REVIEW ON SPONSOR / APPLICANT MEETINGS WITH FDA: HIGHLIGHTS OF NEW GUIDANCE OVER EXISTING

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REVIEW ARTICLE

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ABSTRACT

The United States Department of Health and Human Services has a federal agency called the Food and Drug Administration (FDA or USFDA). A pre-planned assembling of two or more people who have been together for the purpose of getting a common goal via verbal interaction is called a formal meeting. During development stage of any drug or biological products pharmaceutical companies face trouble for both scientific and regulatory point of view, here role of formal meetings comes. Formal meetings between sponsor or applicant and FDA are usually related to development and review of drug and biological products. Center for Drug evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) regulates the formal meetings. These meetings are applicable to Pre – Investigational New Drug Application, Pre – Biologics License Application, New Drug Application for drugs and biological products and not applicable to Abbreviated New Drug Applications (ANDA), application of medical devices and submission of biosimilar biological products. Meetings between FDA and sponsor or applicant are for resolution of dispute, clinical holds discussion, Assessment of protocols of clinical trial, during clinical trials, in between clinical trials – at the phase 1 ending or at the phase 2 ending, to discuss development program. The FDA has classified these formal meetings in different types based on the nature of the request, the information in the meeting request and each meeting type is handled through different procedures. The principles of Good Meeting Management Practices (GMMPs) must be maintained. There are specific requirements and procedures to request, prepare, schedule, conduct and document formal meetings. As the guidance documents for meetings are revised by FDA, Change in procedure and requirements takes place. Any pharmaceutical company need to be in line with new guidance requirements to avoid rejection. Formal meetings between sponsor or applicant and FDA save time, cost and will increase the probability of product approval.

Keywords: FDA, FDA Meeting, Biosimilar Meeting , PDUFA, CDER, CBER, Type A Meeting, Type B Meeting, Type C Meeting, Meeting Request, Meeting Package, FDA Guidance.

INTRODUCTION

Formal meetings between sponsors or applicants and the Food and Drug Administration (FDA) are very important to consider. During drug development timely and enhanced interactive communication of applicant with FDA promotes innovation. To facilitate drug development programs efficiently and effectively is the ultimate goal of the meetings. Center for Drug evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) regulates formal meetings. Any meeting which is requested by a sponsor or applicant is a formal meeting which can be coordinated in any format are considered as formal meeting. These formal meetings can be teleconference, videoconference or face to face. (1–3)

TYPES OF MEETINGS

The meetings that occur between FDA staff and sponsors or applicants are of three types and each meeting type is subject to different procedures:

1) Type A
2) Type B
3) Type C

1) Type A Meeting: Type A meeting is a meeting which is necessary for an otherwise stalled product development program to proceed. Examples include dispute resolution meetings, certain meetings to discuss clinical holds, certain special protocol assessment (SPA) meetings, and a post-action meeting requested within three months after an FDA

regulatory action other than approval (i.e. issuance of a complete response letter). (2)

2) **Type B Meeting:** Type B meetings include the following meetings: pre-IND, pre-emergency use authorization, certain EOP1, EOP2 and pre-phase 3, pre-NDA/BLA, and post-action meetings requested three months or more after an FDA regulatory action other than an approval. Type B meetings also include meetings regarding risk evaluation and mitigation strategies or post-marketing requirements that occur outside the context of the review of a marketing application, and meetings to discuss the overall development program for products granted Breakthrough Therapy designation status. (2)

3) **Type C Meeting:** A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product. (2)

Comparison of Meetings

General comparison between Type A Meeting, Type B Meeting and Type C Meeting is given in Table 1.

