

Best Practices for Communication between FDA and IND Sponsors During Drug Development

Rachel Hartford
Enhanced Communication Team
Office of New Drugs, Immediate Office
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Overview

- Background
- FDA's Philosophy Regarding Communication With IND Sponsors
- Scope of Interactions Between the Sponsor and the Review Team
- Types of Advice that are Appropriate for Sponsors to Seek
- General Expectations for Timing of Communications
- Best Practices and Communication Methods
- Resources for Sponsors
- Additional Contacts

Background

Prescription Drug User Fee Act (PDUFA) V: Enhanced Communication

Enhancing Regulatory Science and Expediting Drug Development:

- Establish dedicated communication liaison staff
- *Draft Guidance for review staff and industry describing best practices for communication during drug development, issued December 2015.*
- *Train all CDER staff involved in the review of Investigational New Drugs (INDs)*

Internal Sources of Input

- Joint Working Group:
 - Center for Drug Evaluation and Research (CDER)
 - Center for Biologics Evaluation and Research (CBER)
- Emails received by the Enhanced Communication Team (ECT)
- Feedback from CDER and CBER Leadership Groups
- Existing FDA Guidance, Manual of Policies and Procedures (MAPP), and Standard Operating Procedures and Policies (SOPP) Documents

Internal Sources of Input – Existing Documents

- Guidance Document - Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products
- CDER MAPP - Good Review Practice: Good Review Management Principles and Practices for Effective IND Development and Review, MAPP 6030.9
- 2011 Report ‘FDA Transparency Initiative: Improving Transparency to Regulated Industry’

External Sources of Input

- [Federal Register notice \(Oct 29, 2014\)](#) announcing docket [FDA-2014-N-1575] resulted in [submissions from 8 parties](#) (BIO, AbbVie, Amneal Pharm, Apotex, Bayer, Celgene, LEO Pharma, and Physicians Committee for Responsible Medicine)
- External emails received by ECT

Guidance Publishes!



The Best Practices for Communication Between IND Sponsors and FDA During Drug Development Guidance for Industry and Review Staff published in December 2015.

Guidance Content

- FDA's philosophy regarding timely interactive communication with sponsors as a core activity;
- The scope of appropriate interactions between the review team and the sponsor;
- Types of advice that are appropriate for sponsors to seek from FDA in pursuing their drug development program;
- General expectations for the timing of FDA response to sponsor inquiries;
- Best practices and communication methods to facilitate interactions between the FDA review team and the sponsor during drug development;
- Expectations for appropriate methods, including the frequency of such communications.

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Communication Philosophy



FDA and IND Sponsors have a shared public health goal of early availability of safe, effective, and high-quality drugs to the American public. However, we have different primary responsibilities.

Communication Philosophy

Sponsors' Primary IND Responsibilities

- soliciting input and guidance from FDA
- managing the overall drug development
- determining the nature and timing of regulatory submissions
- providing well-organized and complete submissions for review

Communication Philosophy

FDA's Primary IND Responsibilities

- ensuring the safety and rights of subjects (all phases)
- ensuring the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety (phases 2 and 3)
- enforcing good clinical practice and human subject protection requirements
- reviewing IND submissions
- taking regulatory actions

Communication Philosophy

FDA's Primary IND Responsibilities Cont'd

- providing feedback on specific trials and overall development programs based on review of IND submissions and in meetings.
- promoting the advancement of regulatory science by:
 - authoring FDA and international guidances
 - conducting and participating in public workshops
 - collaborating with academia
 - publishing in medical and trade journals
 - presenting at professional conferences

Communication Philosophy

General FDA Considerations

- timely review of IND submissions with feedback can result in more efficient development
- provide advice on specific matters relating to an IND (e.g. trial design)
- review divisions determine the extent of review and feedback provided
- breakthrough therapy and fast track drug sponsors receive more intensive guidance on efficient drug development with increased interactions and communications, including meetings

Communication Philosophy

General FDA Considerations Cont'd

- may at any time during the course of an IND communicate about deficiencies or our need for more data or information
- the ability to hold meetings is resource-dependent
- strive to meet the recommended review timelines for IND submissions (MAPP 6030.9)
- Ability to provide advice during drug development is balanced with our critical public health responsibilities (drug safety and NDA/BLA review)

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Scope of Interactions

The review division Regulatory Project Manager (RPM) is the *primary* point of contact for communications between IND sponsors and FDA.

