

Bioresearch Monitoring (BIMO) Data Reviewer's Guide

<Sponsor's Name>

<Compound/Project Name>

<Application Type: Application Number>

List of Studies Included in the BIMO Clinical Data
Application:

Study1 <DM.STUDYID>

Study2 <DM.STUDYID>

.....

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1. Introduction

1.1 Purpose

The purpose of the BIMO Data Reviewer's Guide (BDRG) is to provide an overview of sponsor considerations for preparing and submitting BIMO clinical data (Part I - Clinical study-level information, Part II - Subject-level data line listings by clinical site and Part III - Summary-level clinical site dataset) to support safety and efficacy in the applications that are used by the FDA's Center for Drug Evaluation and Research (CDER) for the planning of Bioresearch Monitoring (BIMO) inspections in electronic Common Technical Document (eCTD) format for <<Choose one: New Drug Applications (NDAs) OR Biologics License Applications (BLAs) OR supplemental New Drug Applications (sNDAs) OR supplemental Biologics License Applications (sBLAs) OR Investigational New Drug Applications (INDs)>> containing clinical data.

This document provides the following information to aid navigation and understanding of BIMO clinical data:

- **Supporting Information, Content and Structure of the Requested BIMO Clinical Data**

Covered in sections 1–10 within this document.

- **Hypertext Links**

There are no external hyperlinks applied in this document, but the location of deliverables in “eCTD Module 5 (M5) -> Clinical Study Reports -> Module 5.3.5.4 -> Other Study Reports and Related Information” are specified with text in section 9.

1.2 Acronyms

Acronym	Translation
ARO	Academic Research Organization
BDRG	Bioresearch Monitoring Data Reviewer's Guide
TCG	Technical Conformance Guide
SAFPOP	Safety Population
EFFPOP	Efficacy Population
<Sponsor-specific non-standard acronyms>	

1.3 BIMO Guidance and Supporting Information

BIMO Guidance and Supporting Information	Version and/or Date
Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions Guidance for Industry	
Bioresearch Monitoring Technical Conformance Guide	
Summary-level Clinical Site Dataset Definition File (define.xml)	
<Add more rows if applicable>	

1.4 Study-related Metadata

Study Identifier	Protocol Number	National Clinical Trial (NCT) Number	Data Cut-off Date	Database Lock Date	Study Status (at Time of Data Cut-off Date)	Comments
<Add more rows if applicable>						

2. Study Description

2.1 List of Studies for which BIMO Clinical Data are Submitted

Study Identifier	Study Title	Study Phase	Comments
<Add more rows if applicable>			

3. Part I – Request for Clinical Study-level Information

3.1 Part I (Item A) – List of All Clinical Sites

The information below is included in the BIMO Part I (Item A) PDF deliverable for each of the major (i.e. pivotal) studies for sites that participated in the study (i.e. sites that have screened one subject with a signed informed consent).

Site Identifier	Current Principal Clinical Investigator Name (Prior Principal Clinical Investigator(s))	Site Address at Time of Clinical Study	Site Contact Information at Time of Clinical Study
SITEID	LASTNAME, FRSTNAME, MINITIAL	FACILITY NAME STREET CITY, STATE, POSTAL COUNTRY	PHONE FAX EMAIL
*Site terminated, or clinical investigator changed at the request of the sponsor before study completion.			

Additional information:

- <Add information as needed>
- <Add information as needed>

3.2 Part I (Item B) – Entities Contact Information and Trial-related Files Location

The information below is included in the BIMO Part I (Item B) PDF deliverable for each of the major (i.e. pivotal) studies.

Entities Type	Name of Entities	Study-related Activities	Address	Location of Study-related Documents and Records Generated (Physical and/or in TMF)	Contact Information CONTACT NAME (If Available): PHONE: FAX (If Available): EMAIL:	Responsible for Documentation	
						Created by	Approved by

Additional information:

- <Add information as needed>
- <Add information as needed>

3.3 Part I (Item C1) – Protocol and Amendments

Study Identifier	List All Protocol/Local Amendment Version Numbers	If Local Amendment (List Country)	Date Effective	Location Reference (Items Included In)
<Add more rows if applicable>				

Additional information:

- <Add information as needed>
- <Add information as needed>

3.4 Part I (Item C2) – Annotated Case Report Form (aCRF)

Study Identifier	Annotated Case Report Form (aCRF)	Location Reference
<Add more rows if applicable>		

Additional information:

- <Add information as needed>
- <Add information as needed>

4. Part II – Subject-level Data Line Listings by Clinical Site

4.1 Subject-level Listings

The following requested listings are presented using <Choose either Option A: By Study, By Site and By Listing OR Option B: By Study, By Site and by Subject Profile.>.

