Statistical Programmer's role in Bioresearch Monitoring (BIMO) package creation:

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Abstract:

Food and Drug Administration (FDA) has suggested that Pharma companies and CROs to include the Bioresearch Monitoring (BIMO) package as part of their regulatory submissions. This BIMO package helps FDA's Office of Bioresearch Monitoring Inspectorate (OBMI) to carry out site-level inspections of clinical research sites to ensure the quality, integrity, and reliability of data, ensure Clinical trials are conducted as per applicable FDA's regulations and make sure that rights, welfare of participants involved in clinical trial are protected. The BIMO package mainly consists of Part I (General study related information and specific Clinical Investigator information, Part II (Subject level listings organised by site and listing type) Part III (Site Level Dataset). Statistical programmers play an important role in creation of Subject-Level Data Listings by Clinical Site, a Summary-Level Clinical Site Dataset (clinsite.xpt), Data definition file (define.xml) and BIMO Data Reviewer guide (bdrg.pdf) which are key components of BIMO package. This article provides details on Statistical Programmer's role in Bioresearch Monitoring (BIMO) package creation.

Introduction:

The pharmaceutical companies submit New Drug Applications (NDAs), Biologics License Applications (BLAs) to FDA to get approval for medicinal products.

These regulatory submissions include clinical trial data and the reports in support of research and marketing applications to FDA to demonstrate reasonable assurance that the Drug is safe and effective. However, these clinical data, and the reports provide information on Participant level data. FDA requires the site level information to conduct site inspections and launched BIMO Program to help with the site inspections.

The Food and Drug Administration (FDA) utilizes the Bioresearch Monitoring (BIMO) program, a multifaceted approach incorporating on-site inspections, data audits, and remote regulatory assessments. This comprehensive program is specifically designed to monitor all facets of the conduct and reporting of research regulated by the FDA. BIMO program mainly Monitors Sponsors/CROs/Study Monitors, Institutional Review Boards, Clinical Investigators and Non-Clinical Laboratories involved in Clinical Trial. The objectives of BIMO Program are three-fold. The first objective is to make sure that rights, welfare of participants involved in clinical trial are protected by ensuring compliance with informed consent and IRB requirements. The second objective Assure the quality, integrity, and reliability of data, and third objective is to ensure Clinical trials are conducted as per applicable FDA's regulations. [1]

Components of BIMO:

BIMO mainly consists of 3 Parts mentioned below.

Part 1: General study related information and specific Clinical Investigator information

Part II: Subject level listings organised by site and listing type

Part III: Site Level Dataset

Following Figure 1 provide an overview of the BIMO Components.

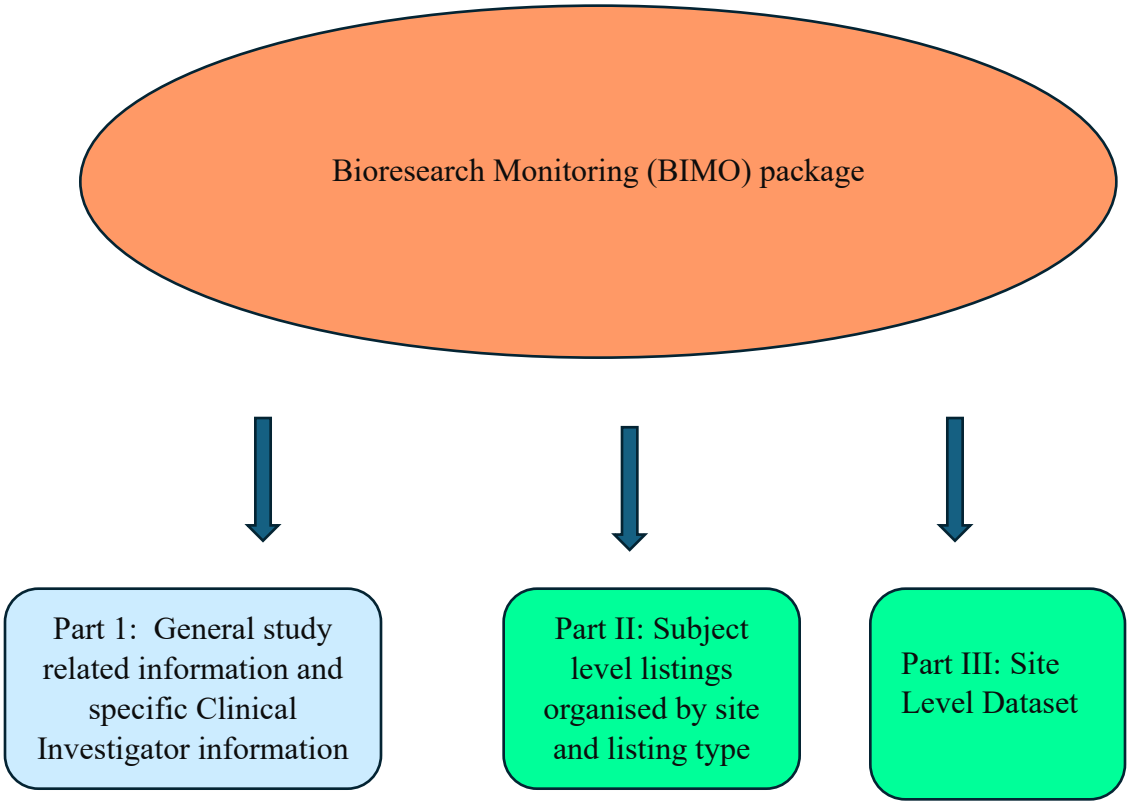

Figure 1: BIMO Components.

Part 1: General study related information and specific Clinical Investigator information:

Part 1 has Clinical Study-Level Information which include several items such as Item A-List of All Clinical Sites PDF, Item B-Entities (Vendor) Contact Information, Item C1-Protocol and Protocol Amendments, Item-C2 Annotated Case Report Form (aCRF), Item-C3 Clinical Data Flow Diagrams.

Following Figure 2 provide an overview of the Part 1 Components.

