When is an IND required?

IND regulations in part 312 require that human research studies be conducted under an IND if all of the following conditions exist:

- The research involves a **drug** as that term is defined in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 321(g)(1)).
- The research is a **clinical investigation** as defined in the IND regulations (21 CFR 312.3).
- The clinical investigation is not otherwise **exempt** from the IND requirements in part 312.

What is a **drug**?

- “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease . . .”
- “articles (other than food) intended to affect the structure or any function of the body of man or other animals.”

What is a **clinical investigation**?

The IND regulations in § 312.3(b) define **clinical investigation** as:

- an experiment in which a drug (approved or unapproved) is administered or dispensed to, or used involving, one or more human subjects.

What is considered **exempt**?

**Research with Marketed (Approved) Drugs may be** exempt [21 CFR 312.2(b)] from IND requirements:

- the drug must be lawfully marketed in the US,
- the study cannot be intended to support a new indication or other significant change in product labelling,
- the study cannot be intended to support a significant change in advertising for the drug or be used to promote the drug, and
- the study cannot significantly increase risks for those taking the drug.

In addition, the investigation must follow Institutional Review Board (IRB; 21 CFR 56) and informed consent requirements (21 CFR 50).

- The investigation is conducted in compliance with the requirements of § 312.7 (i.e., the investigation is not intended to promote or commercialize the drug product).

**IND Exempt Decision Worksheet for Investigators:**


**Sponsor-Investigator Responsibilities:**

The sponsor-investigator of a clinical investigation using a marketed drug is responsible for determining whether the investigation meets the criteria for an exemption.

- The IRB protocol/application should include justification for the study meeting the exempt requirements.
- The IRB submission should include the IND exemption decision worksheet as additional documentation.
- If there is uncertainty about whether the exemption criteria are met, the sponsor-investigator can seek advice from FDA on the applicability of the IND regulations.
Research with Non-FDA Approved/Marketed Articles (Supplements, Food, Vitamins)

A dietary supplement is defined as a product taken by mouth that is intended to supplement the diet and that contains one or more dietary ingredients.

- The dietary ingredients in these products can include vitamins, minerals, herbs and other botanicals, amino acids, other dietary substances intended to supplement the diet, and concentrates, metabolites, constituents, extracts, or combinations of the preceding types of ingredients.

Dietary supplements can be found in many forms such as tablets, capsules, softgels, liquids, or powders

When is an IND Required for research with supplements?

- If the clinical investigation is intended only to evaluate the dietary supplement’s effect on body function or structure, an IND is not required.
  - Examples: Studying the effect of fiber on bowel regularity would not require an IND but investigating the ability of fiber to treat chronic diarrhea would.

- If the clinical investigation is intended to evaluate the dietary supplement’s ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required under part 312.
  - Examples: A clinical investigation designed to evaluate a dietary supplement’s (effect on a disease) ability to prevent osteoporosis or to treat chronic diarrhea or constipation would need to be conducted under an IND.

- The intended use must be clearly stated in the IRB protocol and application.

FDA Guidance for Researchers and IRBs

Guidance for Investigators, Sponsors and IRBs: IND Applications- Determining Whether Human Subjects Research Studies Can Be Conducted Without an IND

FDA Pre-IND Consultation Program for Investigators:  