Review division RPM:

- co-leader of the FDA review team
- comprehensive knowledge of the drug and its regulatory history
- primary contact for facilitating the timely resolution of technical, scientific, and regulatory questions, conflicts, or communication challenges



Scope of Interactions

Other CDER Project Managers that may be contacted directly:

- Office of Pharmaceutical Quality regulatory business project managers (RBPM)
- Office of Surveillance and Epidemiology safety regulatory project managers (SRPM)
- Formal Dispute Resolution Project Manager (FDRPM)



Scope of Interactions

Reviewers are strongly discouraged from having direct communications with sponsors. It is not considered a best practice.

- inquiries directed to RPMs ensure requests are appropriately communicated to and considered by the review team
- direct contact may:
 - interrupt critical public health work
 - lead to responses that have not been vetted
- informal responses may not accurately or comprehensively capture FDA's thinking

Scope of Interactions

‘Rare Instances of Direct Communication’:

- requires supervisory approval
- requires the FDA review team member document in a memorandum to the IND file
- is decided by FDA management on a case-by-case basis, not the IND sponsor





Scope of Interactions

Independent Consultants ...

- with basic drug development questions should use existing FDA resources available online and/or listed in the Additional Contacts section of the guidance
- seeking advice about a specific drug development program should direct requests to the review division RPM and be authorized by the sponsor

Scope of Interactions



Informal Communication Strategy

Can be established early in the development program, adjusted at any time, and may include:

- preferred method (email or phone)
- frequency
- Proposed approaches for managing information requests and responses (bundled vs one-at-a-time)
- shared contact information for alternative back-ups
- mutual expectations for the timing of responses to inquiries

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Appropriate Advice

FDA routinely receives feedback requests. The breadth and frequency can vary based on experience, drug novelty, and development stage.

As FDA resources are limited, sponsors:

- are strongly encouraged to ***first*** seek answers from the multitude of online resources
- may also choose to employ an independent consultant

Appropriate Advice Cont'd

Sponsors have been advised to keep in mind the following:

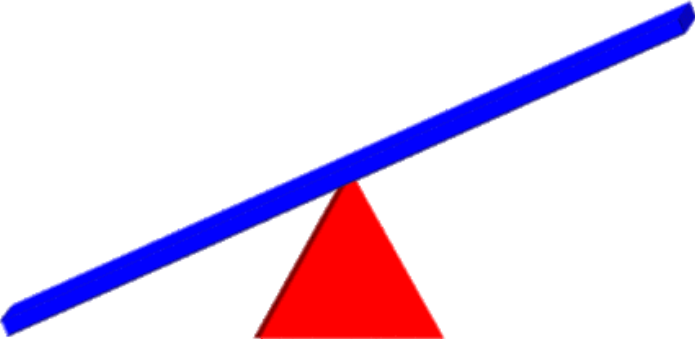
- Guidances, MAPPs, and SOPPs contain policy positions
- General questions may be directed to:
 - Additional Contacts listed in guidance
 - FDA's Enhanced Communication Team
 - CDER's Division of Drug Information
- Questions may be directed to another FDA subject matter expert
- Complex scientific/technical questions should be sent via submission or formal meeting request

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Communication Timing

Overall Considerations

- FDA strives to respond to sponsor questions promptly while balancing FDA public health priorities and other workload responsibilities.
- 
- Responses to safety-related inquiries will be prioritized higher than other inquiries.

Communication Timing

Overall Considerations Cont'd



- A sponsor may perceive a question as simple or clarifying. However, it is often more complex.
- FDA takes a thoughtful and measured approach to answering questions efficiently and comprehensively.
- Complex scientific/technical, policy, or regulatory questions are best posed in a meeting request or in a formal submission.

Communication Timing

Overall Considerations Cont'd



FDA takes a collaborative approach to responding to questions included in meeting packages and in submissions according to their respective pre-specified timelines found in:

- PDUFA Goals Letters
- Good Review Management Principles and Practices for Effective IND Development and Review - MAPP 6030.9
- Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products

Communication Timing



FDA Acknowledgement

For all other sponsor inquiries, received via phone, email, or in a submission **without** a review timeline described in a MAPP, that include specific questions for which sponsors are seeking FDA feedback, FDA project managers will strive to *acknowledge* such communications via phone or email within 3 business days of receipt by the FDA project manager.

Communication Timing

**NEW**

The FDA Acknowledgement Will:

- Include the response itself, if available at the time of the acknowledgement;
- Include an estimated response time frame;
- Indicate that an estimated response time frame will be forthcoming, if a consult with other parties is needed;
- Recommend submitting a formal meeting request if the issues are complex; or
- Recommend contacting another specialized functional area in FDA, if appropriate

The FDA Acknowledgement Will:

1. Include the response, if available at the time of the acknowledgment
2. Include an estimated response time frame
3. Indicate that an estimated response time frame will be forthcoming if a consult with other parties is needed
4. Recommend submitting a formal meeting request if the issues are complex
5. Recommend contacting a specialized functional area, if appropriate
6. All of the Above

Communication Timing

Sponsor Acknowledgement



Similarly, sponsors should:

- Acknowledge receipt of FDA's information requests (written or otherwise)
- Provide the FDA project manager with an estimated response time

It is equally important for sponsors to respond completely and promptly to FDA requests, because delays or lack of response can negatively affect later development.

