESTIGATIONS OF DRUGS AND BIOLOGICS

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Overview

- This guidance is intended to assist investigators in meeting the various Food and Drug Administration (FDA) requirements when using unapproved drugs or biologics in clinical research and treatment.
- Food and Drug Administration (FDA) regulations [21 CFR 312](#) contain procedures and requirements governing the use of unapproved drugs and biologics. All clinical research projects or treatments involving drugs or biologics that are not FDA approved for marketing must be reviewed by the FDA and the IRB. This is done by filing an IND with the FDA and submitting a protocol for review by the Institutional Review Board (IRB).

Investigational New Drug Applications (INDs)

An IND is required for:

- Any use of a drug or biologic not approved for marketing by the FDA, even if no study is being conducted.
- Studies involving a drug or biologic that is not approved by the FDA.
- Studies involving an approved (i.e., commercially available) drug or biologic that is being tested to support a new indication or significant change in labeling of the drug or biologic.
- Studies involving an approved drug or biologic that is being tested to support a significant change in advertising for the drug or biologic.
- Studies involving an approved drug or biologic that is being used or tested in a new route of administration, new dosage level, or new patient population that may increase the risk of the drug or biologic.

An IND is not required for:

- **Clinical Studies:** Any clinical investigation of an approved, marketed drug or biologic requires CHLA IRB review and approval. An IND is not required if all of the following conditions are met:
 - It is **not** intended to be reported to the FDA in support of a new indication for use or to support any other significant change in the labeling; and
 - It is **not** intended to support a significant change in the advertising for the product; and
 - It **does not** involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the product; and
 - It is conducted in compliance with the FDA requirements for IRB review and informed consent; and
 - It is conducted in compliance with the FDA requirements concerning the promotion and sale of drugs ([21 CFR 312.7](#)).

Exceptions:

- When the principal intent of the clinical investigation is to develop information about the safety or efficacy of a drug or biologic, the CHLA IRB may require that the Investigator submit an IND request to the FDA.
- Even when there is no immediate intent to change product labeling or advertising, investigators who are planning rigorous, carefully controlled clinical investigations of an off-label use of an approved drug/biologic should seek an IND. Data from such studies conducted without an IND will not be considered by the FDA.

- **Off-Label Prescriptions:** Neither an IND nor CHLA IRB review is required for off-label use of a marketed drug or biologic as long as such use is **strictly for clinical purposes, and the results are not collected for or presented as research.**

Differences Between a “Sponsor” and a “Sponsor-Investigator” IND

The FDA makes the following distinctions between a “sponsor” and a “sponsor-investigator” and a “commercial IND” and an “Investigator-Initiated IND.”

- **“Sponsor”** means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.
- A **“Commercial IND”** is submitted by a sponsor that intends to market the product upon FDA approval.
- **“Sponsor-Investigator”** means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.
- An **“Investigator-Initiated IND”** is submitted by a physician who both initiated and conducts a clinical investigation.

- See [21 CFR 312.3](#) for other definitions and interpretation of terms related to the topic of investigational new drug applications.

Submitting an IND to the FDA

- **Pre-IND Advice:** Investigators considering submitting an IND application to the FDA should consult the FDA's [Investigational New Drug Application Process](#) web page before submitting an IND application. To contact the appropriate division for the [Pre-IND Consultation Program](#), please refer to the [Pre-IND Consultation List](#).
- **IND Submission:** The IND submission to the FDA and the IRB application should be initiated at the same time. The FDA has 30 days to review the IND application. Likewise, the IRB typically reviews an application within a 30-day window, but it may take longer to secure approval. Subjects may not be recruited or enrolled before FDA and IRB approval.

Expanded Access and Emergency Use of Unapproved Drugs and Biologics for Treatment

- The FDA allows certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs and biologics through expanded access programs. Refer to the Investigator guidance document, "Expanded Access and Emergency Use of a Test Article" for more details.

IRB Review Requirements

- **IND Verification:** The CHLA IRB may review the research before the IND application is submitted to or approved by to the FDA. The FDA does not require local IRB approval before issuing an IND number. When a clinical investigation requires an IND number, the IRB will not issue final approval until the IND number is reported to and verified by the IRB. Verification can be accomplished by providing the following:
 - Sponsor protocol imprinted with the IND number, or
 - Written communication from the sponsor documenting the IND number, or
 - Written communication from the FDA documenting the IND number. **NOTE:** This option is required if the CHLA investigator holds the IND.

- **Investigator's Brochure:** For any study involving an investigational drug or biologic, one copy of the Investigator's Brochure must be submitted with the IRB application.
- **Protocol:** If there is a sponsor or multicenter protocol, a copy of that protocol must accompany the IRB application.
- **Charging for investigational drugs or biologics:** Charging for an investigational drug must be approved by the FDA. Documentation of FDA approval to charge for investigational drugs must be submitted with the application.

Control of Investigational Drugs and Biologics

- CHLA has policies regarding the use of investigational drugs and biologics in order to assure patient safety and comply with JCAHO standards, California law, and California Department of Health Services regulations.
- See [CHLA Policy MM – 088.0: Investigational Drugs](#) for details about the safe handling, dispensing, use, monitoring and disposition of investigational drugs (and biologics) at CHLA.
- Contact the CHLA Investigational Drug Pharmacy for questions: 323-361-6045 or pharmacyIDS@chla.usc.edu.

FDA References

FDA References:

- [FDA Center for Drug Evaluation and Research](#)
- [Information for Sponsor-Investigators Submitting INDs](#)
- [Charging for Investigational Drugs Under an IND](#) - Questions and Answers