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Zifo

Our Guide On Creating A Successful BIMO Data Package

Presented By
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Meet the Speaker

Arvind Sri Krishna MANI

Title: Delivery Manager Japan

Organization: Zifo RnD Solutions

Arvind comes with 15-year experience in the industry and has been with Zifo right from its inception. He has played a significant role in setting up multiple teams for providing clinical services within Zifo and has experience managing projects from across the globe.

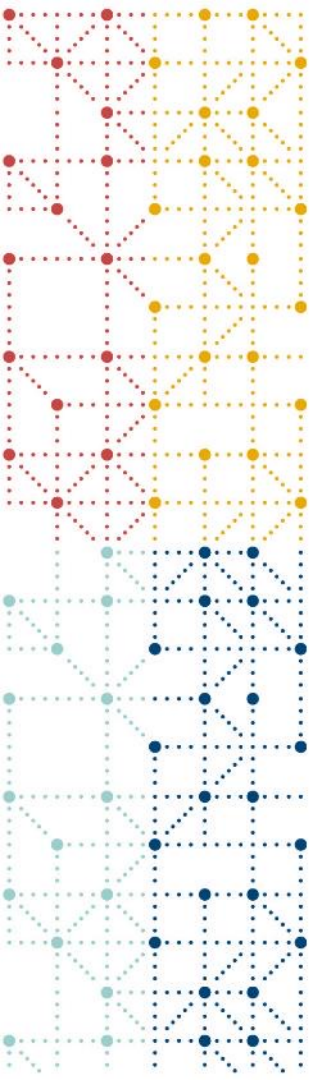
He loves the exposure and the variety in the projects by working with CROs, Technology providers and Pharma companies. He now acts as the delivery manager and point of contact for CDISC and Study Build Projects from Japan. Eager to visit Fujisan the week after the conference.