Table 1: Comparison of Type A Meeting, Type B Meeting and Type C Meeting

Parameter	Type A Meeting	Type B Meeting	Type C Meeting
Meeting Description	• Dispute Resolution • Clinical holds • Special Protocol Assessment (SPA) • Post-action meetings	• Pre-IND • EOP-1 • EOP-2 • Pre-NDA/ Pre-BLA • Pre-emergency • Post-action meetings • REMS or postmarketing requirements • Breakthrough therapy development	Any meeting other than a Type A or Type B meeting
Conformation of scheduling following sponsor request (from time of request)	14 days	21 days	21 days
Time window for meeting to occur (from time of request)	30 days	60 days	75 days
Meeting Package submission due date	Concurrent with the meeting request	At least 1 month before the formal meeting	At least 1 month before the formal meeting

COMMUNICATION WITH FDA

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. (4)

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.

MEETING REQUEST

Usually along with the sponsor or applicant application (BLA, IND or NDA) the meeting request must be submitted through the controlled

document system. If sponsor application is not required to submit then the request must be submitted through fax or e-mail. The sponsor or applicant must contact the review division to prevent the possibility of overlooking of faxed or e-mailed requests because the FDA staff receives the volume of e mails. The faxed or e-mailed requests must be sent on Monday through Friday (except Federal government holidays) during official business hours (8:00 a.m. to 4:30 p.m. EST/EDT). (1)

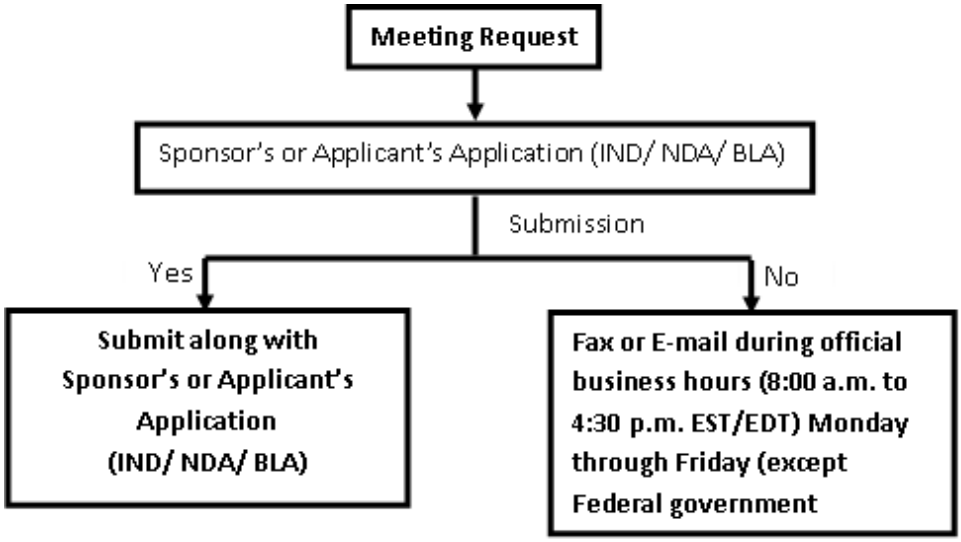

Figure 1: Submission of Meeting Request to FDA

THE FDA RPM (4)

The review division Regulatory Project Manager (RPM) is the primary point of contact for communications between 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. (3)

ASSESSING MEETING REQUESTS

The meeting requests received by the CBER or CDER division director or designee will determine to hold the meeting or not and will respond by granting or denying the meeting to the sponsor or applicant within PDUFA timelines. (1)

MEETING PACKAGE

After grant of meeting sponsor or applicant need to submit meeting package. The meeting package should contain information required for the discussion and should facilitate the FDA to understand sponsor or applicant's confusions, questions, doubts. On time submission of meeting package is very important to ensure that FDA has sufficient time for meeting preparation, for comprehensive study of the meeting agenda, and to accommodate pre-meeting communications. (1)

Meeting Package Submission

The meeting package submission time frames are given in Table 2:

Table 2: Meeting Package submission time frame

Type of Meeting	Meeting Package submission Time frame
Type A	Concurrent with the meeting request
Type B	At least 1 month before the formal meeting
Type C	At least 1 month before the formal meeting

