FDA/CDER SBIA CHRONICLES
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B. Upcoming LIVE Webinars

1. Draft Guidance for Industry on Safety Assessment for IND Safety Reporting – Feb. 1st at 1:30 EST
2. New Requirement for Electronic Submission of Drug Master Files (DMFs): What You Need to Know – Feb 4th at 1pm EST
3. Clinical Outcome Assessment Compendium (COA Compendium) – March 14th at 1 pm

Best Communications Practices with FDA

Having prior industry experience, and now working for CDER's SBIA, I have found that sometimes industry representatives are hesitant to contact their FDA Regulatory Project Managers (RPMs) regarding their IND-related questions. Timely review of IND submissions with appropriate feedback to sponsors can result in greater efficiency of the drug development process and more efficient and robust development programs.

To facilitate improved communications, last month, FDA released the draft guidance, *Best Practices for Communication Between IND Sponsors and FDA During Drug Development* that describes why, what, when, and how to conduct interactions between FDA and sponsors efficiently and consistently in a clear, concise, and timely manner. Communication between FDA and sponsors during drug development and at critical junctures in drug development may ultimately facilitate earlier availability of safe and effective drugs to the American public.

The FDA RPM: The review division regulatory project manager (RPM) is the *primary* point of contact for communications between IND sponsors and FDA during the life cycle of drug development, and has comprehensive knowledge of the drug and its regulatory history. The RPM is also the primary contact for facilitating the timely resolution of technical, scientific, and regulatory questions, conflicts, or communication challenges between the sponsor and the review team**.** If sponsors encounter challenges in obtaining timely feedback to inquiries to the review division RPM, they should contact the RPM's next level supervisor for timely resolution of the issue.

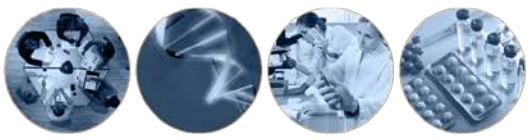
Types of Advice the Sponsor May Seek from FDA: Sponsors often solicit feedback from FDA on both scientific and regulatory issues, especially at critical junctures in their development program. These topics include, but are not limited to the following:

- *Regulatory* (e.g., plans for proprietary name request submission, plans to defer or waive specific studies, development plans for combination products, applicability of an expedited program)

- *Clinical/statistical* (e.g., planned clinical trials to support effectiveness, validity of outcomes and endpoints, trial size, enrichment designs)

- *Safety* (e.g., safety issues identified in nonclinical studies and early clinical trials, size of the overall safety database, concerns related to particular populations, plans for human factors studies, post-approval pharmacovigilance plans, REMS)

- *Clinical pharmacology and pharmacokinetics* (e.g., dose selection, use in specific populations, drug-drug interactions)



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- *Nonclinical pharmacology, pharmacokinetics, and toxicology* (e.g., genetic toxicology, reproductive and developmental toxicology, carcinogenicity, mechanism of action)

- *Product quality* (e.g., proposed shelf life and stability studies, delivery systems, characterization of drug substance/product, facility compliance with good manufacturing practices)

- *Pediatrics* (e.g., proposed pediatric development plan, dosing)

Best Practices and Communication Methods: Central to effective and timely communication between FDA and sponsors is the ability to communicate clearly, both orally and in writing, inside and outside the formal meeting format. Communication via any of the following best practices and communication methods (except meetings where numerous attendees participate) should be conducted via the FDA project manager, typically the review division RPM, rather than FDA reviewers, team leaders, or senior management to ensure that the advice is appropriately vetted and documented.

Complex scientific/technical drug development questions should be directed to the FDA project manager via either a submission or through the formal meeting request process.

Meetings between FDA and Sponsors: Sponsors can request meetings with FDA at any time during drug development to resolve questions and issues. These meetings may also help to minimize wasteful expenditures of time and resources and thus help to speed the drug development and evaluation process. FDA strongly encourages sponsors to request critical milestone meetings such as pre-IND, end-of-phase 1 (EOP1), end-of-phase 2 (EOP2), and pre-NDA/BLA meetings.

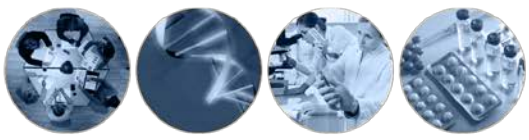
FDA provides feedback to sponsors via the formal meeting process in three main formats: face-to- face meetings, teleconferences, and written response only (WRO). FDA guidances (also refer to the specific guidances for drugs and biosimilars) describe detailed information about meeting requests, packages, scheduling, preparation, conduct, documentation, and timelines for FDA feedback.