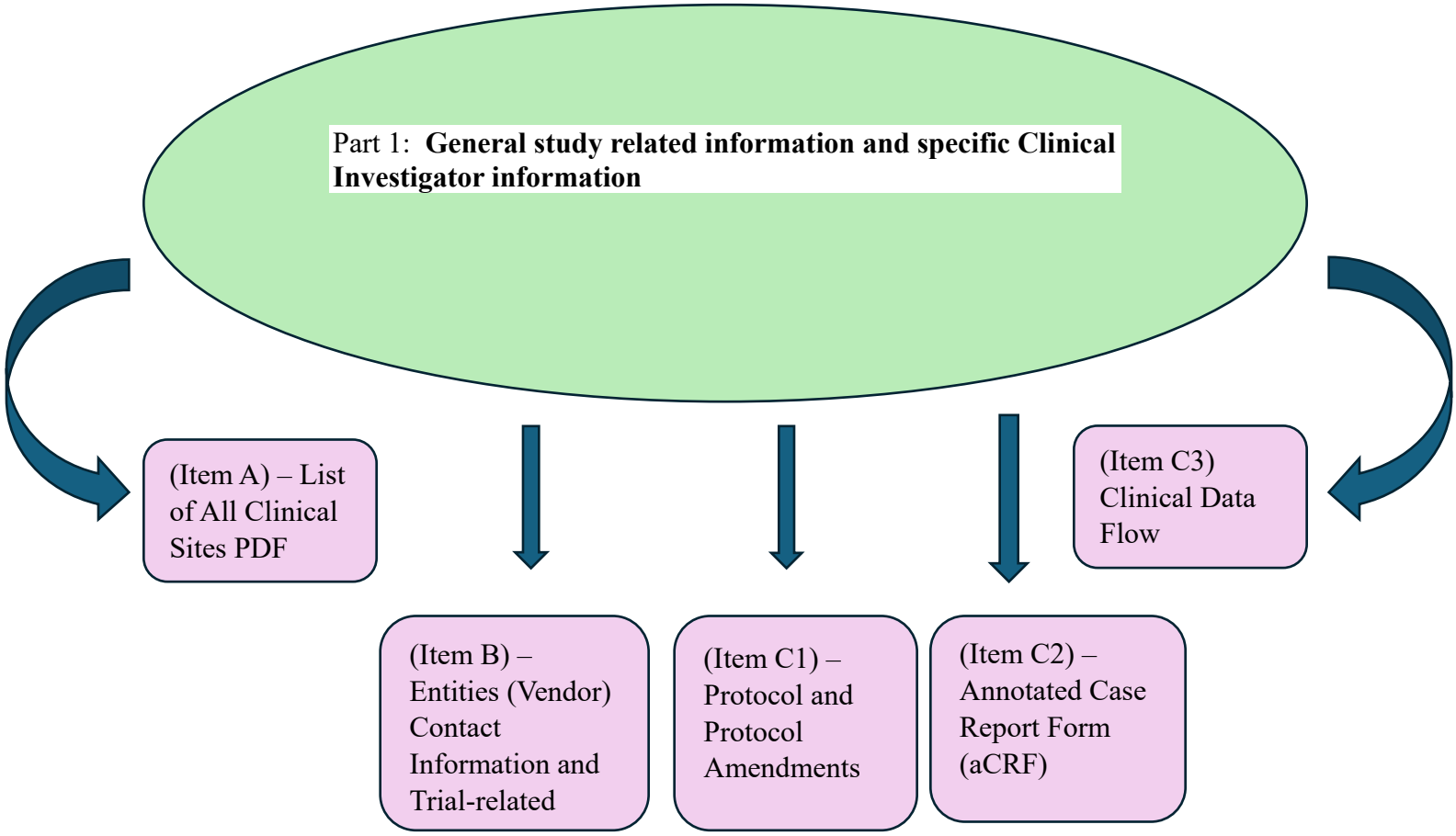

Figure 2: Part 1 Components.

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

Part I (Item A) has details about list of all clinical sites that participated in clinical studies every site and investigator, including contact information as mentioned below.

Protocol Number: A90182			
Site Identifier	Investigator Name (Prior Clinical Investigator(s))	Site Address at Time of Clinical Study (Updated Site Address when exists and available)	Site Contact Information at Time of Clinical Study (Updated Contact Information when exists and available)
SITEID	LASTNAME, FRSTNAME, MINITIAL	FACILITY NAME STREET CITY, STATE, POSTAL COUNTRY	PHONE FAX EMAIL

Table 1: Format for Clinical Site Lists

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

Part I (Item B) has details about List of all Vendors and CRO's to Whom Sponsor Has Contracted Clinical Study Related Activities, along with the location of key study documents such as monitoring plans, training records, and data analysis plans. The location of these study-related documents for each study should be mentioned and indicated with the details whether these were generated by the sponsor or a CRO. The contact information for individuals who can provide location updates should also be provided as mentioned below.

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
Vendor	Labcorp Central Laboratory Services Indianapolis	Central Laboratory Services	8211 SciCor Drive, Indianapolis, IN, 46214-2985 USA	Physical	Courtney Roberts 123-456-789 courtney.roberts@labcorp.com	Vendor	Sponsor
CRO	IQVIA LTD	Data Management (programming and coding)	3 Forbury Place, 23 Forbury Road, Reading RG1 3JH, United Kingdom	**TMF**	Uma Santosh 123-456-789 uma.santosh@iqvia.com	Vendor	Sponsor

Table 2: Entities (Vendor) Contact Information

Part I (Item C1) – Protocol and Protocol Amendments

Part I (Item C1) has details about protocol and protocol amendments. The Reviewer's Guide (RG) should have hyperlinks to protocol and protocol amendments. Following table has details of a sample protocol.

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Table 3: sample protocol

Part I (Item C2) – Annotated Case Report Form (aCRF): Part I (Item C2) has details about different versions of the case report forms, and the final version of the SDTM annotated case report Form. The Reviewer's Guide (RG) should have hyperlinks to aCRF. Following Figure has details of a sample aCRF.

