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Acquiring a Compound with Multiple Clinical Trials? Let's get ready for a Type C meeting! Key Considerations for Preparing Its Regulatory Submission.

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ABSTRACT

Pharmaceutical companies are constantly researching and developing drugs and medicines. In the US, the Food and Drug Administration (FDA) is the ultimate agency that approves the drugs, vaccines, devices and other therapies, to ensure that the new drugs are both safe and effective for their intended uses. Sponsors interact with the FDA requesting specific meetings to discuss their regulatory questions related to their drug development programs. It is very common that pharmaceutical companies acquire drug development programs that are in various stages with multiple clinical trials, for several strategic reasons. Therefore, sponsors will have a broad range of questions while they streamline these newly added compounds towards their regulatory submissions. Type C meetings provide an appropriate forum to seek FDA input on a variety of topics in drug development. In this paper, we provide a comprehensive account covering all essential processes involved in generating various components of Type C meetings.

Introduction

The drug development process is a 5-stage journey from lab to market, starting with Discovery & Development (finding targets), moving to Preclinical Research (lab/animal testing for safety), then Clinical Trials (testing in humans in three phases: safety, effectiveness, comparison), followed by FDA Review (filing for approval, rigorous data examination), and finally, Post-Market Monitoring (ongoing safety surveillance after approval) to ensure new medicines are safe and effective for public use, a process often taking over a decade and costing billions (Fig 1).

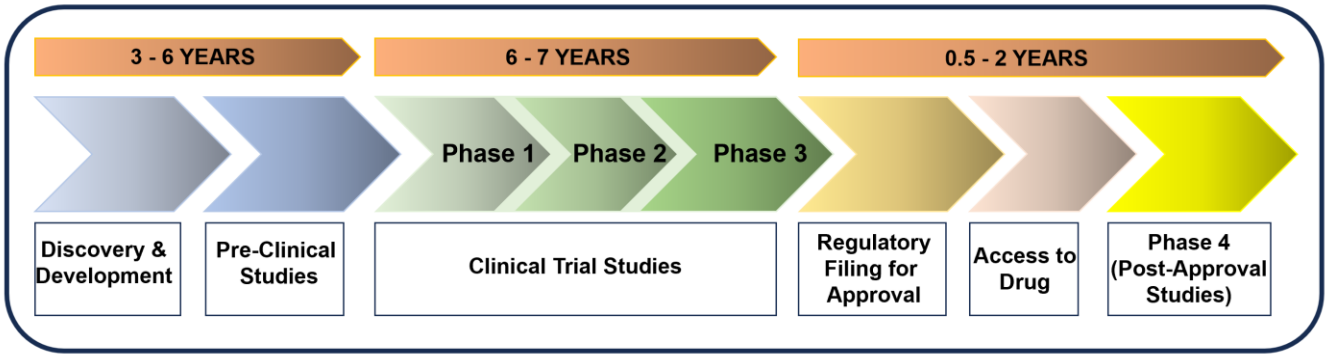
In the US, the Food and Drug Administration (FDA) is the ultimate agency that approves the drugs and medications, to ensure that the new drugs are both safe and effective for their intended uses before they can be marketed to the public. The sponsors have a wide variety of regulatory questions related to the drug development programs and interact with the FDA requesting specific meetings to discuss their regulatory questions. There are six types of meetings available for these interactions as follows: Type A, Type B Pre-IND, Type B EOP (End-of-Phase), Type C, Type D and INTERACT (**IN**itial **T**argeted **E**ngagement for **R**egulatory **A**dvice on **C**BER/CDER Produc**T**s) Meetings. This paper focuses on Type C meetings. It has become very common to witness that pharmaceutical companies acquire drug development programs that are in various stages with multiple clinical trials, for several strategic reasons. Therefore, sponsors will have a broad range of questions while they streamline these newly added compounds towards their regulatory submissions. Type C meetings provide an appropriate forum to seek FDA input on a wide variety of topics at various stages of development to ensure that the submission is in line with FDA expectations. In this paper, we provide a comprehensive account covering all essential processes involved in generating various components of Type C meetings, and the logistics on the interactions between the sponsor and FDA that ensure successful completion of this critical milestone.