Communication Timing

When an FDA Response is Delayed

FDA strives to adhere to all established or estimated response timelines.

The FDA project manager will apprise sponsors if they cannot meet the original estimated response time:

- unexpected complex issues arise during review
- the review team experiences an unexpected shift in priorities or staffing

Communication Timing

When an FDA Response is Delayed Cont'd

Sponsors should contact the following sequentially:

- RPM, for a status update after
 - the expected amount of time for FDA response has passed (for established timelines);
- Or*
- the previously communicated estimated response time has passed
- Chief Project Management Staff (CPMS)
- Appropriate Division Management
- Enhanced Communication Team

Communication Timing

Enhanced Communication Team (ECT)

- is a secondary point of communication for sponsors who are encountering problems in communicating with the review team for their IND
- is a point of contact for general questions about the drug development process or for clarification on which review division to contact with questions
- identifies and disseminates best practices for communication
- contact information:
 - Email: ONDEnhancedComm@fda.hhs.gov
 - Phone: 301-796-0319

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Best Practices and Communication Methods

- General Considerations
- Meetings Between FDA and Sponsors
- Meeting Related Best Practices
- Written Correspondence from FDA
- Submissions from Sponsors
- Acknowledging Receipt of Communications
- Email Between FDA and Sponsors
- General Phone Calls Between FDA and Sponsors
- Faxes Between FDA and Sponsors
- Use of Out-of-Office Messages for FDA and Sponsors



General Considerations

Both FDA and sponsor should have a common understanding of terms and phrasing used in communication.

- use words such as *shall*, *must*, *required*, or *requirement* to convey a statutory or regulatory requirement.
- use the following words to communicate advice (e.g., on trial design), comments, or current thinking often include the following terminology: *advisable*, *critical*, *important*, *may be appropriate*, *should*, *consider*, *discourage*, *encourage*, *prefer*, *recommend*, *suggest*, or *urge*.

These terms should be used consistently by both parties.

Question:

DRG-D2S6-1

View Votes

Edit

End Poll

Which of the following convey a statutory or regulatory requirement?

<input type="radio"/> 1. Should, suggest, prefer	<div></div>	0%	(0)
<input type="radio"/> 2. Shall, must, required	<div></div>	0%	(0)
<input checked="" type="radio"/> No Vote			

☐ Broadcast Results

General Considerations Cont'd

Because there are different business cultures, communication styles, preferences, and documentation needs, there is no single best communication method. Rather, there are best practices that enhance each method.

Meetings - FDA and Sponsors

Meetings are useful in:

- resolving questions and issues raised during development.
- providing valuable scientific and regulatory advice, resulting in more efficient and robust development programs.
- helping sponsors define adequate evidence of effectiveness, safety, and product quality.
- ascertaining FDA's views on the applicable statutory and evidentiary requirements.

Meetings - FDA and Sponsors Cont'd

Meetings between FDA and a sponsor at critical junctures in drug development can be especially helpful in minimizing wasteful expenditures of time and resources, thus speeding the drug development and evaluation process.

These milestone meetings include:

- pre-IND
- end-of-phase 1 (EOP1)
- end-of-phase 2 (EOP2)
- and pre-NDA/BLA meetings



Meeting Best Practices

Sponsors should:

- review information available online before requesting a meeting
- request milestone meetings
- combine drug development issues into the fewest possible meetings
- not ask questions during the meeting that were not included in the meeting package
- not present new data or information during the meeting
- limit questions to what can be reasonably discussed within the duration of allotted meeting time

Meeting Best Practices Cont'd

- The number of questions posed in a Written Responses Only (WRO) request should be no more than what would be *reasonably* expected to be addressed in a meeting.
- Pre-IND and pre-NDA/BLA meetings should include a discussion of what constitutes a complete application.



Written Correspondence from FDA

FDA project managers:

- will use letter templates to ensure consistency and accuracy in regulatory communications
- should send a courtesy copy of communications that are time-sensitive or communicate actions (clinical hold)
 - via secure email or fax (if secure email has not been established)

Submissions From Sponsors

All IND submissions should include an overall summary.

