

Bioresearch Monitoring (BIMO) Data Reviewer's Guide

Sample Drug Company, Inc.

Example_Project3

sBLA: 00003

List of Studies Included in the BIMO Clinical Data
Application:

Study1 <165789>

Study2 <265789>

Study3 <365789>

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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 application 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 Supplemental Biologics license application (sBLA) 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 section 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

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	February 2018
Bioresearch Monitoring Technical Conformance Guide	Version 3.0, 11 th August 2022
Summary-level Clinical Site Dataset definition file (define.xml)	Version 2.1

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
165789	165789	NCT00808067	01DEC2020	01JAN2021	Study Completed	N/A
265789	265789	NCT00808068	01JAN2021	01FEB2021	Study Completed	N/A
365789	365789	NCT00808069	01FEB2021	01MAR2021	Study Completed	N/A

2. Study Description

2.1 List of Studies for which BIMO Clinical Data are Submitted

Study Identifier	Study Title	Study Phase	Comments
165789	A Phase III, multicenter, 12 week open-label study to investigate Pharmacokinetics of test drug in infants with genetically diagnosed spinal muscular atrophy	PHASE III TRIAL	N/A
265789	A Phase III, multicenter, 24 week open-label study to investigate Pharmacokinetics of test drug in infants with genetically diagnosed spinal muscular atrophy	PHASE III TRIAL	N/A
365789	A Phase III, multicenter, 48 week open-label study to investigate Pharmacokinetics of test drug in infants with genetically diagnosed spinal muscular atrophy	PHASE III TRIAL	N/A

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	Total Number of Subjects Enrolled at a Site
SITEID	LASTNAME, FRSTNAME, MINITIAL	FACILITY NAME STREET CITY, STATE, POSTAL COUNTRY	PHONE FAX EMAIL	Count (number >= 0)
*Site terminated, or clinical investigator changed at the request of the sponsor before study completion.				

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

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)
165789	Version 2 (FINAL)	N/A	12DEC2008	Included in the application (refer to section 9)
	Amendment 1	Canada	05SEP2008	Included in the application (refer to section 9)
	Version 1	N/A	28JUN2008	Included in the application (refer to section 9)
265789	Version 2 (FINAL)	N/A	26APR2009	Included in the application (refer to section 9)
	Amendment 1	USA	31OCT2008	Included in the application (refer to section 9)
	Version 1	N/A	01AUG2008	Included in the application (refer to section 9)
365789	Version 1 (FINAL)	N/A	28JUN2018	Appendix 16 of CSR

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

Study Identifier	Annotated Case Report Form (aCRF)	Location Reference
ALL	Final aCRF	It is located in the datasets folder (tabulations\sdtm) of the study

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

4.1 Subject-level Listings

The following requested listings are presented using Option A: By Study, By Site and By Listing.

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 Pharmacokinetic Endpoints (Primary)	There are no Primary and Key Secondary Efficacy Endpoints. There are only Primary Pharmacokinetic endpoints.
165789 and 265789	8a	Listing 8a: Listing of Pharmacokinetic Endpoints Collected as Clinical Events	Not provided: no potential Pharmacokinetic Endpoints were collected as clinical events
365789	8a	Listing 8a: Listing of Pharmacokinetic 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	Not provided: no additional adjudication beyond the standard study data verification by clinical monitors
ALL	11	Listing 11: Listing of Blood Pressure Levels	Additional Listing
ALL	12	Listing 12: Listing of All Blood Pressure Measurement Device used	Additional Listing

Additional information for listings 1 to 12:

- Splitting logic: – For each of the major (i.e. pivotal) studies, listings 1 to 12 are split into 3 Sub-parts (Part 1: From Site 1000 – 1999, Part 2: From Site 2000 – 2999, Part 3: From Site 3000 – 3999)

4.2 Primary Endpoints and Clinical Events

The following table provides information about Primary 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.
165789	Co-primary Pharmacokinetic	Steady-state maximum serum concentration (Cmax) at Week 12 And Steady-state trough serum concentration (Ctrough) at Week 12	For Co-Primary Pharmacokinetic Endpoint 1 at Week 12: Steady-state maximum serum concentration (Cmax) (ADPK.AVAL (where ADPK.PARAMCD='CMAX' and ADPK.AVISIT='Week 12')) For Co-primary Pharmacokinetic Endpoint 2 at Week 12: Steady-state trough serum concentration (Ctrough) (ADPK.AVAL (where ADPK.PARAMCD='CTROUGH' and ADPK.AVISIT='Week 12'))	8
265789	Co-primary Pharmacokinetic	Steady-state maximum serum concentration (Cmax) at Week 24 And Steady-state trough serum concentration (Ctrough) at Week 24	For Co-primary Pharmacokinetic Endpoint 1 at Week 24: Steady-state maximum serum concentration (Cmax) (ADPK.AVAL (where ADPK.PARAMCD='CMAX' and ADPK.AVISIT='Week 24')) For Co-primary Pharmacokinetic Endpoint 2 at Week 24: Steady-state trough serum concentration (Ctrough) (ADPK.AVAL (where ADPK.PARAMCD='CTROUGH' and ADPK.AVISIT='Week 24'))	8