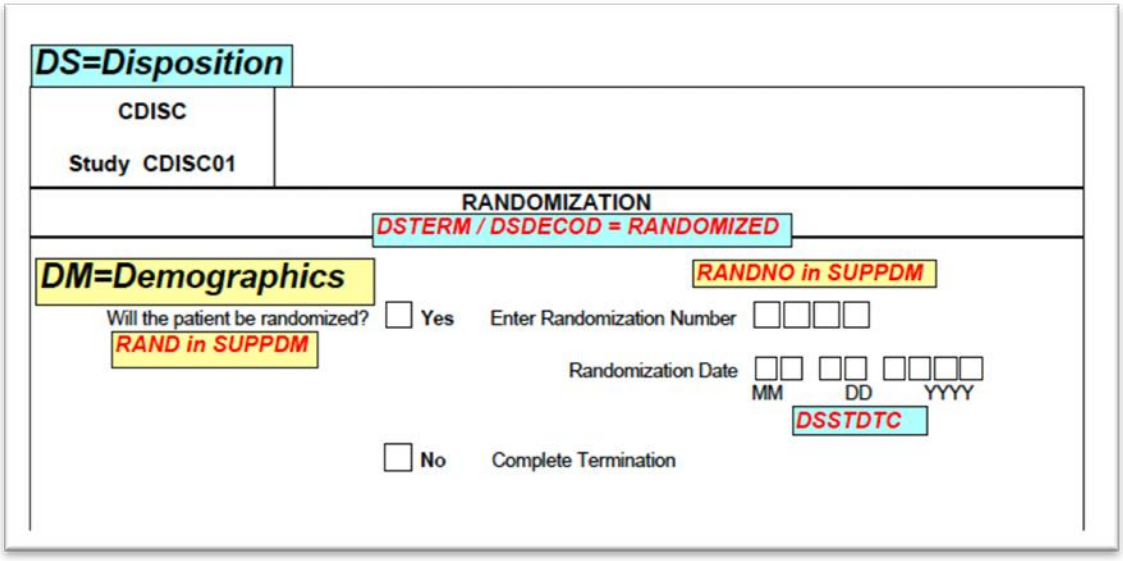
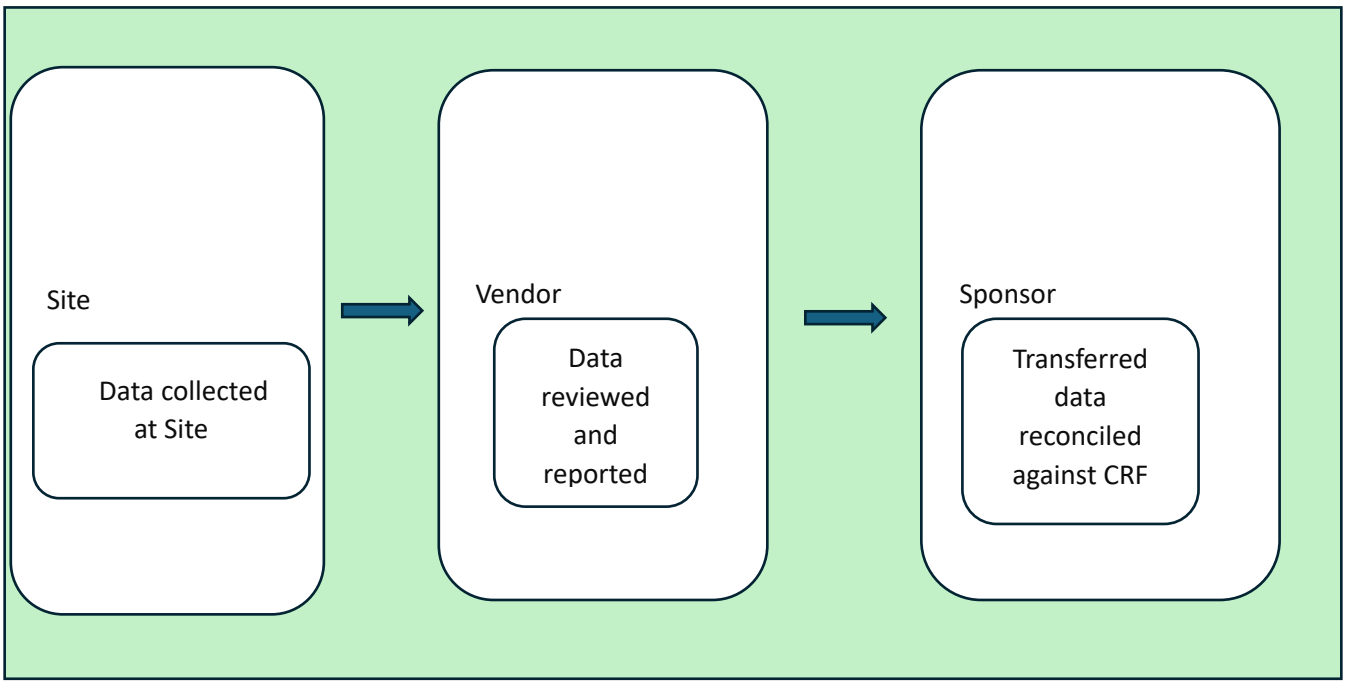


Figure 3: SDTM annotated case report Form.

Part I (Item C3) Clinical Data Flow Diagrams: The Data Flow Diagrams are included as appendix to Part I, in Item C3. They clarify source/movement/location of data. The Data Flow Diagrams are created by Data Management team, however Programming should review them.

Figure 4: Clinical Data Flow Diagram.



Part II: Subject level listings organised by site and listing type:

Part II presents subject-level data listings from pivotal studies, organized by clinical site. The data should include information on consented subjects, treatment assignment, discontinuations, study population, inclusion and exclusion criteria, adverse events, protocol deviations, efficacy endpoints, concomitant medications, and safety monitoring, as outlined in subsequent sections.

Following Figure provide an overview of the Part II Components.