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

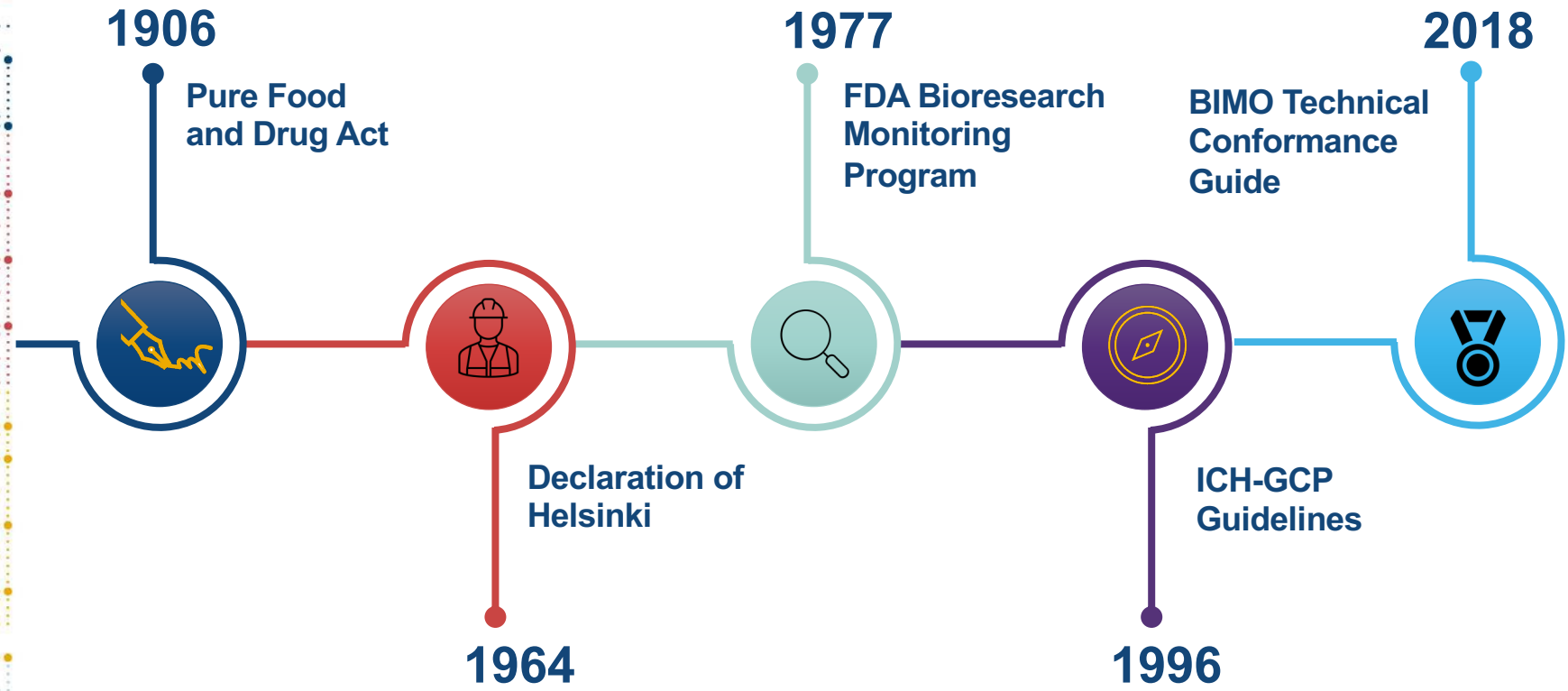
Agenda

1. What is BIMO?
2. BIMO Requirements
3. How Zifo approached BIMO - Examples
4. Challenges



What is BIMO?

History of BIMO



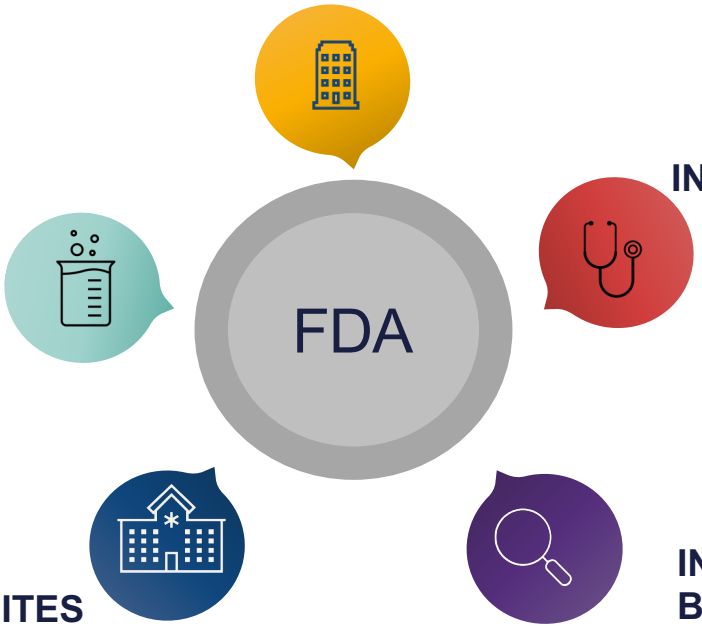
Objectives

- Protect the rights, safety and welfare of human research subjects
- Assure the quality, reliability and integrity of data collected

