
# Fostering Communications in the Drug Development Process

In an ideal setting, sponsors work collaboratively with the US Food and Drug Administration (FDA) during the drug development process, having a shared public health goal of early availability of safe, effective, and high-quality drugs. The FDA describes its philosophy on this topic in *Best Practices for Communication Between IND Sponsors and FDA During Drug Development*, a guidance for industry and review staff issued in December 2017.

As part of the Prescription Drug User Fee Act of 2012 (PDUFA V), covered in the PDUFA Reauthorization Performance Goals and Procedures for Fiscal Years 2013 Through 2017, the FDA's Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) agreed to publish a joint guidance on best practices for timely, transparent, and effective communications between investigational new drug application (IND) sponsors and the FDA. According to the FDA, the timely review of IND submissions with appropriate feedback to sponsors can improve the efficiency of the drug development process.

The IND phase of drug development is the time during which human trials of investigational drugs are conducted. From the FDA's perspective, the IND phase spans the time from the first IND-related submission (including a pre-IND or BIA meeting request or an original IND; see *Formal Meetings with the FDA*, below) to the submission of a marketing application. From the sponsor's perspective, drug development is not limited to the IND phase because it also includes drug discovery and early development of compounds before IND submission and may include clinical trials conducted in other countries outside a US IND.

Sponsors regularly solicit feedback from the FDA on both scientific and regulatory issues during the life cycle of drug development. The agency notes that, during the IND phase, sponsors often solicit advice at critical junctures in their development programmes. Possible topics for consideration include:

- Regulatory (e.g., plans to defer or waive specific studies).
- Clinical/statistical (e.g., validity of outcomes and endpoints).
- Safety (e.g., safety issues identified in non-clinical studies and early clinical trials).
- Clinical pharmacology and pharmacokinetics (PK) (e.g., dose selection and population).
- Non-clinical pharmacology, PK, and toxicology (e.g., genetic toxicology).
- Product quality (e.g., analytical similarity assessment).
- Paediatrics (e.g., proposed paediatric development plan).

The FDA explains in the December 2017 guidance that it recognises that timely and effective communication during the IND phase of drug development provides sponsors with information they seek to inform the design of studies and trials, as well as product quality information, intended to support approval of a future marketing application. Therefore, agency staff aim to respond to sponsor questions promptly, while balancing FDA public health priorities and other work obligations; responses to safety-related inquiries will be prioritised higher than other inquiries.

**Formal Meetings with the FDA**

For drugs developed under expedited programmes—such as breakthrough therapy and fast track—sponsors receive more intensive guidance on an efficient drug development programme with increased interactions and communications with the FDA, including meetings. At critical junctures, the FDA notes, formal meetings with the sponsor can be particularly helpful in minimising wasteful expenditures of time and resources and thus in speeding the drug development and evaluation process.

Milestone meetings under PDUFA include pre-IND, end-of-phase (EOP1), end-of-phase (EOP2), and pre-new drug application (NDA)/biologics licence application (BLA) meetings. Meetings under the Biosimilar User Fee Act (BsUFA) include Biosimilar Initial Advisory (BIA) meetings and Biosimilar Biological Product Development (BPD) Type 1 through Type 4 meetings.

Sponsors can request meetings with the FDA at any time during drug development, and the FDA strongly encourages sponsors to request the critical milestone meetings, and BIA or BPD meetings. The agency's decision to grant or deny meeting requests is resource-dependent and is based on the maturity of the drug's development at the time of the request, taking into consideration the potential utility of the meeting.

Feedback to sponsors via the formal meeting process is provided in three main formats: face-to-face meetings, teleconferences/videoconferences, and written response only (WRO) responses. The FDA notes that detailed information about meeting requests, packages, scheduling, preparation, conduct, and documentation (meeting minutes) are described in other guidances. The associated timelines are described in the PDUFA and BsUFA agreements.

Effective and timely communication between the agency and sponsors promotes understanding of mutual goals and is invaluable to the drug development process, the FDA states. Central to this is the ability to communicate clearly, both verbally and in writing, inside and outside the formal meeting format. It is also key that the FDA and sponsors have a common understanding of terms and phrasing used in communications with each other, and that they are used consistently by both parties.


The December 2017 guidance, which finalises the draft guidance issued on December 9, 2015, does not apply to communications or inquiries from industry trade organisations, consumer or patient advocacy organisations, other government agencies, or other stakeholders not pursuing a development programme under an IND.

**Investigational New Drug Applications (INDs)**

The regulations concerning INDs are stated in 21 Code of Federal Regulations (CFR) part 312 and cover the requirement for an IND, phases of an investigation, general principles of the IND submission, IND content and format, protocol amendments, information amendments, IND safety reporting, annual reporting, and withdrawal of an IND.

In reviewing an IND, the FDA has two primary objectives: (1) to assure the safety and rights of subjects in all phases of an investigation; and (2) in Phases 2 and 3, to help assure that the quality of the scientific evaluation of the drug is adequate to permit an evaluation of the drug's effectiveness and safety (21 CFR 312.22).

On the whole, the 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 (FD&C Act).
- 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. The two categories of clinical investigations that are exempt from the IND requirements, provided the criteria for exemption are met, are certain research involving marketed drug products [21 CFR 312.2(b)] and bioavailability or bioequivalence (BA/BE) studies in humans using unapproved versions of approved drug products [21 CFR 320.31(b) and (d)].


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