Study Identifier	Endpoint Category /Clinical Events	Endpoint / Clinical Events Description	Criterion	Listing No.
365789	Co-primary Pharmacokinetic	Steady-state maximum serum concentration (Cmax) at Week 48 And Steady-state trough serum concentration (Ctrough) at Week 48	For Co-primary Pharmacokinetic Endpoint 1 at Week 48: Steady-state maximum serum concentration (Cmax) (ADPK.AVAL (where ADPK.PARAMCD='CMAX' and ADPK.AVISIT='Week 48')) For Co-primary Pharmacokinetic Endpoint 2 at Week 48: Steady-state trough serum concentration (Ctrough) (ADPK.AVAL (where ADPK.PARAMCD='CTROUGH' and ADPK.AVISIT='Week 48'))	8
365789	Clinical Events	Pharmacokinetic Endpoints collected as Clinical Events	Clinical event date of event (ADCE.CESTDTC), adjudicated (ADCE.CEYN=Yes/No by adjudication committee), date of adjudication (ADCE.CEASTDTC) and the outcome of the adjudication process (ADCE.CEAOUT).	8a

4.3 Safety Monitoring

The following table provides information about safety monitoring in Part II Listing 10 for each of the major (i.e. pivotal) studies.

Study Identifier	Safety Monitoring	Criterion	Listing No.
ALL	Labs	Lab Test- ADLB.PARAM [All Lab test], Analysis Visit - ADLB.AVISIT, Result/ Standard Units ADLB.LBSTRESC, ADLB.LBSTRESU>	10.1
ALL	Vital Signs	VS Test- ADVS.PARAM[All VS Test], Analysis Visit - ADVS.AVISIT, Result/ Standard Units ADVS.AVALC, ADVS. VSSTRESU>	10.2
ALL	ECG	ECG Test- ADEG.PARAM(All ECG Test), Analysis Visit -ADEG.AVISIT, Result/ Standard Units ADEG.EGSTRESC, ADEG.EGSTRESU>	10.3

5. Part III – Summary-level Clinical Site Dataset

5.1 Treatment Variables

For: 165789, 265789 and 365789

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, ARM and TRT01P are equivalent.

ACTARM versus TRTxxA

- If TRTxxA is used, then are the values of ACTARM equivalent in meaning to the values of TRTxxA?

Yes, ACTARM and TRT01A are equivalent.

Are both planned and actual treatment variables used in the analysis?

Yes, planned treatment arm is used in efficacy analysis and summarized by (ITT population) while actual treatment arm is used in safety analysis and summarized by (safety population).

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

Are both planned and actual treatment variables used in the BIMO analysis?

No, only planned treatment TRT01P arm is used for summarizing information within BIMO analysis dataset (clinsite) based on safety population and efficacy population only.

5.2 Primary 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 Type [ENDPTYPE] Endpoint Description [ENDPOINT]	Endpoint Criterion [TRTEFFR1] Safety Population	Censor Criterion [CENSOR1] Safety Population	Endpoint Criterion [TRTEFFR2] Efficacy Population	Censor Criterion [CENSOR2] Efficacy Population
165789	Endpoint Category Co-primary Pharmacokinetic Endpoint Type continuous Endpoint Description Steady-state maximum serum concentration (Cmax) at Week 12	Mean of the Co-primary Pharmacokinetic endpoint 1 at a given site for subjects in SAFPOP i.e. Mean of the Steady-state maximum serum concentration (Cmax) at Week 12 (Mean of ADPK.AVAL where ADPK.PARAMCD='CMA X' and ADPK.AVISIT='Week 12' and ADSL.SAFFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing	Mean of the Co-primary Pharmacokinetic endpoint 1 at a given site for subjects in EFFPOP i.e. Mean of the Steady-state maximum serum concentration (Cmax) at Week 12 (Mean of ADPK.AVAL where ADPK.PARAMCD='CMA X' and ADPK.AVISIT='Week 12' and ADSL.ITTFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing
165789	Endpoint Category Co-primary Pharmacokinetic Endpoint Type Continuous Endpoint Description Steady-state trough serum concentration (Ctrough) at Week 12	Mean of the Co-primary Pharmacokinetic endpoint 2 at a given site for subjects in SAFPOP i.e. Mean of the Steady-state trough serum concentration (Ctrough) at Week 12 (Mean of ADPK.AVAL where ADPK.PARAMCD='CTROU GH' and ADPK.AVISIT='Week 12' and ADSL.SAFFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing	Mean of the Co-primary Pharmacokinetic endpoint 2 at a given site for subjects in EFFPOP i.e. Mean of the Steady-state trough serum concentration (Ctrough) at Week 12 (Mean of ADPK.AVAL where ADPK.PARAMCD='CTROU GH' and ADPK.AVISIT='Week 12' and ADSL.ITTFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing