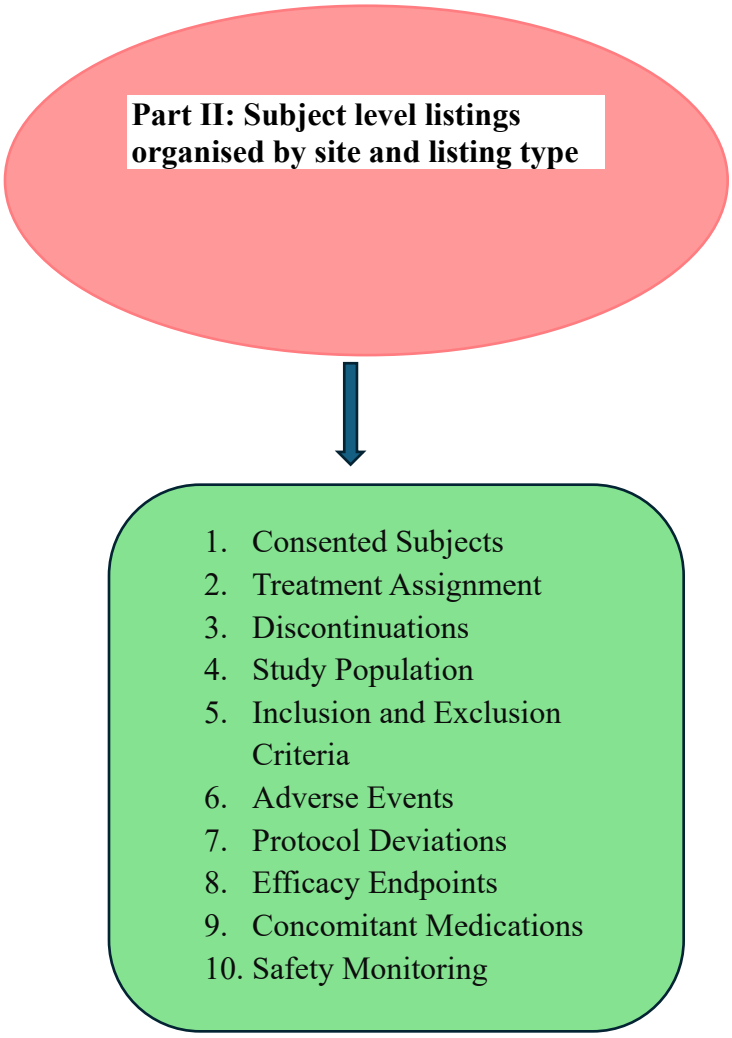


Figure 5: Part II Components.

1. **Consented Subjects (All Screened Participants):**

The listing should include all participants who provided informed consent to enroll in the study, including those subsequently identified as screen failures. For participants who consented but were not randomized to treatment or did not receive the investigational product, the specific reason for not being randomized or treated should be presented.

Participant Identifier	Randomized	Treated	Reason not randomized/not treated
101	No	No	Screen Failure

2. **Treatment Assignment (All Randomized Participants):**

This listing should provide the information about the treatment group to which the Participant was initially randomized. In case a Participant received treatment other than the assigned treatment, the actual treatment received should also be provided.

Participant Identifier	Randomized Treatment	Actual Treatment
101	DRUG ABC	DRUG ABC

3. **Discontinuations (All Randomized Participants):**

This listing should provide the information about All Participants that discontinued during run-in period, study treatment and study completely. For each Participant, the discontinuation date and discontinuation reason should be provided.

Participant Identifier	Treatment	Discontinuation Date	Reason for Study Discontinuation/Study treatment
101	DRUG ABC	12JAN2020	Adverse Event

4. Study Population (All Randomized Participants):

This listing should provide the information about the protocol-defined study population, especially the population in which each Participant was analyzed (such as Randomized, intent-to-treat, safety, Efficacy population). In case the Participants that did not meet inclusion criteria in the particular population, the reason from exclusion from the corresponding population should be provided.

Participant Identifier	Randomized Population	Reason for exclusion from Randomized population	Safety Population	Reason for exclusion from Safety population	Efficacy Population	Reason for exclusion from Efficacy population
101	Yes		Yes		No	Participant did not have at least one postbaseline Efficacy end point assessment

5. Inclusion and Exclusion Criteria (All Screened Participants):

This listing should provide the information about each Participant's inclusion and exclusion criterion mentioned in the protocol.

Participant Identifier	Met Inclusion or Exclusion Criteria	Inclusion or Exclusion Criteria Category	Inclusion or Exclusion Criteria Reason
101	No	Inclusion	Participant did not have minimum Fruit Preference score.

6. Adverse Events (All Treated Participants):

This listing should provide the information about all adverse events including serious adverse events (SAEs), non-serious adverse events (NSAEs), and deaths. It should also contain the date of occurrence, any treatments administered, the severity of the AE, whether the event was deemed serious by the clinical investigator and sponsor, and actions taken. The listing should indicate whether the AE led to the discontinuation of study treatment, the outcome, and the date of resolution.

Participant Identifier	Treatment group	Adverse Event Preferred Term	Adverse Event Start Date	Adverse Event End Date	severity	Serious	Action Taken	Adverse Event led to discontinuation of study therapy	Outcome of AE
101	DRUG ABC	Body pain	8JAN2020	9JAN2020	Moderate	Yes	Dose Changed	Yes	NOT RECOVERED/NOT RESOLVED

7. Protocol Deviations (All Important Protocol Deviations):

This listing should provide the information about all protocol deviations happened during the study. Each listed deviation should include a description and a clear categorization by the sponsor, indicating whether it was considered an important or non-important protocol deviation.

Participant Identifier	Treatment group	Deviation Start date	Deviation Category	Deviation Description
103	DRUG ABC	12FEB2021	NON-IMPORTANT PROTOCOL DEVIATION	Violation of Criteria mentioned in Protocol

8. Efficacy Endpoints (All Randomized Participants):

This listing should provide the information about primary and key secondary efficacy parameters or events. If the endpoints are derived, the raw data variables used to create the derived endpoint should be presented.

8a: Primary efficacy endpoint: If efficacy endpoints are assessed based on a laboratory, imaging, the listing should include test, visit, date of assessment and results.

Participant Identifier	Treatment group	Primary efficacy parameter	Date of Assessment	Visit	Result
109	DRUG ABC	Laboratory test	12FEB2021	Visit 3	Positive

8b: Secondary efficacy endpoint: If efficacy endpoints are collected as clinical events, the listing should include details about clinical event, event date, and the outcome of the adjudication.

Participant Identifier	Treatment group	Secondary efficacy event	date of event	date of adjudication	outcome of the adjudication
107	DRUG ABC	clinical event	13FEB2021	15FEB2021	Exacerbation

9. Concomitant Medications (All Treated Participants**):**

This listing should provide the information about all concomitant medications mentioned in the protocol. The medications start date, stop date, dose used, route of administration, and reason for administration should be included.

Participant Identifier	Treatment group	Medication Term	Medication Start Date	Medication End Date	Dose of Administration	Route of Administration	Reason for Administration
105	DRUG ABC	Tylenol	16MAR2023	18MAR2023	10mg	Oral	Fever

10. Safety Monitoring (All Treated Participants**):**

This listing should provide the information about safety parameters such as Laboratory, Vital signs electrocardiogram. It should also contain visit details, date of assessment and results.

