FDA Type C Meetings on ISS Safety Analysis Strategy and Related Data Requirements

Y. Veronica Pei, MD, MEd, MPH, FACEP

Acting Associate Director
Biomedical Informatics and Regulatory Review Science (BIRRS)
Office of Drug Evaluation Science (ODES)
CDER | US FDA

SBIA Integrated Safety Webinar – March 7, 2024

Learning Objectives

- Understand the types of formal meetings with FDA
- Describe how Type C ISS meeting can be used to support drug development programs
- Describe how to request a Type C ISS Meeting

Formal Meetings with FDA

What: 6 types of formal meetings under PDUFA

Who: Sponsor/Investigators and FDA

Why: Provide advice on drug/biologics development

When: Critical points in product development

Types of Formal Meetings with FDA

Type A	Type B	Type B (end of phase)
Type C	Type D	INTERACT

INTERACT: Initial Targeted Engagement for Regulatory Advice on CDER and CBER Products

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/formal-meetings-between-fda-and-sponsors-or-applicants-pdufa-products

Types of Formal Meetings with FDA

Type A	• Stalled development e.g., clinical holds, dispute resolutions
Type B & Type B (EOP)	• preIND, preNDA/BLA • EOP2
Type C	• Any meeting that does not fit in the other categories
Type D	• Focused topic meetings
INTERACT	• Unique challenges in early development

Type C Meetings on ISS Safety Analysis Strategy and Related Data Requirements (Type C ISS Meetings)

Precede the Pre-NDA meeting

- ≈1 year before pre-NDA meeting
- After drafting analysis plan for ISS
- Before programming work for pooled or other safety analysis

Discuss safety analysis strategy for the ISS and related data requirements

Type C ISS Meetings

- Opportunity to discuss with FDA approach to aggregate safety analysis (e.g., before the pre-NDA meeting)
- Topics:
  - Data pooling for safety analysis
  - Analytic methods
  - Approach to AESI
  - Data standards
  - Submission requirements for datasets

Example Sponsor Questions

- *Does the Agency agree with the proposed pooling strategy?*
- *Does the Agency agree with the proposed Integrated Safety Analysis Plan?*
- *Does the Agency agree with the proposed grouping of MedDRA preferred terms for evaluation of …*
- *Does the Agency agree with the proposed Study Data Standardization Plan?*
- *Are legacy data acceptable if SDTM and ADaM datasets are not available?*
- *Does the Agency agree with the proposal for narratives and case reports forms (CRFs)?*

Meeting Submission Content

- Tabular listing of clinical trials
- Draft ISS statistical analysis plan (SAP)
  - Pooling strategy
  - Rationale for inclusion or exclusion of trials
  - Planned analytic strategies to manage differences in trial designs (e.g., length, randomization ratio imbalances, study populations)
- Method of assignment of study events to a specific study period
- Previously observed and anticipated safety issues

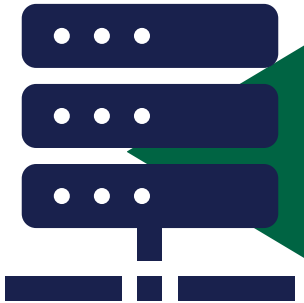
How to Request a Type C ISS Meeting?

Cover Letter: “Discuss Safety Analysis Strategy for the ISS”

Type C Meeting Formats

- Sponsor **<u>may request</u>**:
  - In-person
  - Virtual
  - Teleconference
  - Written response only (WRO)
- Agency may determine that WRO is appropriate

How to Submit a Sample Standardized Dataset?



Cover Letter: “Clinical/Safety Sample Datasets”

Sample Standardized Datasets

- Reviewed for conformance to:
  - Standards
  - Structure
  - Format
- Are **NOT** reviewed as part of marketing application

Can safety analysis strategy and data requirements be discussed during the pre-NDA meeting?

Yes, BUT…

Advantages of Type C ISS Meeting

REGULATORY GUIDANCE

MORE TIME TO PLAN AND MAKE REVISIONS

DEDICATED MEETING ON IMPORTANT TOPIC

Summary

- Request Type C ISS meetings
- Early discussion with Agency on approach to aggregate safety analysis
- Timing: Before preNDA meeting
- Timing: After drafting ISS SAP

Challenge Question

Which of the following statements regarding Type C ISS Meeting is <u>NOT</u> true?

A. They are optional

B. Can be conducted via WRO, in person, or teleconference

C. Best conducted before the preNDA meeting

D. Best conducted before drafting the analysis plan for ISS

Resources

- Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products (Draft Guidance, September 2023). Available at: https://www.fda.gov/media/172311/download

- Study Data Standards Resources. Available at: https://www.fda.gov/industry/fda-data-standards-advisory-board/study-data-standards-resources

- Study Data Technical Conformance Guide - Technical Specifications Document. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/study-data-technical-conformance-guide-technical-specifications-document

FDA U.S. FOOD & DRUG ADMINISTRATION