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Expansion of Meetings with the US FDA

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Sponsors of investigational medicinal products (IMP) are encouraged to seek guidance from the FDA throughout the course of development in order to maximise the likelihood of regulatory approval.

The FDA offers opportunities for Sponsors to request guidance on a development program free of charge and irrespective of the stage of development.

To ensure Sponsors receive valuable feedback from FDA, it is critical to request the correct type of meeting from the correct division. This should be carefully considered against the type of IMP, phase of development and scope of questions for which the Sponsor is seeking advice.

Evolution of Meetings Offered by FDA

The FDA has traditionally offered Type A, Type B and Type C meetings to Sponsors of an IMP seeking general guidance on a development program (**Table 1**).

Table 1 - Scope of Type A, B and C Meetings with FDA

Meeting	Scope	Example(s) of Topics
Type A	To discuss a stalled development program or important safety issue.	• Dispute resolution meeting • A trial is on clinical hold
Type B	To discuss a development program prior to a critical regulatory submission (pre-approval) or post approval; to discuss the development of products which have been granted BTD or RMAT.	• Pre-IND meeting • Pre-NDA or pre-BLA meeting • Pre-emergency use authorization meeting • Post-marketing requirement meetings • Product has been granted BTD or RMAT
Type B (EOP)	To discuss a development program in transition to the next phase of clinical development.	• End-of-phase 1 meetings for products with "accelerated development", "accelerated drug approval" or "accelerated biologic approval" status • End-of-phase 2 meetings
Type C	To discuss topics which are not outlined in the scope of another meeting under PDUFA guidance.	• CMC changes on manufacturing process • Nonclinical questions regarding completed testing • Clinical trial design issues or potential protocol changes • Questions on NDA planning prior to EOP milestone

Abbreviations: BTD = breakthrough designation; CMC = chemistry, controls and manufacturing; EOP = end-of-phase; IND = investigational new drug; NDA = new drug application; PDUFA = Prescription Drug User Fee Act; pre-BLA = pre-biologics license application; pre-IND = pre-investigational new drug; pre-NDA = pre-new drug application; RMAT = regenerative medicinal advanced therapy.

In June 2018, the FDA launched a new meeting track known as Initial Targeted Engagement for Regulatory Advice on CBER Products (INTERACT), targeting Sponsors of novel early-stage biologics presenting unique challenges in early development and not yet ready for a pre-IND meeting. The scope of this meeting was extended to include products regulated by CDER in September 2022, with the aim of enhancing support for Sponsors of innovative drugs (**Table 2**). At the same time, the FDA announced the introduction of Type D meetings for Sponsors seeking guidance on a narrow set of development issues requiring a shorter response turnaround.

Table 2 - Scope of Type D and INTERACT Meetings with FDA

Meeting	Scope	Example(s) of Topics
Type D	To discuss a narrow set of issues critical to development where timely feedback is required.	• Clarification or follow-up issue to another meeting • A short query on an innovative development approach
INTERACT	To discuss a novel development program that poses unique challenges early in development, prior to a pre IND meeting.	• Recommendations on a FIH trial • Unusual CMC issues Note: Not to be confused with Type B pre-IND meeting

Abbreviations: CMC = chemistry, manufacturing and controls; FIH = first in human; INTERACT = Initial Targeted Engagement for Regulatory Advice on CDER/CBER products; pre-IND = pre-investigational new drug.

This paper will discuss the expansion of PDUFA meetings implemented by the FDA User Fee Reauthorisation Act of 2022 (PDUFA VII, 2023 – 2027) and provide a reflection on the relevance of Type D meetings and the expansion of INTERACT meetings based on Scendea's collective experience since their implementation.

Introduction to Type-D Meetings

SCOPE

The FDA introduced Type D meetings for Sponsors of an IMP who require timely feedback on a narrow set of issues which are deemed critical to development. This is limited to a maximum of 2 focused topics and involvement of no more than three disciplines.

Examples of Type D meetings could include, but are not limited to:

- A follow-up question from another formal meeting that has brought up a new issue or clarification on a written response only (WRO) or on meeting minutes.
- A specific issue on which the Sponsor is seeking Agency input on, with only 3-5 associated questions in total.
- A general question about an innovative development approach that does not require extensive advice.

TIMING

Upon submission of the meeting request and briefing package, which are to be submitted together, the Sponsor should expect a response from FDA within 14 calendar days from receipt of the request, detailing whether a meeting has been granted or rejected, or whether written responses will be issued.

The FDA will arrange the meeting or written responses within 50 calendar days from receipt of the request, approximately 25 days quicker than a Type C meeting.

BENEFITS

In theory, the Type D meeting function offers benefits over other meeting types:

- Enables timely feedback on a question that does not require extensive review, requiring less time to compile meeting materials and submit the request.

- Prevents and/or minimizes delays in development for Sponsors with critical and time-sensitive queries.
- Facilitates specific feedback on a narrow issue or topic, generating streamlined FDA responses.
- Enables easier request for FDA clarification following formal feedback and allows iterative confirmation in writing from FDA.

CONSIDERATIONS

Since its implementation, Scendea has supported clients in successfully navigating Type D interactions with the FDA. In order to ensure a Type D meeting is the most appropriate avenue, the Sponsor should carefully consider the following:

- Is the nature of the query within scope of a Type D meeting? If the Sponsor is seeking advice on a variety of topics, this is not the best way forward. If too many questions are posed or multi disciplinary feedback is requested, the FDA will likely suggest a Type B or C meeting and a longer response timeframe should be expected.

