Investigational New Drug (IND) Policy and Guidance

Investigational test articles are only allowed to be used in approved research protocols under the direction of approved researchers. For guidance on labeling investigational new drugs or the use of supplements in a clinical trial, please refer to the policy Study Drugs and Supplements.

Definitions:

Clinical investigation: any experiment in which a drug is administered or dispensed to, or used involving one or more subjects

Drug: articles intended for use in the diagnosis, cure, mitigation, treatment of prevention of disease… [21 USC 321 (g)(1)(B)], articles (other than food) intended to affect the structure or any function of the body… [21 USC 321 (g)(1)(C)]; a drug is defined by intended use, not the nature of the substance (e.g. cranberry juice)

Investigational New Drug: new drug or biologic that is used in clinical investigation, and in certain cases, for clinical treatment

What is an IND?

An Investigational New Drug Application (IND) is a request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. 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.

Types of INDs

There are three IND types:

- An Investigator IND is submitted by a physician. The physician initiates and conducts the clinical investigation and directions the investigational drug administration or dispensation. A physician might submit an IND to propose studying an unapproved drug, or an approved product for a new indication or in a new patient population.
- Emergency Use IND allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND in accordance with 21CFR, Sec. 312.23 or Sec. 312.20. It is also used for patients who do not meet the criteria of an existing study protocol, or if an approved study protocol does not exist.
- Treatment IND is submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.

When should an IND application (IND) be submitted to the FDA?

An IND application is required when research involves a drug, the research is a clinical investigation, and the clinical investigation is not exempt from IND regulations.

FDA regulations require sponsors and sponsor- investigators (of individual investigator-initiated studies) to determine whether an IND is required for a particular study. The sponsor should be able to determine whether the IND regulations apply to a planned clinical investigation as required under 21 CFR 312.2(a). If a sponsor is uncertain whether an IND is required, the sponsor should contact the appropriate review division (i.e., for the therapeutic area being studied) in the appropriate FDA Center for advice (21 CFR 312.2(e)).

IND Exemptions

Whether an IND is needed to conduct a clinical investigation of a marketed drug primarily depends on the intent of the investigation and the degree of risk associated with the use of the drug in the investigation. A clinical investigation of a marketed drug is exempt from the IND requirements if all of the criteria for an exemption in § 312.2(b) are met:

- The drug product is lawfully marketed in the United States AND
- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug AND
- The investigation is not intended to support a significant change in the advertising for the drug AND
- The investigation does not involve a route of administration, dosing level, or patient population that significantly increases the risk (or decreases the acceptability of the risk) associated with the use of the drug product (21 CFR 312.2(b)(1)(iii)) AND
- The investigation is conducted in compliance with the requirements for review by an IRB (21 CFR part 56) and with the requirements for informed consent (21 CFR part 50) AND
- The investigation is not intended to promote or commercialize the drug product.

IRB Review of IND studies

The IRB must review the qualifications of the investigator and the adequacy of the investigational site for studies using an IND. The Human Protections Administrator (HPA) will verify that the IND is valid, either with the sponsor, submission of information from the sponsor, or verification with the FDA. The IND number can be verified either by the IND number being identified in the associated sponsor protocol or by a letter from the FDA attached to the protocol confirming than an IND number has been obtained.

The regulations at 21 CFR 56.107(a) require that an IRB "...be able to ascertain the acceptability of the proposed research in terms of institutional commitments and regulations, applicable law,

and standards of professional conduct and practice..." In addition, the regulations at 21 CFR 56.111 require that an IRB determine that the proposed research satisfies the criteria for approval, including that "...risks to subjects are minimized... [and] reasonable in relation to anticipated benefits, if any, to subjects..." In order to fulfill these responsibilities, the IRB needs information about the qualifications of the investigator(s) to conduct and supervise the proposed research.

When reviewing a proposed study, the IRB should ask the investigator if the sponsor determined that an IND is or is not required and the basis for the determination. If the sponsor has determined that an IND is not required, the IRB may request that the investigator provide a copy of any available supporting documentation (e.g., letter from the sponsor or FDA, other basis for that determination). Per FDA guidance, if during its initial review of a study, the IRB questions whether an IND is required, but is unable to resolve this issue, the IRB will follow procedures for resolving controverted issues (e.g., notifying the clinical investigator in writing of the IRB's concerns and delaying approval of the study until the matter is resolved).

Use of approved drugs off-label in the course of medical treatment

Use of a marketed product for treatment with no intention of collecting data for clinical research purposes, and when the intent is the "practice of medicine", does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE), or review by an Institutional Review Board (IRB).

Do clinical investigations using supplements need an IND?

Some clinical investigations using supplements required an IND; other studies using supplements may not require one. For guidance the use of supplements in a clinical trial, please refer to the policy Study Drugs and Supplements.

To apply for an IND, please refer to FDA guidance:

https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-application-procedures-overview

Questions about whether a product (drugs) is subject to IND regulations: call FDA 301-796-3400

Questions about whether a product (biologics) is subject to IND regulations: call FDA 301-827-2000