



Submitting Summary Level Site Data: Overview, Implementation, and Case Studies

Rob Woolson

Jeff Abolafia

Ben Vaughn

BIMO Summary Level Clinical Site Dataset

What is it?

... a single dataset that includes data from all pivotal studies used to support safety and efficacy in an application

[Specifications for Preparing and Submitting Summary Level Clinical Site Data for CDER's Inspection Planning \(FDA DRAFT Guidance: Technical Specifications, November 2012\).](#)

The Guidance

Guidance for Industry Providing Submissions in Electronic Format — Summary Level Clinical Site Data for CDER's Inspection Planning

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of the publication of the *Federal Register* notice announcing the availability of draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD, 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document please contact Jonathan Helgott: 301-796-5636, Jonathan.Helgott@FDA.hhs.gov, or Paul Cleves: 301-796-0173, Paul.Cleves@FDA.hhs.gov.

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Specifications for Preparing and Submitting Summary Level Clinical Site Data for CDER's Inspection Planning

Revision History

Date	Version	Summary of Changes
11/08/11	1.0	Original Version
10/15/12	1.1	Updated example values in Appendix 2
11/7/12	1.2	Updated Country codes from alpha-2 to alpha-3

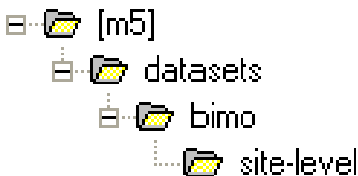
Background

“... CDER has determined that to plan efficiently for clinical site inspections and to meet the PDUFA goal dates for marketing applications, CDER prefers to receive summary level site data.”

Dataset Purpose

1. Identify and characterize each study
2. Identify the sponsor
3. Document the NDA or BLA number
4. Describe individual clinical investigator sites, including financial disclosure information
5. Identify treatment arm
6. Document endpoint types
7. Report primary endpoint results by site and treatment arm

The Essentials

- **Name:** clinsite.xpt
- **Format:** SAS® transport file
- **Structure:** one record per pivotal study, clinical site, treatment arm, and primary endpoint
- **Documentation:** define file, reviewer guide
- **Location:** 

```
graph TD; m5[m5] --> datasets[datasets]; datasets --> bimo[bimo]; bimo --> site-level[site-level]
```

One Dataset – Many Goals ...

“The summary level clinical site dataset is intended to characterize the individual clinical investigator sites, describe aspects of the studies with which those clinical investigator sites are associated, and present the characteristics and outcomes of the study at the site level.”



Data Source/Origin**Information****Study-level metadata**

Study Number; Title, Number of Sponsors; Sponsor Name(s); IND Number; Study Conducted Under IND?

Regulatory affairs database

NDA Number; BLA Number; Supplement Number

Raw/SDTM/Legacy Analysis/ADaM dataset(s)

Site Identifier; Treatment; Number of Subjects Enrolled; Subjects Screened; Subjects Discontinued; Treatment Efficacy Endpoint Estimate; Treatment Efficacy Endpoint; Site-specific Treatment Effect (and variation); Number of Censored Observations; Number of non-SAEs Number of SAEs; Deaths

Protocol/Statistical Analysis Plan

Text description of Primary Endpoint(s); Primary Endpoint Variable Type.

None – hardcode per guidance

Domain Abbreviation

CTMS (or other separately maintained database)

Number of Protocol Violations

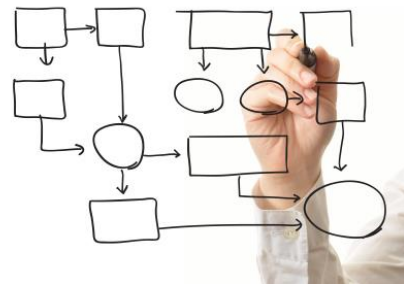
FDA 1572 forms

Maximum financial disclosure amount by any single investigator by site; total financial disclosure by site (for all principal and sub-investigators); investigator names, phone numbers, fax numbers, email addresses, and postal address information (country, state, province, postal code, street, etc.)

Plan Ahead

This is not your 'standard'
standardized dataset

Some essential steps to successfully creating a
submission-ready BIMO dataset ...





Essential Steps

Start the data assembly process as early as possible.

- ✓ Ideal starting time
- ✓ Consolidate essential regulatory information
- ✓ Availability for the pre-NDA/BLA meeting

Step 1

Identify and select a BIMO
dataset coordinator.

Step 2



Create a data/information source inventory and action log.

Collect:

- Requisite source data
- The functional area and owner of the data
- Source data status

Establish:

- Planned data format
- Required additional analyses
- Production, validation, and QC plan
- Production, validation, and QC plan owner

Step 3

Create BIMO dataset
programming specifications.

Step 4



Program, validate, and QC
the BIMO dataset.

Step 5



Prepare for additional FDA requests

- The FDA has consistently requested supportive by-study, by-site patient level listings and other supportive data summaries.
- Sponsors should anticipate additional FDA requests and allocate resources to comply.

Step 6

Case Study 1



Case Study 1

Clinical Development Program:

- Multi-national, multi-center development program including three phase II studies and four phase III studies. Data were submitted as a part of a 505(b)(1) marketing application.

Data source status:

- Source data included raw data, legacy analysis data, SDTM datasets, ADaM datasets, and a regulatory affairs database.

Challenges and Discussion

- ✓ 4 CROs. 7 Studies.
- ✓ Multiple data formats
- ✓ Analysis method limitations
- ✓ FDA communication & request

Case Study 2



Case Study 2

Clinical Development Program:

- Multi-center development program including four phase III studies. Data were submitted as a part of a 505(b)(2) marketing application.

Data source status:

- Source data included SDTM datasets, ADaM datasets, and a regulatory affairs database.

Challenges and Discussion

- ✓ 2 CROs
- ✓ Multiple data formats
- ✓ Non-parametric analysis of primary end point
- ✓ FDA request

Recommendations

1)

Create guidelines to accommodate primary analyses that are non-parametric.

2)

Include supportive by-study, by-site patient level listings as an element in the relevant guidance documents.

3)

Create additional specifications for:

- Missing or non-missing values
- Placeholder records for arms that do not occur at a given site
- Studies with multiple phases/treatment comparisons
- Cases where the safety and efficacy populations are not the same

4)

BIMO dataset metadata should comply with standardized metadata guidelines.

Questions



Thank you for attending.

Send questions or comments to:

Rob Woolson (rob_woolson@rhoworld.com)

Jeff Abolafia (jeff_abolafia@rhoworld.com)

Ben Vaughn (ben_vaughn@rhoworld.com)