Drug Development Process & Its Regulation by FDA – Overview

As a first step, during the early stages of research and development (R&D), researchers identify a biological target (like a protein or gene or even a biological pathway) involved in a disease and search for molecules that can affect it, leading to a promising compound. These identified targets are moved into preclinical research that involves laboratory and animal studies to assess initial safety, toxicity, and potential effectiveness, establishing foundational data for human trials. Based on the outcome of this pre-clinical phase, the targets are moved into the clinical research (popularly known as clinical trials) phase that includes three major phases: Phase 1 - Small group of

healthy people (or patients) to check safety and dosage, Phase 2 - Larger group of patients to evaluate effectiveness and side effects, and Phase 3 - Large-scale trials to confirm effectiveness, monitor side effects, and compare to existing treatments. Upon completing the clinical trials successfully, the sponsor submits a New Drug Application (NDA) with all data for the FDA Review. Typically, FDA teams (doctors, chemists, statisticians) review for safety, efficacy, and benefit-risk. Often, Post-Market Safety Monitoring (Phase 4) is required under the monitoring by the FDA and company to detect long-term or rare side effects, ensuring continued safety after approval. The overall cost of the drug development process and complexities and challenges involved in this business can be easily understood if we know how many compounds that were screened initially during the discovery and development stage and how many finally became the actual approved drug. For every 5,000–10,000 compounds initially screened, roughly 250 enter preclinical testing, about 5–10 progress to human trials, and ultimately only one drug is approved for use! Figure 1 presents a bird's eye view about the drug development process.

Fig. 1. Drug Development Process:



Who owns the drug development process? Here comes the distinctions between two terms – Sponsor and Contract Research Organization (CRO). A sponsor funds and owns a clinical trial (like a pharma company), holding ultimate responsibility, while a CRO is an outsourced expert hired by the sponsor to plan, manage, and execute trial activities (like site monitoring, data management, regulatory filings), acting as the key middleman between the sponsor and research sites, allowing sponsors to focus on their core product development. In short, sponsor is the owner and funder, while the CRO is the executor or manager.

The U.S. Food and Drug Administration (FDA) has several centers and offices under its umbrella, among which two major centers are the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). These two centers differ in their responsibilities, regulatory scope, and review processes: CDER is primarily responsible for evaluating and regulating small molecule drugs (chemical drugs), including most prescription drugs and over the counter (OTC) drugs. CBER is primarily responsible for evaluating and regulating biological products, including vaccines, cell therapies, gene therapies, blood products, and allergenics. Office of Therapeutic Products (OTP) is part of the CBER, and it regulates advanced biologics like gene/cell therapies. Key differences in the scope and functions between CBER and CDER are listed in **Table 1**.

Small Molecules are usually chemically synthesized from simple chemicals, small (under 1 kDa) in size, with defined chemical structures. They often interact with multiple targets, leading to broad effects but also potential side effects (e.g., organ damage). Often, they are administered orally as pills or capsules. Whereas the biologics are derived from living organisms (cells, tissues) and much larger than small molecules with complex 3D structures (proteins, antibodies, vaccines). They are highly specific, "precision-guided" action on single targets, with fewer off-target effects. Usually, biologics are administered via injection or infusion to bypass the digestive system.

PDUFA (Prescription Drug User Fee Act) is a U.S. law that allows the FDA to collect fees from drug companies to fund the drug review process, speeding up the approval of safe and effective medicines while improving communication and development. Reauthorized every five years, the current iteration (PDUFA VII) runs through FY 2027, enabling the FDA to hire more staff, upgrade systems, and meet performance goals for timely drug access, with final decisions often occurring on "PDUFA dates".

Table 1. Key Differences Between CDER and CBER

ROLES	CDER	CBER
Responsibilities	Primarily responsible for evaluating and regulating small molecule drugs (chemical drugs), including most prescription drugs and over the counter (OTC) drugs.	Primarily responsible for evaluating and regulating biological products, including vaccines, cell therapies, gene therapies, blood products, and allergenics.
Regulatory scope	Regulates drugs such as pain medications, antibiotics, anticancer drugs, and drugs other than blood products	Regulates the products typically derived from living organisms or living sources, and their production and quality control processes differ significantly from chemical drugs
Review process	Responsible for reviewing New Drug Applications (NDAs), including preclinical data, clinical trial results, and evaluating the safety and efficacy of drugs.	Responsible for reviewing Biologics License Applications (BLAs), which include evaluating the manufacturing process, facilities, and the safety and efficacy of the products themselves.
Organizational structure	Encompasses several offices, including the Office of New Drugs (OND), Office of Drug Evaluation, etc., with each office responsible for reviewing specific types of drugs.	Encompasses several offices, including those responsible for reviewing specific product categories, such as the Office of Vaccines, Office of Cell and Gene Therapy, etc.
Other Responsibilities	Oversees drug labeling, advertising, marketing, and drug shortage issues.	Oversees the labeling and advertising of biological products and ensures compliance with manufacturing processes.