Participant Identifier	Treatment group	Category of Test	Name of Test	Date of Test	Visit	Result	Reference Range Indicator
103	DRUG ABC	Hematology	Hemoglobin	18MAY2023	Visit 3	14g/dl	Normal

Part III: Site Level Dataset:

Part III include several files a 'clinsite' dataset in xpt format, an associated define file in xml format and Reviewer´s Guide.

Following Figure 3 provide an overview of the Part III Components.

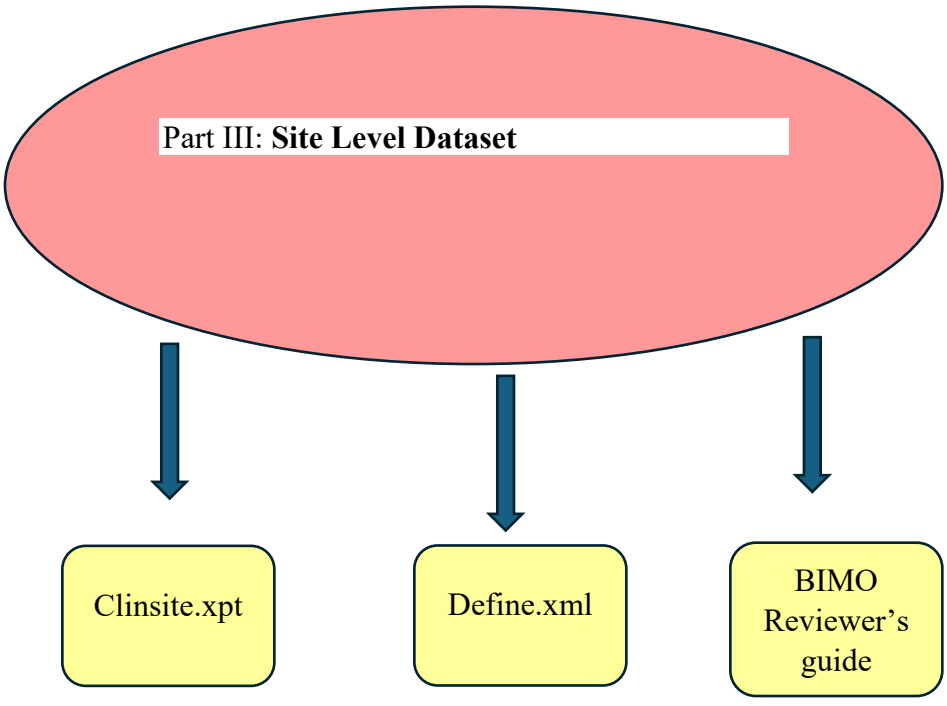


Figure 6: Part III Components.

Clinsite.xpt:

Clinsite is a single summary-level clinical site dataset that contains data from all pivotal studies. This dataset should include data from the safety population (SAFPOP) and primary efficacy population (EFFPOP), organized by clinical site and treatment arm for each major study. For sites involved in multiple studies, data must be reported independently for each study for clarity. The ClinSite dataset is created using a combination of sources. These include clinical study data in SDTM and ADaM formats. Additionally, a spreadsheet from Clinical Operations is incorporated, which contains investigator contact information and financial disclosures. Following is a sample clinsite.xpt file.

STUDYID	TITLE	SPONCNT	SPONSOR	IND	UNDERIND	NDA	BLA	SUPPNUM	SITE ID
STU-123	Randomized double blinded study	1	ABC Pharma	0987	Y	0789	-	-	007

ARM	COHORT	SAFPOP	EFFPOP	SCREEN	DISCSTUD	DISCTRT	END POINT	ENDP TYPE	TRT EFFR1	TRT EFFR2
DRUG ABC	-	31	25	52	7	5	Change from Baseline	Binary	1.27	1.32

CENSOR1	CENSOR2	NSAE	SAE	DEATH	IMPDEV	NOIMPDEV	FINLDISC	LAST NAME	FRST NAME
-	-	3	2	1	5	7	< $25,000	Wilson	Rick

MINITIAL	PHONE	FAX	EMAIL	COUNTRY	STATE	CITY	POSTAL	STREET	STREET1
A	123	321	Rw123@mail.com	USA	NC	Duram	27703	Main street	South lane

Clinsite Dataset Specification: Following is the specification with the details of variables as mentioned in in appendix 3 of FDA BIMO Technical Conformance Guide**.** [3]

S.NO.	Variable Name	Variable Label	Category and source
1	STUDYID	Study Identifier	Study Information from Protocol
2	TITLE	Study Title	Study Information from Protocol
3	SPONCNT	Sponsor Count	Sponsor Information from Protocol
4	SPONSOR	Sponsor Name	Sponsor Information
5	IND	IND Number	Regulatory Information
6	UNDERIND	Under IND	Regulatory Information
7	NDA	NDA Number	Regulatory Information
8	BLA	BLA Number	Regulatory Information
9	SUPPNUM	Supplement Number	Regulatory Information
10	SITEID	Study Site Identifier	Site Information
11	ARM	Description of Planned Treatment Arm	Study Design
12	COHORT	Description of Planned Cohort	Study Design
13	SAFPOP	Number of Subjects in Safety Population	Population
14	EFFPOP	Number of Subjects in Efficacy Population	Population
15	SCREEN	Number of Subjects Screened	Population
16	DISCSTUD	Number Subjects Discont. Study	Population/Disposition
17	DISCTRT	Number Subjects Discont. Study Treatment	Population/Disposition
18	ENDPOINT	Primary Endpoint	Outcome
19	ENDPTYPE	Primary Endpoint Type	Outcome
20	TRTEFFR1	Treatment Efficacy Result for SAFPOP	Outcomes/Results

S.NO.	Variable Name	Variable Label	Category and source
21	TRTEFFR2	Treatment Efficacy Result for EFFPOP	Outcomes/Results
22	CENSOR1	Censored Observations in SAFPOP	Outcomes/Results
23	CENSOR2	Censored Observations in EFFPOP	Outcomes/Results
24	NSAE	Number of Non-Serious Adverse Events	Safety Information
25	SAE	Number of Serious Adverse Events	Safety Information
26	DEATH	Number of Deaths	Safety Information
27	IMPDEV	Number of Important Protocol Deviations	Protocol Deviations
28	NOIMPDEV	Num of Non-Important Protocol Deviations	Protocol Deviations
29	FINLDISC	Financial Disclosure Amount	Regulatory/Disclosure
30	LASTNAME	Investigator Last Name	Investigator Information
31	FRSTNAME	Investigator First Name	Investigator Information
32	MINITIAL	Investigator Middle Initial	Investigator Information
33	PHONE	Investigator Phone Number	Investigator Contact
34	FAX	Investigator Fax Number	Investigator Contact
35	EMAIL	Investigator Email Address	Investigator Contact
36	COUNTRY	Country	Investigator Contact
37	STATE	State	Location Information
38	CITY	City	Location Information
39	POSTAL	Postal Code	Location Information
40	STREET	Street Address	Location Information
41	STREET1	Street Address Continued	Location Information

Table 4: Clinsite Dataset variables

The total of 41 variables were specified in the current BIMO Technical Conformance Guide, which are mandatory. Sponsors can add additional variables bases on study requirements.