- Would a video teleconference be preferable to a written response? In Scendea's experience, Type D meetings most often result in written responses only (WRO), although video teleconferences are possible. If the Sponsor is eager to initiate a verbal dialogue with FDA, the Type D meeting may not be the most suitable option.

- When does the Sponsor intend to submit the request? It is important to be aware that the meeting request and briefing document must be submitted in parallel. Sponsors should ensure that the briefing document is prepared in advance of submitting the request if the intention is to submit as soon as possible.

- Is this a standalone query that could be resolved with a request for clarification email? Although the Type D meeting can be a useful tool to address a new issue that has arisen from FDA feedback from a prior meeting, it does not replace the option of requesting clarification from the Agency if a single follow-up query arises from previous feedback.

- The shorter timeline associated with the Type D meeting does not preclude the potential for preliminary FDA responses. FDA preliminary responses could be issued up to 5 days prior to a scheduled Type D meeting. If applicable, the Sponsor may be asked to respond no later than 3 days from receipt of the preliminary responses.

Expansion of INTERACT Meetings to include CDER

SCOPE

INTERACT meetings are intended for novel development programs that could present unique challenges early in development, prior to a pre-IND meeting. Sponsors of innovative drugs can now request an INTERACT meeting with CDER early in development, in addition to developers of biologics under review by CBER.

The INTERACT meeting is intended to support the Sponsor in overcoming novel challenges that may have a rate-limiting impact on IND submission but does not replace the purpose of a pre-IND meeting. Examples of INTERACT meeting topics with CDER could include, but are not limited to:

- Questions on a novel drug platform or candidate for which there is no existing guidance or other information to reference from FDA.
- Issues that a Sponsor must address prior to a pre-IND meeting for novel drug platforms or candidates.
- Queries on the development of innovative devices in combination with a drug.
- Discussion of New Approach Methodologies.

TIMING

The process for requesting an INTERACT meeting with CDER is identical to the process for biologics regulated by CBER, and follows the same timelines and principles. Similarly to the Type D meeting, an INTERACT meeting request should be submitted together with the briefing document. Following submission, the Sponsor can expect a response from FDA within 21 days acknowledging whether a meeting has been granted and if a video teleconference or WRO is expected. If a meeting is granted, it should be scheduled by FDA within 75 days from receipt of the request.

BENEFITS

The expansion of INTERACT meetings to include products regulated by CDER was intended to benefit Sponsors of innovative drugs who are early in their development, offering several advantages:

- Initiates early dialogue with CDER and allows the relevant division to familiarize with the development program at an early stage of development.
- An additional opportunity to engage with CDER, free of charge, before a Sponsor is ready to approach the FDA on pre-IND questions.
- Enhanced access for Sponsors developing novel, challenging or innovative drugs to encourage the development of more innovative approaches, no longer restricted to CBER.

CONSIDERATIONS

Since the scope of INTERACT was expanded, Scendea has supported clients in managing INTERACT meetings with CDER. Sponsors of novel or innovative drugs should consider several factors prior to requesting this type of meeting:

- Which stage of development is the product in? If an INTERACT meeting is requested too late in development, the FDA are likely to reject the request or propose an alternative type of meeting. Likewise, it is possible for FDA to reject an INTERACT meeting if requested prematurely; a specific investigational product should have been identified for evaluation in a clinical study.

- What is the scope of the questions that the Sponsor wishes to put forward? Posing questions that are most suited to a Type B pre-IND meeting is one of the most common reasons for rejection of an INTERACT meeting.

- When does the Sponsor intend to submit the request? Similarly to Type A and Type D meetings, the meeting request and briefing document must be submitted concurrently. Sponsors should ensure that both documents are prepared in parallel to prepare for timely submission.

- The FDA may issue preliminary responses up to 5 days prior to a scheduled INTERACT meeting. In this scenario, the Sponsor should be prepared to respond within 3 days from receipt of the preliminary responses. If a meeting is still deemed necessary, the Sponsor is expected to send a revised meeting agenda indicating which questions are considered resolved and which questions require further discussion.

Summary

Sponsors of IMPs should initiate early discussions amongst team members to plan for appropriate interactions with FDA throughout the product lifecycle. It is paramount that the Sponsor selects the most appropriate meeting type in order to obtain the most valuable feedback and optimize product development.

The introduction of Type D meetings and INTERACT meetings with CDER now offers additional avenues to engage with FDA. Whilst the shorter timeframe associated with the Type D meeting response can be an advantage for time-sensitive queries, the timing remains relatively close to other meeting types when considering the length of a full development program. Similarly, the expansion of INTERACT meetings to include products regulated by CDER enhances opportunities for early engagement with FDA, however it is crucial that the product is at an appropriate stage of development prior to IND submission.

The Sponsor should carefully consider the scope of questions being posed and which meeting type would be the most suitable option. Verbal interactions with FDA are encouraged to improve familiarity and better understand the FDA's attitude towards a development program, so it is always beneficial to consider the need for direct interactions. Once a meeting type has been selected, questions can be positioned strategically depending on the needs and objectives of the request. Thorough preparation will promote timely, transparent and pertinent feedback to maximise development and strengthen the likelihood of regulatory approval.

References:

Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products - U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), September 2023

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