Sponsor’s Interactions with FDA pertinent to Its Drug Development Programs

Since the introduction of the Prescription Drug User Fee Act (PDUFA) VII for fiscal years 2023 - 2027, the FDA published a revised draft guidance in September 2023, providing several recommendations regarding the conduct of formal meetings between the FDA and Sponsors. These meetings are intended to focus on issues around the development and review of drugs or biological products. The draft guidance, entitled "Formal Meetings Between the FDA & Sponsors or Applicants of PDUFA Products," is important because it provides the sponsors and applicants with tangible information and additional clarity concerning the Agency's expectations for these meetings.

The sponsors need to interact with the FDA to align their drug development plans with regulatory expectations, ensuring safety, efficacy, and faster market approval by getting crucial feedback, avoiding costly pitfalls, and meeting legal requirements for new medicines. The key reasons for sponsor-FDA interactions can fall under any of these categories:

Guidance & Alignment: Get expert advice on complex products (like cell/gene therapies) and align development strategies with agency expectations to streamline the path to approval.

Risk Mitigation: Identify and address potential deficiencies early, preventing clinical holds, submission delays, or marketing refusals.

Regulatory Compliance: Understand and meet stringent requirements for study design, data quality, patient safety, and monitoring.

Product-Specific Feedback: Receive tailored advice on Chemistry, Manufacturing, and Controls (CMC), nonclinical data, and clinical trial design.

Strategic Planning: Discuss overall development pathways, milestone achievements, and future study designs (Phase 1, 2, 3) to build a robust program.

The sponsor interactions with the FDA are structured engagements throughout drug/biologic development, primarily via formal meetings for guidance, and informal methods like emails, phone calls, and submissions. These interactions facilitate crucial feedback, from early-stage discussions to milestone reviews, ensuring compliance and robust development programs, with formal meetings offering a chance for deep dives into scientific and regulatory aspects. There are six types of formal meetings under PDUFA that occur between requesters and FDA staff. They are as follows:

1. **Type A Meeting** – this is necessary for an otherwise stalled product development program to proceed or to address an important safety issue
2. **Type B Meeting** – This is also called as Milestone Meeting or an Entitled Meeting to discuss product development and next steps. These meetings are crucial to keep product development moving forward.
3. **Type B (end-of-phase (EOP)) B Meeting** – This typically occurs after the completion (or near completion) of a clinical stage (Phase 1 or Phase 2) to discuss the results of that stage, what they mean, and discuss proceeding to the next stage of clinical trials with FDA. This meeting helps sponsors gain assurance from FDA that they are on the right track with their clinical development, are ready to move to the next stage, and are aligned on the next clinical study.
4. **Type C Meeting** – This refers "any meeting other than a Type A, Type B, Type B (EOP), Type D, or INTERACT meeting regarding the development and review of a product, including meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use".
5. **Type D Meeting** – This is fairly a newer category meant for offering rapid, focused feedback on narrow regulatory issues that do not require a full Type A or B meeting.
6. **INTERACT Type B Meeting** – **IN**itial **T**argeted **E**ngagement for **R**egulatory **A**dvice on **C**DER and CBER Produc**T**s is a meeting at a specific time early in product development. The appropriate timing for an INTERACT is when a sponsor has identified the investigational product to be evaluated in a clinical study and conducted some preliminary preclinical proof-of-concept studies with the intended investigational product but has not yet designed and conducted definitive toxicology studies.

The FDA draft guidance document for industry, named "Formal Meetings Between the FDA and sponsors or Applicants of PDUFA Products Guidance for Industry", released in September 2023, provides detailed information about various FDA meetings/Interactions between the sponsors and the Agency and the considerations that a sponsor must have when preparing for a formal meeting with the FDA. Based on this document, we present comprehensive schedule of various FDA Meetings in Table 2.

Table 2. Summary of FDA Meetings & procedural timelines.

FDA Meeting Request/WRO Request Response Timelines	
Meeting Type (any format)	**Response Time (calendar days from receipt of meeting request/WRO request)**
A	14 days
B	21 days
B (EOP)	14 days
C	21 days
D	14 days
INTERACT	21 days

Table 2. Summary of FDA Meetings & procedural timelines (Continued)

FDA Meeting Scheduling Time Frames	
Meeting Type (any format)	**Scheduling (calendar days from receipt of meeting request)**
A	30 days
B	60 days
B (EOP)	70 days
C	75 days
D	50 days
INTERACT	75 days
FDA WRO Response Timelines	
Meeting Type (any format)	**WRO Response Time (calendar days from receipt of WRO request)**
A	30 days
B	60 days
B (EOP)	70 days
C	75 days
D	50 days
INTERACT	75 days