Written Correspondence from FDA: FDA project managers will use established letter templates to ensure consistency and accuracy in regulatory communications. Project managers should send a courtesy copy of written FDA correspondence to sponsors when such communications are time-sensitive or communicate actions.

Submissions from Sponsors: FDA regulations describe general principles of, as well as content and format requirements for INDs. Complete and well-organized sponsor submissions can increase the efficiency of FDA review. FDA encourages sponsors to identify issues or areas of concern in their submissions by describing them fully and soliciting feedback on specific areas of concern where further progression in drug development depends largely on receiving FDA feedback. If sponsors omit important information, do not identify the regulatory intent of the submission, or provide insufficient detail, they run the risk of not receiving timely FDA feedback. In addition, sponsors must adhere to required timelines for their submissions.

Some submissions have regulatory-mandated timelines for reviewing and providing feedback to the sponsor that are described by statute or regulation (e.g., some safety-related submissions, complete response to clinical hold) while other submissions have FDA-established goals for review and feedback (e.g., in a MAPP). Timelines for FDA feedback regarding IND submissions are discussed in MAPP 6030.9.

Acknowledging Receipt of Communications: FDA project managers will send written acknowledgment of receipt of certain submissions that have review timelines. They will also strive to acknowledge receipt of questions received from sponsors via telephone calls, emails, and other submissions within 3 business days of receipt by the project manager. The acknowledgment may include the response itself; an estimated response time frame; notification that the question(s) have been consulted to other offices/centers with an undetermined response time frame; a recommendation to submit the questions via a formal meeting request; or redirection to another specialized functional area in FDA.



Sponsors should likewise acknowledge receipt of FDA information requests and provide an estimated response time. Delays in responding, or lack of response, to FDA information requests can negatively affect later development. Sponsors should acknowledge receipt of FDA's information requests, and provide the RPM with an estimated response time.

Email between FDA and Sponsors: Sponsors should establish secure email with FDA to allow for informal communications that may include commercial confidential information. Use of secure email allows transparent and complete communication between FDA and sponsors. However, it is not a substitute for formal submissions (e.g., new INDs and amendments). Formal submissions should be submitted to the respective center's document room (paper submissions) or via the electronic gateway, as applicable.

General Telephone Calls between FDA and Sponsors: General or administrative questions are suitable for informal telephone communications between sponsors and FDA project managers. However, when complex, regulatory, or technical issues are discussed via telephone between the sponsor and the FDA project manager, the caller should follow-up with a written communication to document the discussion and/or respond to information requested during the conversation.

Faxes between FDA and Sponsors: Although it is not a substitute for formal submissions, a fax can be used when secure email has not been established between FDA and sponsors. Before transmitting the fax, sponsors and FDA project managers should contact their respective counterparts to arrange for confirmation of receipt.

Use of Out-of-Office Messages by FDA and Sponsors: IND sponsors and FDA staff should alert others to their unavailability by using email and voicemail out-of-office messages.

Keep in mind that questions that may appear to the sponsor to be simple or clarifying questions are often more complex and necessitate significant review and communication among FDA review team members, including conducting an internal meeting(s), before an answer can be provided.

Because FDA resources are limited, sponsors are strongly encouraged to first seek answers to their questions from the multitude of FDA resources available to them. FDA policy positions are typically documented and described in FDA guidances, MAPPs, and SOPPs. Complex scientific/technical drug development questions should be directed to the FDA project manager via either a submission or through the formal meeting request process. Finally, general questions that cannot be answered by using existing resources can be directed to an FDA project manager, to the designated enhanced communication staff, CDER's Division of Drug Information, or CDER SBIA. Sponsors also can employ an independent consultant for assistance in conceiving strategic drug development and regulatory plans. This allows both sponsors and FDA to conserve their respective resources to address the more complex and challenging drug development issues.

We encourage you to learn more in the draft guidance *Best Practices for Communication Between IND Sponsors and FDA During Drug Development*, and to view our web-based learning course *Engaging with FDA during New Drug Development* for further information.

Cheers,
Renu Lal, Pharm.D.
CDER Small Business and Industry Assistance

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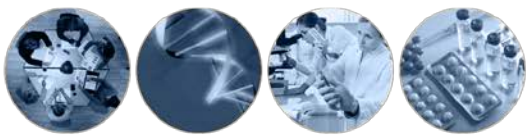

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