Study Identifier	Endpoint Category Endpoint Type [ENDPTYPE] Endpoint Description [ENDPOINT]	Endpoint Criterion [TRTEFFR1] Safety Population	Censor Criterion [CENSOR1] Safety Population	Endpoint Criterion [TRTEFFR2] Efficacy Population	Censor Criterion [CENSOR2] Efficacy Population
265789	Endpoint Category Co-primary Pharmacokinetic Endpoint Type Continuous Endpoint Description Steady-state maximum serum concentration (Cmax) at Week 24	Mean of the Co-primary Pharmacokinetic endpoint 3 at a given site for subjects in SAFPOP i.e. Mean of the Steady-state maximum serum concentration (Cmax) at Week 24 (Mean of ADPK.AVAL where ADPK.PARAMCD='CMA X' and ADPK.AVISIT='Week 24' and ADSL.SAFFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing	Mean of the Co-primary Pharmacokinetic endpoint 3 at a given site for subjects in EFFPOP i.e. Mean of the Steady-state maximum serum concentration (Cmax) at Week 24 (Mean of ADPK.AVAL where ADPK.PARAMCD='CMA X' and ADPK.AVISIT='Week 24' and ADSL.ITTFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing
265789	Endpoint Category Co-primary Pharmacokinetic Endpoint Type Continuous Endpoint Description Steady-state trough serum concentration (Ctrough) at Week 24	Mean of the Co-primary Pharmacokinetic endpoint 4 at a given site for subjects in SAFPOP i.e. Mean of the Steady-state trough serum concentration (Ctrough) at Week 24 (Mean of ADPK.AVAL where ADPK.PARAMCD='CTROU GH' and ADPK.AVISIT='Week 24' and ADSL.SAFFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing	Mean of the Co-primary Pharmacokinetic endpoint 4 at a given site for subjects in EFFPOP i.e. Mean of the Steady-state trough serum concentration (Ctrough) at Week 24 (Mean of ADPK.AVAL where ADPK.PARAMCD='CTR OUGH' and ADPK.AVISIT='Week 24' and ADSL.ITTFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing

Study Identifier	Endpoint Category Endpoint Type [ENDPTYPE] Endpoint Description [ENDPOINT]	Endpoint Criterion [TRTEFFR1] Safety Population	Censor Criterion [CENSOR1] Safety Population	Endpoint Criterion [TRTEFFR2] Efficacy Population	Censor Criterion [CENSOR2] Efficacy Population
365789	Endpoint Category Co-primary Pharmacokinetic Endpoint Type Continuous Endpoint Description Steady-state maximum serum concentration (Cmax) at Week 48	Mean of the Co-primary Pharmacokinetic endpoint 5 at a given site for subjects in SAFPOP i.e. Mean of the Steady-state maximum serum concentration (Cmax) at Week 48 (Mean of ADPK.AVAL where ADPK.PARAMCD='CMA X' and ADPK.AVISIT='Week 48' and ADSL.SAFFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing	Mean of the Co-primary Pharmacokinetic endpoint 5 at a given site for subjects in EFFPOP i.e. Mean of the Steady-state maximum serum concentration (Cmax) at Week 48 (Mean of ADPK.AVAL where ADPK.PARAMCD='CMA X' and ADPK.AVISIT='Week 48' and ADSL.ITTFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing
365789	Endpoint Category Co-primary Pharmacokinetic Endpoint Type Continuous Endpoint Description Steady-state trough serum concentration (Ctrough) at Week 48	Mean of the Co-primary Pharmacokinetic endpoint 6 at a given site for subjects in SAFPOP i.e. Mean of the Steady-state trough serum concentration (Ctrough) at Week 48 (Mean of ADPK.AVAL where ADPK.PARAMCD='CTROU GH' and ADPK.AVISIT='Week 48' and ADSL.SAFFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing	Mean of the Co-primary Pharmacokinetic endpoint 6 at a given site for subjects in EFFPOP i.e. Mean of the Steady-state trough serum concentration (Ctrough) at Week 48 (Mean of ADPK.AVAL where ADPK.PARAMCD='CTR OUGH' and ADPK.AVISIT='Week 48' and ADSL.ITTFL='Y') per SITEID per ARM per ENDPOINT.	Set to missing