Type C Meeting – Background and Objectives

As the draft guidance highlights, “A Type C meeting is any meeting other than a Type A, Type B, Type B (EOP), Type D, or INTERACT meeting regarding the development and review of a product, including meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use”. As this reflects, the Type C meeting is an opportunity for a formal discussion to address any scientific or regulatory aspects that can arise during the drug development processes, especially the ones that were not covered by the Type A (stalled development) or Type B (milestone) meetings. Indeed, this is an opportunity to raise questions and concerns about any of the drug development steps to avoid delays and align with FDA expectations. These meetings are typically 60 minutes and occur within 75 days of the request, with sponsors submitting a briefing package to get guidance. Hence, the Type C FDA meeting is unique as it provides the following key features:

Flexibility: Addresses diverse issues that don't fit other categories, from early-stage research to Phase 4.

"Catch-All": Covers topics like nonclinical studies, protocol changes, biomarker use, labeling, manufacturing, or pediatric study plans.

Timing: Can occur at any point in the product lifecycle, offering proactive guidance.

Specific Use Case: A notable Type C meeting type is for discussing new surrogate endpoints not yet used for approval.

From our experience, following representative topics are common as most of the sponsors would have questions under these and seek further advice and feedback from the FDA prior to their final application. Raising important questions well ahead of the submission will help sponsors to plan their submission logistics accordingly without any ambiguity.

Study Design & Protocols: Overall clinical trial design, refining endpoints, revising the selection of biomarkers relevant to the study, potential amendments in the trial design

Data Interpretation: Discussing results, Aligning on study results interpretations, and their regulatory implications.

Regulatory Strategy: Addressing eligibility for designations like Breakthrough Therapy or navigating specific pathways.

Follow-up to previous FDA comments: Seeking additional guidance on review feedback.

Nonclinical: Issues with nonclinical studies, pre-clinical data modelling, pharmacological parameters

Manufacturing & Quality: Updates and issues related to production.

New Surrogate Endpoints: A specialized Type C meeting exists to discuss using novel biomarkers for approval.

Early Consultation: Early discussions on novel concepts like new surrogate endpoints or rare disease challenges.

Any deviations in the technology platform: Use of R, submission of datasets other than SAS XPT files

Issues from the legacy studies – status on the contents from the legacy studies' packages that were completed prior to their acquisition, any critical missing elements and their implications in the submissions.

Stakeholders and Cross-functional teams involved in Type C Meeting Preparation

Having learned about the objectives and the scopes of the Type C meeting, here we shift the focus to the key stakeholders of this meeting. The key participants are the sponsors (applicants) and the representatives from the FDA's CDER or CBER, depending on the nature/type of the study drug being discussed. With the sponsor's side, who are all the key players. As we know, any pharma or biotech company includes diverse cross-functional teams. The following cross-functional teams play key roles in preparing Type C meeting materials and logistics:

- Regulatory team
- Medical Writing
- Safety and Efficacy Leads
- Statistician
- Statistical Programming
- Technology & Platform development (Clinical programming) team
- Institution's CDISC & Submission Standards team

In practice, the regulatory team leads all the logistical efforts and coordinates with the leads from these cross -functional teams for preparing the write up for the Type C meeting and maintaining the communications between the FDA and the sponsor teams. In other words, the regulatory team is the Point-of-Contact for this effort from the sponsor side. Among these cross-functional teams, the contributions from the Statistical programming team are critical from the contents point of view. Because the programming team deals with clinical data as well as producing the reports (in the context of study documents, SAP and mock-up shells) for their delivery and the rest of the cross -functional teams' review. Therefore, statistical programming teams bear the responsibility for communications that are pertinent to any aspects of the data related items, starting from data capture through generation of clinical data reports, and programming platforms.

Prior Considerations on the essential tasks that support various components of the Type C Meeting

Considering the broader scope of the Type C meeting, one can anticipate the spectrum of details that are being garnered across multiple cross-functional teams. Other than the tasks that involve regulatory expertise, gathering the details for the rest of the components will be usually led by the programming lead. It is highly helpful to handle the whole process efficiently when a programming lead starts to envision about the requirements and time frame

for mobilizing the details several months ahead of the submission of the meeting request. In this context, we are sharing here our perspectives and tips from our experience.