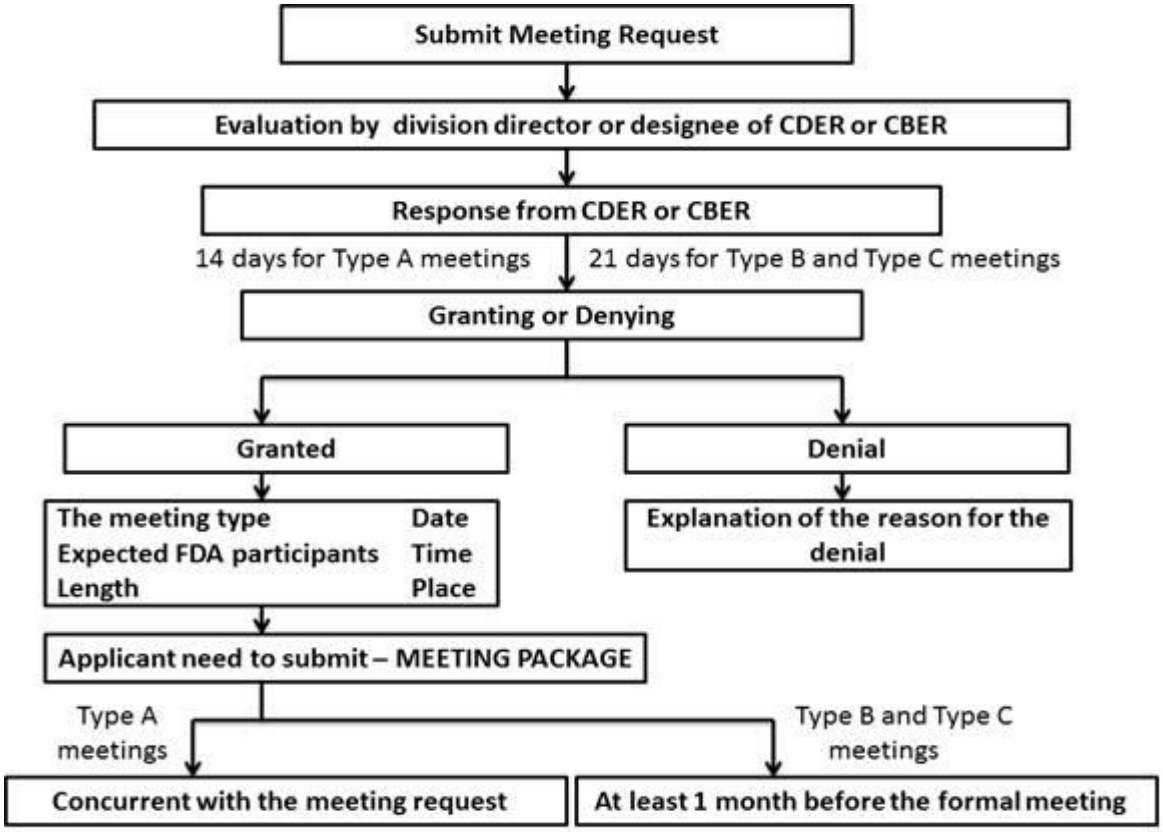

Figure 2: Assessing Meeting Request

Meeting Package Content

The meeting package contains the summary of the information related to the product and other supplementary information required to solve issues raised by the sponsor or applicant. The content of meeting package varies based on the indication, phase of product development, product and issues required to be discussed. General content of Meeting package is as follow:

- Product name and application number (if applicable).
- Chemical name and structure.
- Proposed indication.
- Dosage form, route of administration, and dosing regimen (frequency and duration).
- A list of all individuals, with their titles and affiliations, who will attend the requested meeting from the requester's organization, including consultants and interpreters.
- A background section that includes the following:
  - A brief history of the development program and the events leading up to the meeting.
  - The status of product development (e.g., chemistry, manufacturing, and controls; nonclinical; and clinical, including any development outside the United States, as applicable).
- A brief statement summarizing the purpose of the meeting.
- A proposed agenda, including estimated times needed for discussion of each agenda item.
- A list of the final questions for discussion grouped by discipline and with a brief summary for each question to explain the need or context for the question.
- Data to support discussion organized by discipline and question. Full study and trial reports or detailed data generally are not appropriate for meeting packages; the summarized material should describe the results of relevant studies and clinical trials

with some degree of quantification, and any decision about clinical trials that resulted.

THE CONDUCT OF FORMAL MEETING (1)

An FDA staff member will chair the meeting and it starts with introduction and the agenda. To maximize the time for the discussion, all presentations are required to keep brief because the meeting will not be longer to accommodate a presentation. FDA attendees and the requester attendees give summary of the important points, any agreements, any clarifications, and actions required to be done by sponsor or applicant at the end of the meeting. The summary is presented by sponsor or applicant to ensure the mutual understanding of meeting outcomes and actions required to be done by sponsor or applicant. The summary can be given after the discussion of each question or at the end of the meeting.

MEETINGS DOCUMENTATION

Meeting documentation agreements, disagreements, outcomes and action required to be done by sponsor or applicant is critical for assurance of the preservation of information for meeting attendees and for any future references. The official records of the meeting are FDA minutes. All the sponsor or applicant and FDA attendees get the official finalized FDA minutes within 30 days of the conduct of the meeting. (1)

FDA GUIDANCE DOCUMENT

As the guidelines changes same way change in guidance document is done by FDA periodically. It is the duty of the regulatory professional (sponsor or applicant) to know it and get thorough knowledge of what changes are done to existing guidance document and get updated to the new regulatory requirement. Sponsor or applicant needs to work as per new requirements. The significant change in guidance document "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products, March 2015" compared to FDA's exsting guidance document "Guidance for Industry Formal Meetings Between the FDA and Sponsors or Applicants, May 2009" is given in Table 3. (1,3,5)

Table 3: Comparison of FDA's 2009 (Existing) and 2015 (New) guidance documents of Formal meetings between FDA and sponsor or applicant

MEETING TYPE	EXISTING GUIDANCE (2009)	NEW GUIDANCE (2015)
Type A Meeting designation	**Existing:** Meetings that are necessary for an otherwise stalled development program to proceed or to address an important safety issue, including: • Dispute resolution meetings • Meetings to discuss clinical holds • Special protocol assessment meetings	**Added:** • **Post-action meetings requested within 3 months** after an FDA regulatory action other than an approval (i.e., issuance of a complete response letter).
Type B Meeting designation	**Existing:** • Pre-IND meetings • Certain end-of-phase 1 meetings for subpart E or subpart H or similar products • End-of-phase 2/pre-phase 3 meetings • Pre-NDA/pre-BLA meetings	**Added:** • **Pre-emergency** use **authorization meetings.** • **Post-action meetings** requested 3 months after an FDA regulatory action other than approval. • **Risk evaluation and mitigation strategies (REMS) or post-marketing requirements** meetings that occur outside the context of the review of a marketing application. • **Breakthrough therapy develop-**

			ment meetings (meetings to discuss overall development programs for breakthrough therapy-designated products).
Type C Meeting Designation		Existing: Any meeting other than a Type A or Type B meeting regarding the development and review of a product	N/A
Meeting Timing (Days after FDA's receipt of request)	**Type A**	30 days	30 days
	Type B	60 days	60 days
	Type C	75 days	75 days
		If a sponsor or applicant requests a meeting date that is beyond timeline	
		CDER or CBER will work with the sponsor or applicant to determine the earliest agreeable date.	Meeting date should be within 14 calendar days of the requested date.
Meeting package due date	**Type A**	At least 2 weeks before the formal meeting.	Concurrent with the meeting request
	Type B	At least 4 weeks before the formal meeting.	At least 1 month before the formal meeting
	Type C	At least 4 weeks before the formal meeting.	At least 1 month before the formal meeting
Response to Pre-IND Questions		Only face-to-face meetings, videoconferences, or teleconferences	Sponsors can now request written responses for pre-investigational new drug application and Type C meetings
These Meeting types not applicable to		**Existing:** • Abbreviated New Drug Application (ANDA)	**Added:** • Applications for biosimilar biological products • Submissions for medical devices

