**Tip #1: What is an IND exemption**

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 are met:

- The drug product is lawfully marketed in the United States.
- 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.
- In the case of a prescription drug, the investigation is not intended to support a significant change in the advertising for the drug.
- The investigation does not involve a route of administration, dose, patient population, or other factor that significantly increases the risk (or decreases the acceptability of the risk) associated with the use of the drug product.
- The investigation is conducted in compliance with the requirements for review by an IRB and with the requirements for informed consent.
- The investigation is not intended to promote or commercialize the drug product.

**Tip #2: Who makes the determination about IND exemption?**

The sponsor-investigator must submit the argument for IND exemption to COMIRB as part of the IRB review materials. The IRB will determine the need for an exemption. In cases where the IRB is not comfortable making the determination, the sponsor-investigator will be advised to seek guidance from the FDA. Advice and guidance may be obtained from the FDA either formally or informally.

**Informal inquiries have the following features:**

- They can be communicated either orally or in writing (written communication includes email, fax, or other written correspondence).
- They pose only relatively uncomplicated questions about a planned clinical investigation that FDA can answer based on somewhat limited information.
- The inquirer is not seeking a formal written response.

In response to an inquiry intended to be informal, FDA can (1) provide an informal (qualified, nonbinding) response, either orally or in writing, concerning the applicability of the IND regulations based on its understanding of the planned clinical investigation; (2) ask for additional information before providing an informal response; or (3) determine that the inquiry poses a complex question that should be submitted as a formal inquiry. FDA will not retain and track informal responses to inquiries concerning the applicability of the IND regulations to planned clinical investigations.

**Formal inquiries have all of the following features:**

- They are in writing (can be paper or electronic).
- They pose a question of any level of complexity.
- The inquirer is seeking a formal written response or FDA determines that a formal written response should be given (i.e., that the inquiry cannot be answered informally).
- The documentation contains enough detail to permit FDA to provide a formal response concerning the applicability of the IND regulations to a planned clinical investigation (e.g., a study protocol, information about the drug product).
In response to a formal inquiry, FDA may provide a formal written response concerning the application of the IND requirements to a planned clinical investigation or may determine that it has insufficient information to provide a formal response and seek additional information before providing a response. The scope of any formal response would be limited to the conduct of a clinical investigation consistent with the investigation described in documentation provided to FDA. If there are significant changes to the protocol or other aspects of the planned investigation after FDA has provided a response, that response may no longer be valid. FDA will archive formal inquiries and FDA responses to those inquiries.