In our experience, it is best practice to create folders in a share point or MS Teams area where all the stakeholders can access, review and edit necessary documents during the whole process. While we listed the documents that are expected to be submitted along with the Type C document to FDA, there are several background tasks and documents required to be prepared and reviewed diligently as these feed into the required components of the Type C meeting. Preparing the essential documents and making them available for easy access are highly helpful for efficiently collecting necessary input in the relevant documents. Typically, the programming lead can garner the efforts for procuring these items in the common area. In our experience, the following representative tasks helped our team steer our efforts and thus significantly contributed to the Type C meeting preparations.

- Deciding on the studies to be included in the submission: An excel spreadsheet containing the list of studies and study level contacts (lead programmer, statisticians, data management contact, vendor contacts) for reaching out for any questions, Study ID from the past, Study ID given by the current organization after their acquisition.
- List of studies with their protocol titles, brief scope, phase, vendors for SDTM and ADaM components, study start date, study end date (for the completed studies).
- List of studies/trials with their technical details – CDISC versions being used SDTM and ADaM parts, WHO Med Dictionary details, MedDRA versions, CDISC Controlled Terminology (NCI CT versions),
- List of non-clinical studies – protocol titles, brief scope, CDISC SEND and Controlled Terminologies, if any, versions, study start date and study end date, contact specifics after their acquisition with the current organization (mostly project managers from the pre-clinical section).
- Investigator Brochure – This is one of the very resourceful documents as it gives complete picture of the therapeutic compound/biologic and the related trials (both clinical and non-clinical studies). Usually, it is a live document and must be available from both medical and regulatory teams.
- A thorough checklist on the components from the packages of all studies that were completed prior to their acquisition. This is highly helpful to understand the lapses and gaps from the acquired studies. Though this checklist offers little help with the Type C document, this document is enormously helpful in our experience while we plan for their submission.

Recommended components for a Type C Document

Having explored the scope and contents of the Type C meeting, let's delve into the logistics and documents / documents to be included during the Type C Meeting request. Under this section, we provide an overview of the potentially required documents to be included during the type C meeting request. Though the exact contents may vary depending on the indication as well as the nature of the studies included under a compound, the following items are highly anticipated. Further, we highlight our perspectives from the acquired studies.

Study Protocol:

The protocol for any clinical trial is the essential, detailed blueprint for a study, outlining its goals, design, methods (who, what, when, how), participant eligibility, safety measures, and statistical plans, acting as the rulebook to ensure participant safety, data integrity, and scientific validity while guiding all researchers involved. It's a comprehensive document reviewed by ethics boards (IRBs) and regulators (like the FDA) before a trial starts, ensuring ethical conduct and scientific rigor.

For any ongoing pivotal trials, updated versions of the protocol and eCRFs are easily available within the study teams at any given time. However, when the compound is acquired along with the completed studies from an external organization, ensuring the availability of these study documents is one of the challenging tasks. It is highly recommended that the programming lead gains access to the folders of the studies that have already been completed to ensure that these documents are actual documents that were being followed while conducting the respective studies. If there is any discrepancy between the version being used in the study and the version that is available in the folder, then the programming lead can reach out to the concerned teams that are involved during the study acquisition. However, a review to ensure the presence of the following key components in the available versions of the protocols will be highly desirable:

Background & Rationale: Why study is needed.
Objectives: Specific questions the trial aims to answer.
Study Design: How the trial is structured (e.g., phases, randomization).
Eligibility Criteria: Who can and can't join (inclusion/exclusion).
Treatment Plan: Interventions, doses, procedures, and tests.
Safety & Adverse Events: Monitoring and reporting risks.
Statistical Plan: How data will be analyzed to determine success.
Ethics: Protecting participants (IRB/Ethics Committee)

Statistical Analysis Plans (SAP):

SAP is a detailed blueprint for analyzing research data, outlining variables, statistical methods, patient populations, and output formats (tables, figures) before data collection is complete, ensuring transparency, rigor, reproducibility, and preventing bias by specifying analyses like primary, secondary, subgroup, and missing data handling, crucial for clinical trials and regulatory submissions.

For any ongoing pivotal trials, updated versions of the SAPs are easily available within the study teams at any given time. However, when the compound is acquired along with the completed studies from an external organization, it is almost impossible to verify every line of the SAP. However, the study team may ensure that SAP covers the following key components:

Introduction: Study background, objectives, hypotheses, and endpoints.
Study Design: Details on randomization, treatment groups, and study duration.
Analysis Populations: Definitions for Full Analysis Set (FAS), Per-Protocol, Safety& Efficacy populations
Data Handling: Procedures for data cleaning, organizing, and handling missing data.
Statistical Methods: Specific tests (t-tests, ANOVA, regression), significance levels, and multiplicity adjustments.
Primary & Secondary Analyses: Detailed plans for main and supporting outcomes.
Subgroup & Sensitivity Analyses: Pre-specified exploratory analyses and “what-if” scenarios (e.g., worst-case/best-case).
Questionnaire Tools: ePRO and eCOA related analysis, Details on the use of Global and Study-specific questionnaire tools and related analysis data and outputs
Output: Specifications for tables, listings, and figures (TLFs).
Software: The statistical software to be used (e.g., SAS, R).