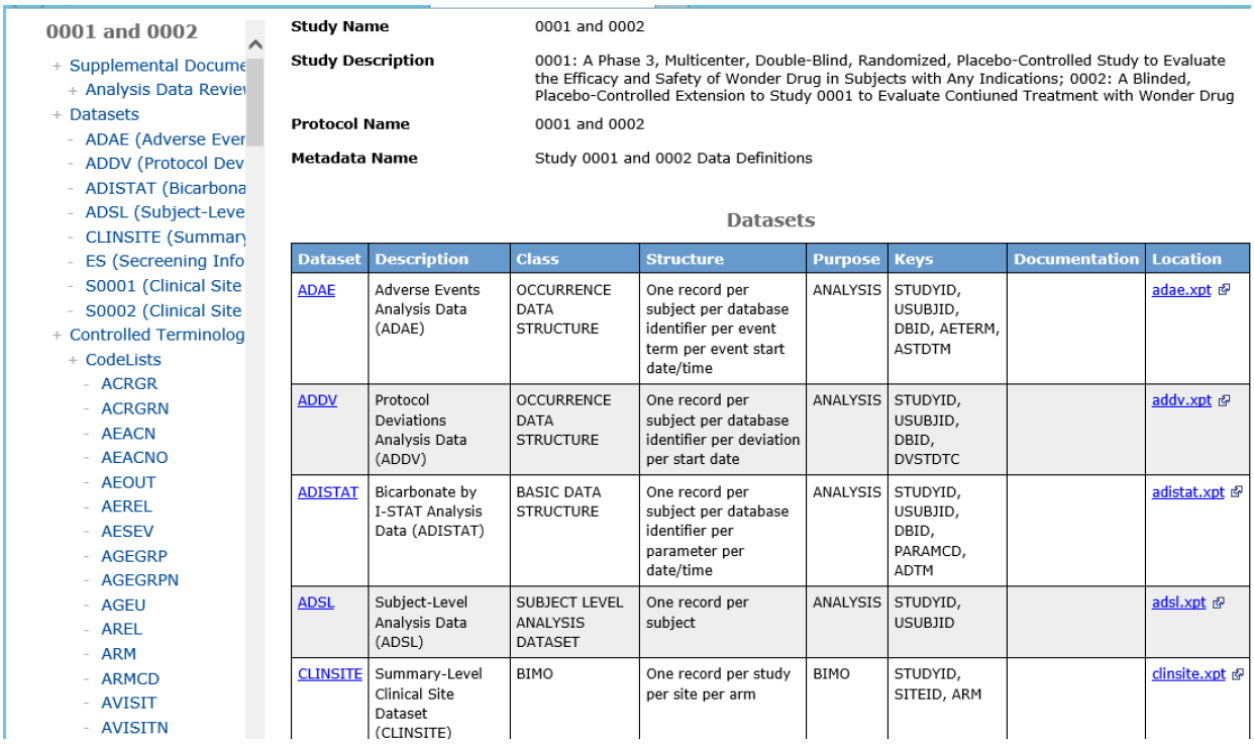
Categories: These variables can be classified into 10 categories as shown in Table 5 below.

S.NO.	Variable category	Description	Variables	Data Source
1)	Study level Information	Study title, sponsor details	STUDYTL, SPONCNT, SPONNAME	Protocols ADSL
2)	Regulatory Information	Scope of the application (IND/NDA/BLA), and relevant reference numbers	IND, UNDERIND, NDA, BLA, SUPPNUM	Regulatory affairs
3)	Study Treatment and Population	Arm or treatment group, cohorts, enrollment and study populations	ARM, COHORT, SAFPOP, EFFPOP	ADSL
4)	Screening information	Total number of Participants screened at particular site	SCREEN	ADSL
5)	Disposition Information	Participant treatment, study discontinuations at particular site	DISCSTUD, DISCTRT	ADSL
6)	Endpoints Information	primary endpoint and it's type whether it's "Continuous," "discrete," or "other"	ENDPOINT, ENDPTYPE	statistical analysis plan
7)	Efficacy Information	Population-wise endpoints, Treatment Safety, Efficacy results and censoring details	TRTEFFR1, TRTEFFR2, TRTEFFS1, TRTEFFS2, CENSOR1, CENSOR2	Protocol ADaM Efficacy Datasets such as ADRS, ADEFF, ADTTE
8)	Safety Information	SAEs, non-SAEs, death details	NSAE, SAE, DEATH	ADAE
9)	Protocol Violation	Important and non-Important protocol deviations	IMPDEV, NOIMPDEV	ADPRODEV
10)	Site-level Information	site details, financial disclosure and Primary clinical investigator contact information	SITEID, FINLDISC, LASTNAME, FRSTNAME, MINITIAL, PHONE, FAX, EMAIL, COUNTRY, STATE, CITY, POSTAL, STREET, STREET1	Site contact information and financial disclosure file provided by the Clinical Operations team

Table 5: Categories of Clinsite Dataset variables

Define.xml: Data Definition document describes Clinsite Dataset meta data. The define file can be Created using Pinnacle 21 or Macros. It contains comments, methods and calculations used for deriving the variables of Clinsite Dataset, including a description of source analysis datasets and associated variables used to derive the variables. The Define.xml have hyperlinks to Clinsite.xpt file and Reviewer's Guide (RG).