Study Identifier	Listing No.	Listing Title	Comments
ALL	1	Listing 1: Listing of Consented Subjects	
ALL	2	Listing 2: Listing of Treatment Assignment	
ALL	3	Listing 3: Listing of Discontinuations	
ALL	4	Listing 4: Listing of Study Population	
ALL	5	Listing 5: Listing of Inclusion and Exclusion Criteria	
ALL	6	Listing 6: Listing of Adverse Events and Deaths	
ALL	7	Listing 7: Listing of Protocol Deviations (all, i.e. Non-Important and Important, Protocol Deviations)	
ALL	8	Listing 8: Listing of Efficacy Endpoints	
ALL	8a	Listing 8a: Listing of Efficacy Endpoints Collected as Clinical Events	
ALL	9	Listing 9: Listing of Concomitant Medications	
ALL	10	Listing 10: Listing of Safety Monitoring	
ALL	10a	Listing 10a: Listing of Safety Endpoints Collected as Clinical Events	

Additional information for listings 1 to N <N= no. of listings included in Part II>:

- Splitting logic: Provide details of any splitting logic that has been used in the presentation of listings, e.g. for labs by site, subject, CAT/SUBCAT
- <Add information as needed>

4.2 Primary, Key Secondary Endpoints and Clinical Events

The following table provides information about Primary, Key Secondary Endpoints in Part II Listing 8 and corresponding endpoints collected as clinical events in Part II Listing 8a for each of the major (i.e. pivotal) studies.

Study Identifier	Endpoint Category / Clinical Events	Endpoint / Clinical Events Description	Criterion	Listing No.
<Add more rows if applicable>				

4.3 Safety Monitoring and Clinical Events

The following table provides information about safety monitoring in Part II Listing 10 and corresponding endpoints collected as clinical events in Part II Listing 10a for each of the major (i.e. pivotal) studies.

Study Identifier	Safety Monitoring / Clinical Events	Criterion	Listing No.
<Add more rows if applicable>			

5. Part III – Summary-level Clinical Site Dataset

5.1 Treatment Variables

For: <Study Identifier>

Use of ADaM Treatment Variables in the CSR Analysis

ARM versus TRTxxP

- Are the values of ARM equivalent in meaning to the values of TRTxxP?
<Yes/No> (insert additional text here or a mapping table or a figure)

ACTARM versus TRTxxA

- If TRTxxA is used, then are the values of ACTARM equivalent in meaning to the values of TRTxxA?
<Yes/No> (insert additional text here or a mapping table or a figure)
- Are both planned and actual treatment variables used in the analysis?
<Yes/No> (insert additional text here or a mapping table or a figure)

Use of ADaM Treatment variables in the BIMO analysis dataset (clinsite)

- Are both planned and actual treatment variables used in the BIMO analysis?
<Yes/No> (insert additional text here or a mapping table or a figure)

5.2 Primary and Key Secondary Endpoints Summary

The following table provides information about the endpoints summarized in the Part III clinsite dataset for each of the major (i.e. pivotal) studies.

Study Identifier	Endpoint Category	Endpoint Criterion	Censor Criterion	Endpoint Criterion	Censor Criterion
	Endpoint Type [ENDPTYPE]	[TRTEFFR1]	[CENSOR1]	[TRTEFFR2]	[CENSOR2]
	Endpoint Description [ENDPOINT]	Safety Population	Safety Population	Efficacy Population	Efficacy Population
<Add more rows if applicable>					

5.3 Clinical Site Dataset Supporting Information

The following table provides supporting information about Part III Summary-level Clinical Site Dataset for each of the major (i.e. pivotal) studies.

Study Identifier	Variable Name [Variable Label]	Description
	/	
	General	
<Add more rows if applicable>		

5.4 Conformance Inputs

The information below describes the validation inputs used to evaluate conformance for the clinsite dataset (clinsite.xpt) and its define.xml for each of the major (i.e. pivotal) studies.

Specify the software name and version used to evaluate conformance on the clinical site dataset (clinsite.xpt).

(Text here) <Choose one: SAS <Version no. >/Pinnacle 21 <Version no. >/Manual review/<Others specify>

Specify the version of the validation guidance used (i.e. CDISC, FDA BIMO TCG, with version and date) for the clinical site dataset (clinsite.xpt).

(Text here) <Example: FDA BIMO Technical Conformance Guidance Version 3.0, 11th August 2022>

Specify the software name and version used to evaluate conformance on the clinical site dataset (define.xml).

(Text here) <Choose one: SAS <Version no. >/Pinnacle 21 <Version no. >/Manual review/<Others specify>

Specify the version of the validation guidance used (i.e. CDISC, FDA BIMO TCG, with version and date) for the clinical site dataset (define.xml).