Study Data Standardization Plan (SDSP):

SDSP is an important document and communication tool between the sponsor and the FDA. The purpose of the SDSP is to document and communicate a plan for describing the sponsor’s application of data standards in non-clinical and clinical studies across a development program. Indeed, it requires enormous level of input across various sections of the studies, especially if the submission involves multiple studies. Template for preparing the SDSP is available at the PHUSE site, and the programming leads must visit the PHUSE site to download the latest version of the template. It is recommended to start preparing this document with the current template available from the PHUSE.

According to the Study Data Technical Conformance Guide (October 2024), sponsors should prepare a document called the study data standardization plan (SDSP) for each of their development programs to describe the submission of standardized non-clinical and clinical study data to the FDA. For New Drug Applications (NDA) and Biologics License Applications (BLA), the SDSP should be in Electronic Common Technical Document (eCTD) section 1.13.9 General Investigational Plan. For Investigational New Drugs (IND), the SDSP should be in eCTD section 1.20 General Investigational Plan for an Initial IND.

The sponsors are encouraged to start the SDSP early, even in pre-IND stage, to identify potential standardization issues early in the development process. It should be shared with the FDA during key regulatory interactions and when deemed necessary by either the sponsor or the FDA. The SDSP should then be updated in subsequent communications with the FDA as the development program expands and additional studies are planned. The

document is often used as part of briefing packages for pre-NDA and pre-BLA meetings to confirm agreement on what and how study data will be submitted but can be shared for earlier FDA interactions as needed.

The SDSP contains tabular lists of non-clinical and clinical studies in the development program with details about each study such as protocol number, study title, study type, study status, start date, and standards used for study data.

Bioresearch Monitoring (BIMO) Package Planning:

FDA's Bioresearch Monitoring (BIMO) program is a comprehensive program of on-site inspections, data audits, and remote regulatory assessments designed to monitor all aspects of the conduct and reporting of FDA regulated research. The BIMO program was established to assure the quality and integrity of data submitted to the agency in support of new product approvals and marketing applications, as well as, to provide for protection of the rights and welfare of the thousands of human subjects and animals involved in FDA regulated research. It has become a cornerstone of the FDA preapproval process for new medicines, medical devices, food and color additives, veterinary products and, tobacco products introduced to the U.S. consumer.

The BIMO program is unique in the scope of its compliance programs and regulations which are shared by all six of FDA's Centers such as, CBER, CDER, CDRH (Center for Devices and Radiological Health), CFSAN (Center for Food Safety and Applied Nutrition), CTP (Center for Tobacco Products), and CVM (Center for Veterinary Medicine).

This is one of the topics that sponsors usually would like to get many clarifications. In brief, FDA's current BIMO Technical Conformation Guide provides guidance on the content and format for all three parts of the BIMO package, namely Study documents, Site Level Listings and CLINSITE dataset. Besides, BIMO Data Reviewer's Guide is also needed, and this is being guided by the BDRG template being released by the PHUSE working group. Though it is recommended that the BIMO package needs to be generated based on the recommendations, still sponsors are different stages of adopting these two guidelines due various technical and logistical reasons.

When a therapeutic compound has been acquired with studies that were initiated/completed by external organization, the sponsor may have many questions and Type C meeting can be a forum that the sponsors can list their questions to seek feedback from the FDA. Some of the questions can be related to the following topics:

1. Being an acquired compound, there could be several gaps in the available data as well as the components of the study package to the extent that the sponsor may not be able to provide the BIMO package in full compliance with the guidelines. The sponsor can highlight the gaps ahead of the submission during the Type C preparation and get additional clarifications.
2. It is possible that a good number of sites that were recruited by the previous company may not exist now and some of the site-level information may not be available. The CLINSITE dataset must include the site level details in the variables listed in the BIMO TCG. If the sponsor cannot generate the CLINSITE data per TCG, sponsor can explain this ahead of time.
3. Sponsor can list the titles of the Site-level Listings and ask for the FDA's feedback.
4. For any reason, if the preparation of BDRG is not feasible as per the template released from the PHUSE site, then sponsor can explain the background surrounding its ability to adhere to the PHUSE template and provide a brief description of the template that the sponsor wishes to submit.