The summary usually comprises the first page of the submission and should:

- explain the regulatory and developmental context
- list the objectives of the submission
- include any questions for FDA response

FDA Acknowledgement of Sponsor Questions



NEW



NEW

Sponsor inquiries should be ***acknowledged*** within 3 business days of receipt by the project manager



NEW

Email - FDA and Sponsors

Secure email:

- is not a substitute for formal submissions
- allows for informal communication that may include commercial confidential information
- may be established by contacting SecureEmail@fda.hhs.gov
- can be confirmed by using address validation tool

FDA communication via **unsecure** email cannot include commercial confidential information (e.g., trade secrets, manufacturing, or patient information).

Question:

DRG-D2S6-2

View Votes

Edit

End Poll

FDA communication via unsecure email cannot include:

<input type="radio"/> 1. Patient information	<div></div>	0%	(0)
<input type="radio"/> 2. Trade secrets	<div></div>	0%	(0)
<input type="radio"/> 3. Manufacturing information	<div></div>	0%	(0)
<input type="radio"/> 4. All of the above	<div></div>	0%	(0)
<input checked="" type="radio"/> No Vote			

☐ Broadcast Results

General Calls - FDA and Sponsors

Phone Calls:

- are not a substitute for formal submissions
- are suitable for general or administrative questions
- if complex, regulatory, or technical issues arise, the **caller** should follow-up with a written communication (e.g., email, sponsor submission, FDA correspondence) to document the discussion and/or respond to information requested during the conversation

General Calls – FDA and Sponsors Cont'd

- provide back-up contact information, names and telephone numbers for communicating time-sensitive issues (e.g., notification of clinical hold).
- include back-up contact information in out-of-office messages, whenever appropriate.

Faxes - FDA and Sponsors

Faxing:

- is not a substitute for formal submissions
- can be used when secure email has not been established
- before sending, arrange for confirmation of receipt
- include a coversheet

Out-of-Office Messages - FDA and Sponsors

- use email and voicemail out-of-office messages
- include an expected return time
- contact information for other staff that are covering, particularly for time-sensitive communications (e.g., notification of clinical hold).
- FDA project managers should also include contact information for their division's Chief Project Management Staff.

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Resources

FDA develops and maintains Web pages, portals, and databases, and participates in interactive media as a means of providing self-service tools for its stakeholders, including IND sponsors.

Sponsor use of these tools allows for more effective utilization of limited FDA resources in providing advice on scientific and regulatory issues that fall outside of established guidance, policy, and procedures.

Resources

- FDA Guidances
- FDA Policy and Procedures (MAPPs)
- FDA Basics for Industry
- FDA Interactive Media (Facebook, Pinterest, Twitter, Flickr, Blogs, Podcasts, etc.)
- FDA Presentations
- FDA Labeling and Approvals (Drugs@FDA)
- FDA Rules and Regulations
- Code of Federal Regulations



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Additional FDA Contacts

Sponsors may use certain FDA points of contact for responses to basic or procedural drug development questions ***not*** directly linked to an existing or planned development program.

Contacts are in specific functional areas and serve as an alternative means to obtain general information or address issues that arise in the context of the regulatory process.

CDER Additional Contacts

- Controlled Substance Staff
- Division of Drug Information - druginfo@fda.hhs.gov
- Division of Pediatric and Maternal Health
 - Pediatric: pedsdrugs@fda.hhs.gov
 - Maternal Health: cdelerpmhs@fda.hhs.gov
- Enhanced Communication Team - ONDEnhancedComm@fda.hhs.gov
- Import/Export
 - General Imports Compliance CDERImportsExports@fda.hhs.gov
 - Export Certificate and Compliance CDERExportCertificateProgram@fda.hhs.gov
- Ombudsman - CDERombudsman@fda.hhs.gov
- Rare Diseases Program
- Small Business & Industry Assistance Program - CDERSBIA@fda.hhs.gov

Additional Contacts Cont'd

Office of Special Medical Programs

- Advisory Committee Oversight and Management Staff
- Office of Combination Products - combination@fda.gov
- Office of Good Clinical Practice - gcp.questions@fda.hhs.gov
- Office of Orphan Products Development - orphan@fda.hhs.gov
- Office of Pediatric Therapeutics - OPT@fda.hhs.gov

CBER

- Manufacturers Assistance and Technical Training Branch - industry.biologics@fda.hhs.gov
- Ombudsman - cberombudsman@fda.hhs.gov

Additional Contacts

- When sponsors contact one of these resources via email, they should copy the review division RPM when the questions and subsequent responses may have bearing on review division activities.
- When an FDA resource is responding directly to a sponsor via email, copy the review division RPM and/or respective FDA project manager, when known and when appropriate.

Questions?

Please complete the session survey:

surveymonkey.com/r/DRG-D2S6