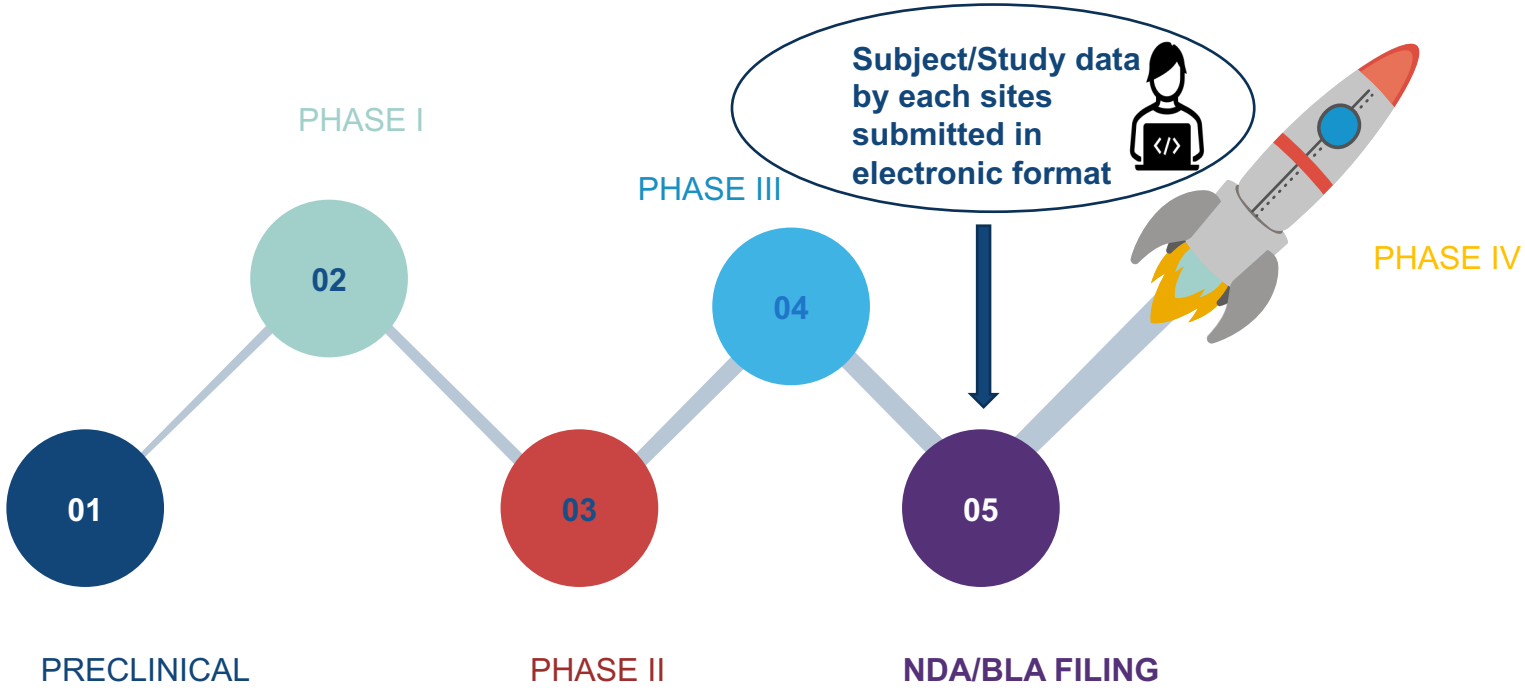
Bioresearch MOnitoring

Data audits

On-site inspections



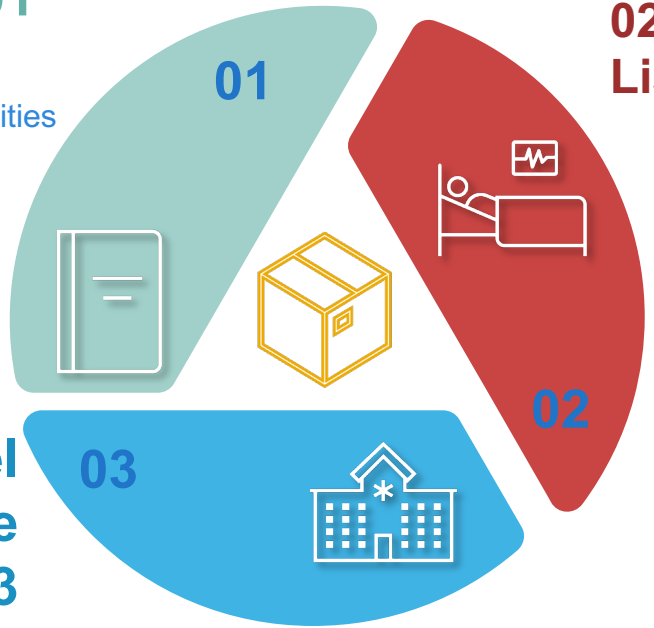
Role of Statistical Programmers in BIMO



BIMO Requirements

Study Level-01

- General Site Info
- List of Contracted activities
- Annotated CRFs
- Protocol documents