Questions related to the software tools and clinical data formats being used in the study:

In recent years, pharmaceutical industry has been witnessing a huge shift towards exploring open-source tools such as Python, R and any machine learning tools for their potential application in clinical data analysis and submission. Many pharmaceutical companies are in various stages in adopting these open-source tools, especially R as their tool in programming for generating data and the outputs. Especially when the study packages include mix of usage of R and SAS as their programming tools in generating outputs. The Type C meeting can serve as a good opportunity to seek FDA's advice or approval for submitting the outputs that were generated by both SAS and R.

Traditionally, the submission of SAS-generated XPT has been widespread practice. However, recent trends witness the discussions about the use of CDISC-JSON files instead of the traditional XPT files. The FDA is actively adopting CDISC Dataset-JSON as the future standard for electronic study data submissions, moving away from traditional XPT files, with version 1.1 addressing early pilot issues. This JSON-based format is a modern, efficient alternative

that supports enhanced metadata and better integration with current data science tools, allowing for smaller files and easier processing while maintaining data integrity for regulatory review. There are several key aspects of FDA's Dataset-JSON as follows:

Standard: Based on Clinical Data Interchange Standards Consortium (CDISC) Dataset-JSON v1.1.

Purpose: To replace SAS XPORT (XPT) as a primary transport format for study data in regulatory applications (IND, NDA, BLA, etc.).

Benefits: Smaller file sizes, richer metadata, vendor neutrality, and easier use with modern programming languages (Python, R).

Status: FDA has successfully completed pilots, confirmed data integrity, and is working on internal system updates for full adoption.

When to Request an FDA Type C Meeting?

Request an FDA Type C meeting for general drug development questions not covered by Type A (stalled programs) or Type B (major milestones like pre-IND/NDA) meetings, often for non-critical but important topics, early phase feedback (like EOP2A), or specific issues, scheduling it within 75 days of FDA receipt, and submitting your detailed package about 47 days prior. Use Type C for guidance on development pathways, biomarker discussions, or clarification on regulatory requirements, ensuring you have specific objectives and questions ready

A Type C meeting is a versatile option for sponsors needing FDA input on topics that don't fit within the scope of Type A or Type B meetings. Sponsors should consider requesting a Type C meeting when they need feedback on these non-critical yet important aspects of their drug development program. To ensure timely scheduling, it's advisable to submit the meeting request approximately 75 days before the desired meeting date. This proactive approach allows for thorough preparation and more productive discussion with FDA.

Scheduling and Timelines for a Meeting Request

Type C meetings follow FDA-established timelines. FDA will respond to a meeting request within 75 days of receiving it. Meetings can be conducted like face-to-face discussions, conference calls, or written responses only (WRO). The background package can be submitted at the time of the meeting request or 47 days before the date of the meeting (or expected written response in the case of a WRO meeting). Good questions, a well-structured meeting request, and data-supported briefing document are the keys to a productive discussion.

Planning and Logistics on the Sponsor side – Key Factors for a Successful Outcome

Having decided on the scope and specific details related to the requirement for the Type C meeting and need to collect information across multiple cross-functional teams, one obvious question that the reviewers of this paper will be interested in is who would steer and coordinate the efforts for this effort. Typically, in a well-established organization with well-defined divisions for steering various aspects of drug development, mostly an experienced lead level staff from a regulatory division would steer the activities. However, since most of the inputs are related to statistical analysis, clinical data and programming aspects, a lead person from a programming team also will steer this task. If programming team leads these tasks, still a regulatory staff will shadow these activities due to the requirement of extensive knowledge about the agencies and submissions. Hence, this differs from organization to organization.

In this paper, we have covered various aspects of Type C meetings, right from the definition of various interactions between sponsors and the FDA, through complete logistical details involved in this part of the drug development cycle. From our experience and observations from other submissions, we can holistically list the following key factors for successful FDA Type C Meeting.

Prior to the Meeting:

1. Precise planning for regular meetings for collecting various details and preparation are the key elements. Ensure that the sponsor's team staff visit the FDA's site regularly to get an updated guidance document.