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] / General	Description
165789, 265789 and 365789	General	Out of all studies part of our application, we are only submitting BIMO clinical data for only these 3 studies (165789, 265789 and 365789) as discussed and agreed upon in our pre-submission meeting with the FDA dated 10Jan2023.
165789, 265789 and 365789	CENSOR1 [Censored Observations in SAFPOP] and CENSOR2 [Censored Observations in EFFPOP]	Study does not contain any time-to-event primary/key secondary endpoint, so these variables value will be missing in the clinical site dataset (clinsite.xpt) and mentioned in its define.xml.

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 clinical site dataset (clinsite.xpt).

Manual review

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).

FDA BIMO Technical Conformance Guidance Version 3.0, 11th August 2022

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

Manual review

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).

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
165789, 265789 and 365789	clinsite	Data and define.xml	For Variable NOIMPDEV, Variable Label in the dataset should match the variable label described in BIMO TCG.	As per the latest BIMO TCG (e.g. Version 3.0, 11th August 2022, the variable label length is 43 which is ≥ 40 and not as per eSub data requirement and hence we have modified the variable label and kept variable label length ≤ 40 ('Number of Non-Important Protocol Dev')
165789, 265789 and 365789	clinsite	Data and define.xml	Within the endpoint related variables (ENDPTYPE, ENDPOINT, TRTEFFR1, CENSOR1, TRTEFFR2, and CENSOR2) only primary PK endpoints are summarized.	Sponsor has provided only primary PK endpoints as this is the key endpoints to support the pharmacokinetic result of the study drug and moreover there are no primary efficacy endpoints defined within the study analysis.

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
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 system –used to capture this information	Not collected on the CRF
Subject Site Transfer Information	Subject Site Transfer Information	Sponsor system –used to capture this information	Not collected on the CRF

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
165789	CAN: 134667 – site terminated due to compliance issue	N/A
265789	USA: 135776 – site terminated due to compliance issue	N/A
365789	N/A	N/A

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 <DDMMMYYYY>	Reason for Transfer	Comments
123456	123456-100103-1020	100102	100103	15DEC2019	Subject moved to a new location.	N/A
123456	123456-100104-1020	100102	100104	19DEC2019	Subject moved to a new location.	N/A

Note:

- For BIMO Requests Part I (Item A), II and III, the sponsor has considered these subjects under their switched site.
- When a subject transfer multiple sites, the sponsor has considered these subjects only under their last switched site.

7.3. Identical Site ID Used in Multiple Studies

Site #	Study Identifiers	Comments
300315	165789 and 365789	N/A

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
165789	For BIMO Request Part I (Item A), II and III there are 200 sites ([160] sites that have enrolled at least 1 subject and [40] sites that have only screen failure subjects).	Note: sites that have enrolled a subject can also have screen failure subjects also.
265789	For BIMO Request Part I (Item A), II and III there are 220 sites ([190] sites that have enrolled at least 1 subject and [30] sites that have only screen failure subjects).	Note: sites that have enrolled a subject can also have screen failure subjects also.
365789	For BIMO Request Part I (Item A), II and III there are 140 sites ([100] sites that have enrolled at least 1 subject and [40] sites that have only screen failure subjects).	Note: sites that have enrolled a subject can also have screen failure subjects also.

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) study (165789, 265789 and 365789)**
 - 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
165789 and 265789: [<Study #>-Protocol-and-Amendments-Version#<details>.pdf]
365789: [Appendix 16 of CSR]
 - Part I (Item C2) – Annotated Case Report Form (aCRF)
ALL: [It is located in the datasets folder (tabulations\sdtm) of the study]
 - 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 [define2-0-0.xsl]
 - BIMO Data Reviewer's Guide [bdrdg.pdf]

10. Appendix

For defining Eligibility: Inclusion/Exclusion Criteria list mentioned in the finalized Protocol:

Code	Description
IC01	Signed written Informed Consent Form
IC02	Age 18-80 years at the time of signing Informed Consent Form
IC03	Life expectancy >=12 months
EC01	Pregnancy or lactation or intending to become pregnant during study
EC02	P23titive test results for chronic infection
EC03	Known history of HIV status