BIOSIMILAR MEETINGS (6)

These are the formal meetings between biosimilar biological product sponsors or applicants and the Food and Drug Administration (FDA). These meetings are applicable to biosimilar biological products sponsor or applicant who intended to submit application under 351(k) of the Public Health Service Act (PHS Act). These meetings are not applicable to abbreviated new drug applications (ANDA) or new drug applications (NDA) under section 505 of the FD & C Act or to biologics license applications (BLAs) under section 351(a) of the PHS Act. Types of biosimilar meetings with FDA and it's similarity with definite type of PDUFA meeting with FDA is given in Table 4.

Table 4: Types of meeting between biosimilar biological product sponsor or applicant and FDA

Meeting Type	Purpose	Timeline for meeting* (Days from receipt of request by the FDA)	Similar Type PDUFA meeting
Biosimilar Initial Advisory meeting	Feasibility of development as a biosimilar under Section 351(k)	90 days	Type B Pre- IND Meeting
BPD Type 1 meeting	Stalled program: Clinical holds Special protocol assessment Safety issue	30 days	Type A Meeting

	meriting discussion Dispute resolution meetings		
BPD Type 2 meeting	Issue in ongoing program meriting discussion	75 days	Type C Meeting
BPD Type 3 meeting	Evaluation of bio-similarity, need for additional study, study design/analysis	120 days	Type C Meeting
BPD Type 4 meeting	Discuss format and content of biosimilar BLA	60 days	Type B Pre-BLA Meeting
*If Sponsor or applicant requests a meeting date beyond timeline, the FDA will work with the sponsor or applicant to determine the earliest agreeable date.			

ANNUALLY MEETINGS WITH FDA

As per Federal Register, on the bases of the current expectations of workload and development, estimation done by FDA that approximately 15 sponsors and applicants (respondents) may request approximately a total of 30 formal meetings, and submit approximately 30 information packages, with CDER annually, and approximately 1 respondent may request approximately 2 formal meetings, and submit approximately 2 information packages, with CBER annually. (7)

CONCLUSION

Formal meetings provide an important forum for sponsor or applicant to present information, and for FDA to provide specific and targeted advice. FDA promotes innovation through intense and well-timed interactive communication with sponsors during drug development. The ultimate goal of FDA is to smooth the conduct of development programs efficiently and effectively. Formal meetings are classified in different types by FDA and it is very important to request right meeting at right time for the questions sponsor's or applicant's have in the development phase. Formal Meetings are done earlier in development phase and later meetings shows high impact on success at best. These meetings can be particularly helpful for orphan drug products, new chemical entities, drugs having novel indications and biologics, where the Regulatory pathway is not plotted and/or aspects of the clinical trials are uncertain. Success of these meetings depends on particularity of sponsor's meeting agenda, objective and ability in asking questions regarding the format and content of their upcoming IND/BLA/NDA submission. Preparation for the meeting is very crucial for sponsors and applicants. A formal meeting facilitates the understanding of product development and regulatory related doubts to the sponsor or applicant. Ultimately and wise versa FDA can get benefits from these type of productive meetings as well. FDA gets better knowledge of the data submitted by sponsor or applicant and can have collaborative expectations with the sponsor or applicant and among the review team. These meetings discussions also enhance predictability, communications and transparency between applicant or sponsor and FDA.

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CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest.

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