Focus should be based specific requirement pertinent to the type of the investigation drug/compound and the therapeutic area or disease indication that is under the study

2. Define Clear Objectives:
   Know exactly what regulatory guidance or specific input that a sponsor needs from the FDA.
   Specify the key questions and regulatory challenges that a sponsor needs FDA input on.
   Focus on objectives: Limit the agenda to essential topics for precise, actionable feedback from the FDA.
3. Prepare a Strong Briefing Package:
   Concise & Focused: Keep it to essential background and data, avoiding voluminous materials (typically 50-100 pages).
   Targeted Questions: Limit to a few (e.g., max 10 for 60 mins) clearly worded questions, including sub-questions, directly addressing your goals.
   Sufficient Data: Provide enough organized data to support the questions without overwhelming the reviewers.
4. Understand Meeting Scope: Clarify if the sponsor is seeking binding feedback or advisory discussion.
5. Prepare Your Team: Assign roles, align messaging, and ensure team members are ready to speak.

Execution of the Meeting:

1. Skip Presentations: Use the allotted time for discussion and getting answers, not for presenting background.
2. Stay Focused & Manage Time: Stick to the agenda and ensure time for key points and answers.
3. Be Clear & Concise: Avoid jargon; don't hide concerns, propose solutions.
4. Listen Actively: Pay attention to feedback, body language, and voice tone; correct misinterpretations immediately.
5. Summarize & Confirm: Use the last few minutes to summarize outcomes, action items, and next steps.

Post-meeting events:

1. Document & Distribute Minutes: Promptly share summaries of discussions, outcomes, and action items.
2. Feedback Implementation: Integrate FDA feedback into the development plan and follow through on agreed actions.

What to anticipate from the FDA after Type C meeting?

After a Type C meeting with the FDA, sponsors can anticipate receiving formal, written minutes within 30 calendar days, outlining the discussion, key agreements, and recommendations regarding the drug development program. These minutes act as the official record, guiding next steps, while allowing sponsors a 20-day window to request clarification if necessary.

Official Minutes (Within 30 Days): The FDA provides a summary document detailing discussion, agreements, and action items.

Actionable Advice: The agency will give feedback on topics like non-clinical studies, protocol amendments, or manufacturing, which must be incorporated into the development plan.

Clarification Period: If necessary, sponsors have 20 days to ask for clarification on the meeting minutes, with the FDA responding within 20 days.

Documentation Alignment: Ensure all project team members review the minutes to align on the agreed-upon regulatory path.

Next Regulatory Steps: The advice may require updating protocol designs, initiating new studies, or revising CMC (Chemistry, Manufacturing, and Controls) strategies.

Conclusion

This paper emphasized most of the important steps as efficient ways for handling Type C meeting pertinent to a sponsor's complex drug development program. As highlighted, each clinical trial is unique. Especially when a sponsor acquired a compound with relevant clinical trials that were completed in part or fully from the external source and streamlined these studies into their pipeline, they pose multiple challenges. Under these circumstances, A Type C meeting provides an opportunity to address any regulatory challenges and clarify expectations and align strategies. The sponsors can enhance their chances of successful outcomes and steer a productive relationship with the FDA via understanding the scopes and significance of these steps.

1. Understanding the gaps and defining the questions, scopes and expectations for study-specific situations well ahead
2. Planning and garnering necessary information across the cross-functional teams
3. Developing a clear communication and execution of strategy internally as well as with the agency and execution
4. Key factors include crystal-clear objectives, a focused, concise briefing package with well-organized data (around 50-100 pages, max 10 questions for 60 mins) to support targeted questions, and a streamlined meeting agenda with designated speakers, emphasizing discussion over presentations and active listening for actionable feedback, followed by thorough follow-up on commitments
5. Executing the follow-up actions upon receipt of the results of the Type C meeting from the FDA as these actions highlights the importance of translating discussions into actionable outcomes, ensuring that insights gained are effectively integrated into development plans.

In conclusion, the significance and criticality of the Type C meetings cannot be overstated. The significance of this meeting and its outcome are beyond the adherence to the compliance level, but it creates an opportunity for aligning sponsor's pipeline goals with agency's expectations and drug development processes. By clear planning and proactive engagement, sponsor teams can improve their chances of favorable feedback and contribute to the overall success of their organizations in bringing innovative therapies to market. In general, experience from the previous submission and handling of various meetings with the Agency brings valuable lessons and experiences that can easily translate into the forthcoming new drug development applications. Hence, embracing the practices that we have described in this paper is not only highly beneficial, but they pave the way for fostering a culture of continuous improvement and achieving excellence in regulatory compliance. If a sponsor is in its early stage of its growth and preparing the Type C package for the first time, it is highly helpful to hire an external consulting firm that is very specialized in FDA regulations and well experienced in handling various meetings and submission with FDA. Recruiting such a firm well ahead is one of the common practices for a smaller organization since these expert firms provide very elaborate discussions and guidance through the course of action with mock sponsor-FDA meetings.

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