(Text here) <Example: FDA BIMO Technical Conformance Guidance Version 3.0, 11th August 2022>

5.5 Conformance Issues Summary

The following table provides summary from the validation input and checks used to evaluate conformance for the clinsite dataset (clinsite.xpt) and its define.xml for each of the major (i.e. pivotal) studies.

Study Identifier	Dataset	Issue (Data and/or define.xml)	Diagnostic Message	Explanation
<Add more rows if applicable>				

6. External Datasets and Sources

The following table lists all external datasets sources that are used as an input for the BIMO clinical data for each of the major (i.e. pivotal) studies.

External Datasets Sources	Description	Source	Comments
Screen failure file	Consented screen failure subject information file	<Sponsor/CRO system – used to capture this information>	Not collected on the CRF
Minor Protocol Deviations	Non-important Protocol Deviations	<Sponsor/CRO system – used to capture this information>	Not collected on the CRF
Financial Disclosure Amount	Financial disclosure amount (US\$) by site containing disclosures for the clinical investigator and all sub-investigators	BIMO Module 1: FD Tracker	Not collected on the CRF
Principal Clinical Investigator and Site Contact Information	Investigator Last Name Investigator First Name Investigator Middle Initial Investigator Phone Number Investigator Fax Number Investigator Email Address Country State City Postal Code Street Address Street Address Continued	<Sponsor/CRO system – used to capture this information>	Not collected on the CRF
Subject Site transfer information	Subject Site transfer information	<Sponsor/CRO system – used to capture this information>	Not collected on the CRF
<Add more rows if applicable>			

7. Site-specific Matters

7.1 Site Concerns

The following table provides site information related to site concerns and site additional information for the sites that may/may not be present in the BIMO clinical data (Part I - Clinical study-level information, Part II - Subject-level data line listings by clinical site and Part III - Summary-level clinical site dataset) for each of the major (i.e. pivotal) studies.

Study Identifier	Site # with Concerns (If any)* <Grouped by Country Code>	Comments
<Add more rows if applicable>		

Note: *Only sites with site concerns are listed.

7.2 Subjects Transferred Between Sites

The following table provides information related only to subjects that transferred between sites. This information is used in the BIMO clinical data (Part I - Clinical study-level information, Part II - Subject-level data line listings by clinical site and Part III - Summary-level clinical site dataset) for each of the major (i.e. pivotal) studies.

Study Identifier	Subject Identifier	Enrolled Site #	Switch Site #	Switch Date <DDMMYYYY>	Reason for Transfer	Comments
<Add more rows if applicable>						

Note: For BIMO Requests Part I (Item A), II and III, the sponsor has considered these subjects under their <enrolled/switched> site.

7.3 Identical Site ID Used in Multiple Studies

Site #	Study Identifiers	Comments
<Add more rows if applicable>		

8. Site Summary

The following table provides a site summary (total number of sites, sites that have enrolled at least 1 subject with a signed informed consent, sites that have only screen failed subjects with a signed informed consent and site additional information <freeform text>) for the sites used in the BIMO clinical data (Part I - Clinical study-level information, Part II - Subject-level data line listings by clinical site and Part III - Summary-level clinical site dataset) for each of the major (i.e. pivotal) studies.

Study Identifier	Site Summary	Comments
<Add more rows if applicable>		

9. eCTD Folder Structure Skeleton for BIMO Items in MODULE 5

MODULE 5 – CLINICAL STUDY REPORTS

5.3.5 Reports of Efficacy and Safety Studies (Indication)

5.3.5.4 Other Study Reports

- BIMO
 - For each of the major (i.e. pivotal) studies [unique study identifiers from DM.STUDYID in ascending order separated by a comma]
 - Part I (Item A) – List of All Clinical Sites
[<Study #> Listing All Clinical Sites.pdf]
 - Part I (Item B) – Entities Contact Information and Trial-related Files Location
[<Study #> Contracted Clinical Study-Related Activities.pdf]
 - Part I (Item C1) – Protocol and Amendments
[<Study #> Protocol and Amendments.pdf]
 - Part I (Item C2) – Annotated Case Report Form (aCRF)
[<Study #> Sample Annotated CRF.pdf]
 - Part II – Subject-level Data Line Listings by Clinical Site
[<Study #> Data Line Listings by Clinical Site.pdf]
 - Site-level Part III – For all major (i.e. pivotal) studies combined
 - Summary-level Clinical Site Dataset [clinsite.xpt]
 - Data Definition file [define.xml] and Stylesheet [Stylesheet filename with file extension]
 - BIMO Data Reviewer's Guide [bdrp.pdf]

10. **Appendix**

Provide supplemental information in the Appendix.