Sample Define.xml file:



0001 and 0002

- + Supplemental Docume
- + Analysis Data Revie
- + Datasets
  - ADAE (Adverse Ever
  - ADDV (Protocol Dev
  - ADISTAT (Bicarbona
  - ADSL (Subject-Leve
  - CLINSITE (Summary
  - ES (Secreening Info
  - S0001 (Clinical Site
  - S0002 (Clinical Site
- + Controlled Terminolog
  - + CodeLists
    - ACRGR
    - ACRGRN
    - AEACN
    - AEACNO
    - AEOUT
    - AEREL
    - AESEV
    - AGEGRP
    - AGEGRPN
    - AGEU
    - AREL
    - ARM
    - ARMCD
    - AVISIT
    - AVISITN

Study Name 0001 and 0002

Study Description 0001: A Phase 3, Multicenter, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Wonder Drug in Subjects with Any Indications; 0002: A Blinded, Placebo-Controlled Extension to Study 0001 to Evaluate Contiuned Treatment with Wonder Drug

Protocol Name 0001 and 0002

Metadata Name Study 0001 and 0002 Data Definitions

Datasets

Dataset	Description	Class	Structure	Purpose	Keys	Documentation	Location
ADAE	Adverse Events Analysis Data (ADAE)	OCCURRENCE DATA STRUCTURE	One record per subject per database identifier per event term per event start date/time	ANALYSIS	STUDYID, USUBJID, DBID, AETERM, ASTDTM		adae.xpt
ADDV	Protocol Deviations Analysis Data (ADDV)	OCCURRENCE DATA STRUCTURE	One record per subject per database identifier per deviation per start date	ANALYSIS	STUDYID, USUBJID, DBID, DVSTDTC		addv.xpt
ADISTAT	Bicarbonate by I-STAT Analysis Data (ADISTAT)	BASIC DATA STRUCTURE	One record per subject per database identifier per parameter per date/time	ANALYSIS	STUDYID, USUBJID, DBID, PARAMCD, ADTM		adistat.xpt
ADSL	Subject-Level Analysis Data (ADSL)	SUBJECT LEVEL ANALYSIS DATASET	One record per subject	ANALYSIS	STUDYID, USUBJID		adsl.xpt
CLINSITE	Summary-Level Clinical Site Dataset (CLINSITE)	BIMO	One record per study per site per arm	BIMO	STUDYID, SITEID, ARM		clinsite.xpt

BIMO Reviewer's guide: BIMO Reviewer´s Guide (RG) is a helpful document for FDA reviewers and includes the additional details about part I, II and III in the BIMO package. It should contain a description of the BIMO components with hyperlinks to Module 5 deliverables. and should be in pdf format. One of the important sections in Reviewer´s Guide is Section 7 which has details about Site-specific Matters. Section 7.1 provides site information related to site concerns and Section 7.2 provides has details about Subjects Transferred Between Sites.

PHUSE have released a package for BIMO RG which provides further information, template and examples. Please find the sample PHUSE Template below.

<Sponsor's Name> BIMO Data Reviewer's Guide

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BIMO Reviewer's guide: Section 9 of BIMO RG has description of the BIMO components with hyperlinks to Module 5 deliverables.

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

MODULE 5 – CLINICAL STUDY REPORTS

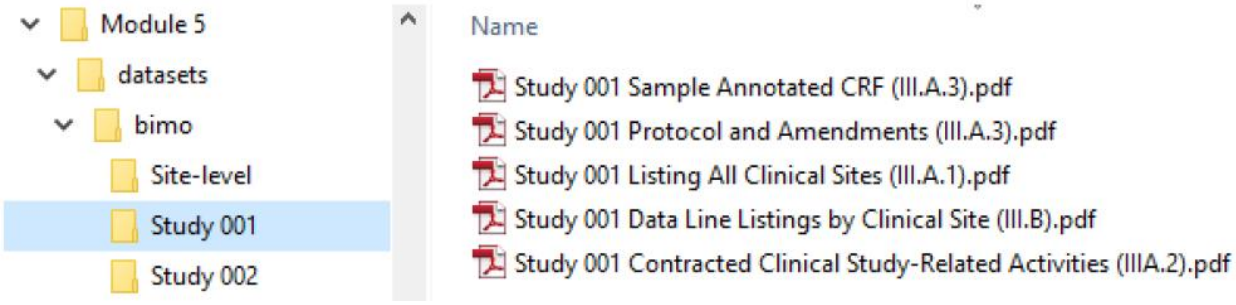
5.3.5 Reports of Efficacy and Safety Studies (Indication)

5.3.5.4 Other Study Reports

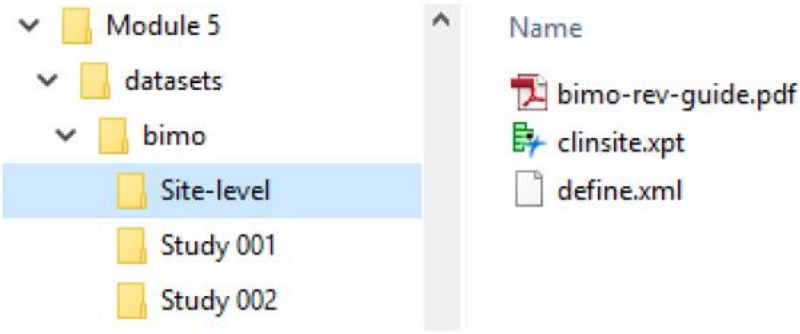
- BIMO
  - **For each of the major (i.e. pivotal) studies [unique study identifiers from DM.STUDYID in ascending order separated by a comma]**
  - Part I (Item A) – List of All Clinical Sites
    [<Study #> Listing All Clinical Sites.pdf]
  - Part I (Item B) – Entities Contact Information and Trial-related 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 **[bdrg.pdf]**

M5 Folder Structure:

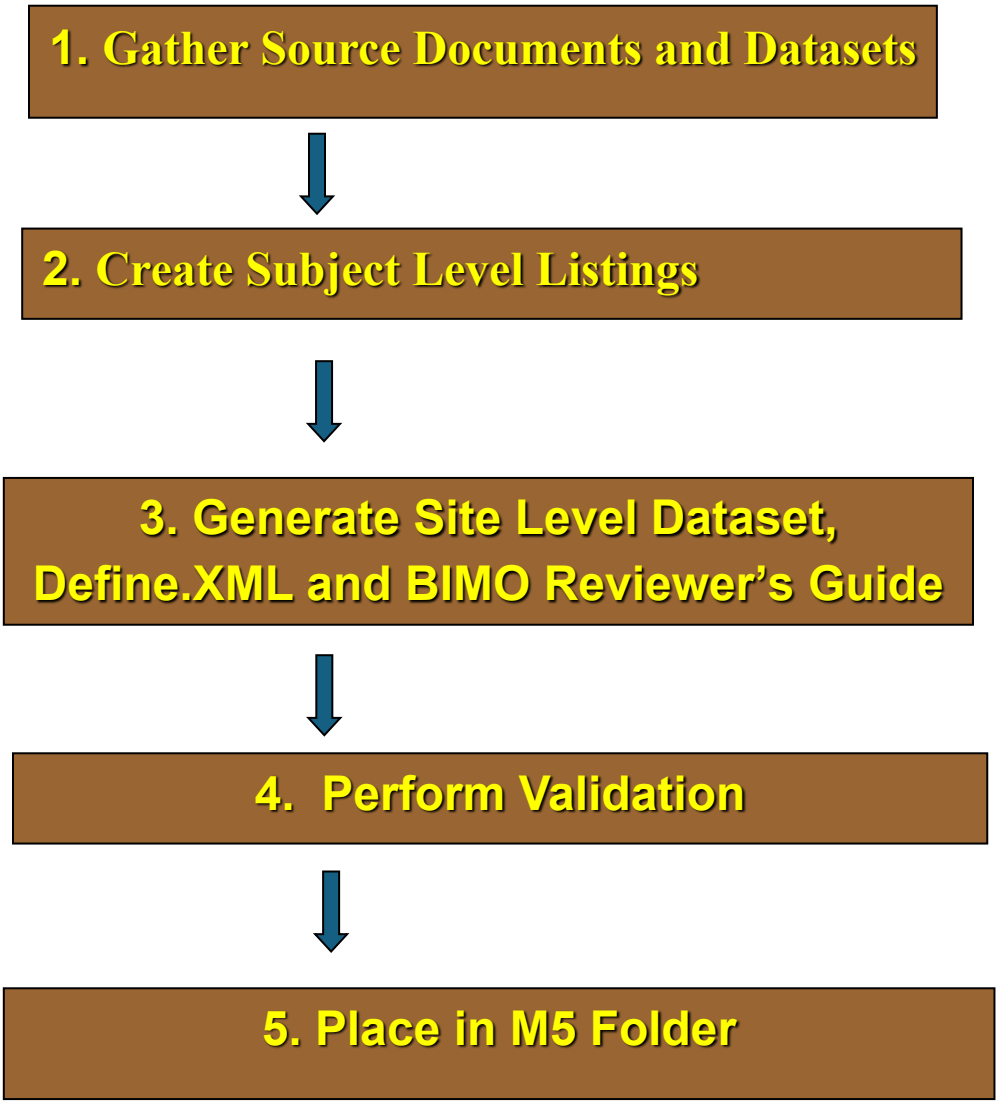
Clinical Study-Level Information and Subject-Level Line Listings by Clinical Site should be placed in the Study-level folder within Module 5 Folder Structure.



The Site-Level Dataset Define File and BIMO Data Reviewer's Guide should be placed in the Site-level folder within Module 5 Folder Structure.



Overview of BIMO Package creation: The following process flow diagram provides the Overview about different steps involved in BIMO Package creation.



Different Stake Holders involved in BIMO package creation: Following table has details about different stake holders and their responsibilities in BIMO package creation.

Study Documents and Deliverables	Clinical Operations	Study Management	Data Management	Statistics	Statistical Programming Team
Part I (Item A) List of All Clinical Sites PDF	✓				
Part I (Item B) Entities (Vendor) Contact Information and Trial-related Files Location	✓				
Part I (Item C1) Protocol and Protocol Amendments		✓			
Part I (Item C2) Annotated Case Report Form (aCRF)		✓			
Part I (Item C3) Clinical Data Flow Diagrams			✓		
Investigator Contacts List	✓				
Part III (Item A) Financial Disclosure Details	✓				
Participant level listings Mock shells				✓	
Participant level listings Programming				✓	✓
CLINSITE dataset Specification				✓	✓
CLINSITE dataset Programming				✓	✓
Define.XML Creation				✓	✓
BIMO Reviewer's guide Creation				✓	✓

Table 6: Categories of Clinsite Dataset variables

Guidance documents required for creation of BIMO package: Following documents has important guidance and information which will be helpful in BIMO package creation.

1) Bioresearch Monitoring Technical Conformance Guide.
2) Standardized Format for Electronic Submission for Marketing Applications Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for Center of Biologics Evaluation and Research Submissions.
3) Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions.
4) Bio-research Monitoring Data Reviewers Guide (BDRG) Package
5) Processes and Practices Applicable to Bioresearch Monitoring Inspections.

Conclusion:

FDA has introduced Bioresearch Monitoring (BIMO) program to help with their site-inspections. This program involves conducting site inspections, audits, and remote assessments to ensure regulatory compliance and data integrity in FDA-regulated research. It is designed to monitor all aspects of clinical trials and plays a critical role in protecting human rights and focuses on participant safety, regulatory adherence, and the reliability of submitted study data.

The BIMO submission package is structured into three main components: Part I consists of general study and clinical investigator information, including a list of clinical sites, vendor contact information, trial-related file locations, protocols, annotated case report forms, and clinical data flow diagrams. Part II contains subject-level listings organized by site and listing type, and Part III consists of site-level datasets, including clinsite.xpt, define.xml, and the BIMO Reviewer's Guide. Statistical programmers are primarily responsible for generating Parts II and III, includes detailed subject-level data outputs and structured datasets to support regulatory review. Statistical programmers are primarily involved in creating Part II and Part III of BIMO package.

References:

1) Bioresearch Monitoring Program Information https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/fda-bioresearch-monitoring-information/bioresearch-monitoring-program-information)

2) Office of Bioresearch Monitoring Inspectorate https://www.fda.gov/about-fda/oii-inspectorates/office-bioresearch-monitoring-inspectorate-obmi

3) Bioresearch Monitoring Technical Conformance Guide
https://www.fda.gov/media/85061/download

4) Standardized Format for Electronic Submission for Marketing Applications Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for Center of Biologics Evaluation and Research Submissions.

5) Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions.

6) Bio-research Monitoring Data Reviewers Guide (BDRG) Package
https://advance.hub.phuse.global/wiki/spaces/WEL/pages/26807874/Bio-research+Monitoring+Data+Reviewers+Guide+BDRG+Package

7) Processes and Practices Applicable to Bioresearch Monitoring Inspections.

CONTACT INFORMATION

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