02 - Individual subject Listings by site

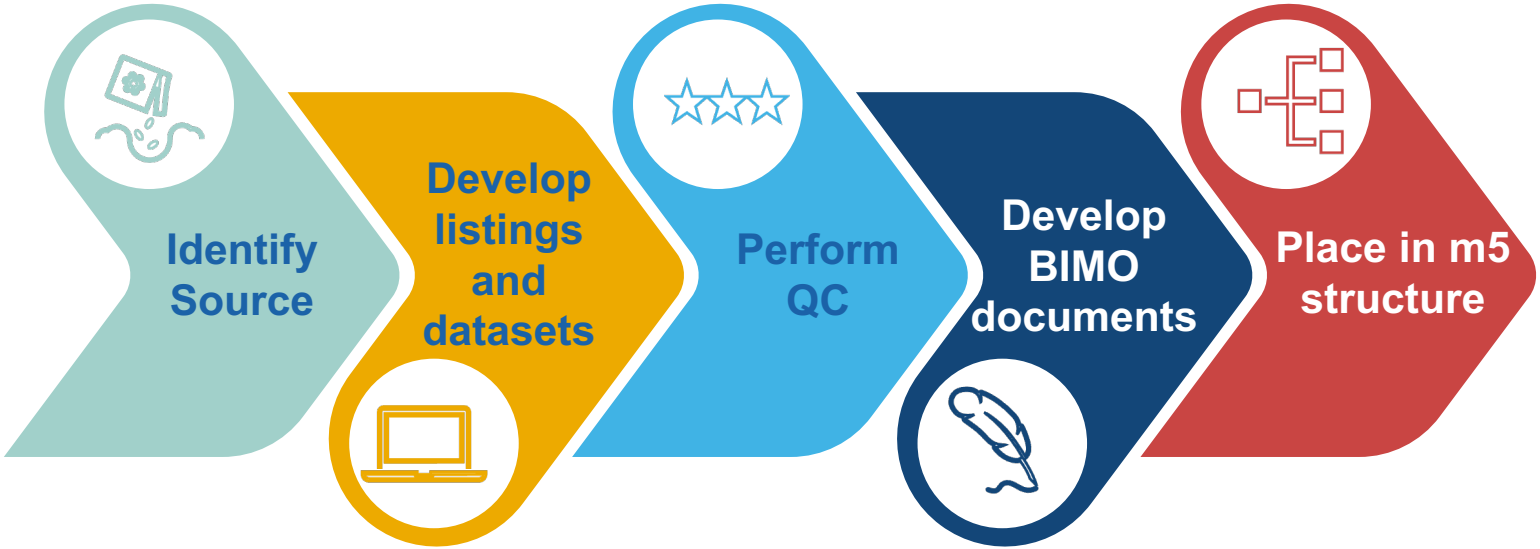
Summary-Level Clinical Site - 03

- Clinsite.xpt
- Define.xml

How Zifo Approached BIMO - Examples

Quick Tips for Sponsors

- Draft a plan for the BIMO data package
- Share the draft plan with FDA at a pre-NDA meeting or a similar form of communication
- Update and finalize the BIMO data plan with feedback from the FDA reviewers
- Execute the BIMO data plan
- Create eCTD documentation for the clinsite dataset


Identify Source
Develop listings and datasets
Perform QC
Develop BIMO documents
Place in m5 structure

Part 01 : General Site info

Table A: Format for Clinical Site Lists

Protocol Number: Protocol Title			
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**
0001*	Doe, John M.	Doe University Department of Medicine 1 Main St., Suite 100 Silver Spring, MD 20850 USA	Phone: 1-555-555-5555 Fax: 1-555-555-5555 Email: john.doe@mail.com
0002	Doe, Jean (Smith, John)	Doe University Department of Medicine 1 Main St., Suite 100 Silver Spring, MD 20850 USA	Phone: 1-555-555-5555 Fax: 1-555-555-5555 Email: john.smith@mail.com (Phone: 1-555-555-5554 Email: jean.doe@mail.com)
003	Dietric-Fischer, Inge	Hartmannstrasse 7 5300 Bonn 1 Germany	Phone:49-555-555-5555 Fax: 49-555-555-5555 Email: Dietric.Fischer@web.de
* Site terminated, or clinical investigator changed, at request of sponsor before study completion.			

- Information related to site and Investigator
- Receive the data from Sponsor
- Submit this listing as pdf

What to do if we have multiple studies

A separate table should be provided for each clinical study

Part 02 :Individual subject Listings by site

List of Subject Level Data line listings

1. Consented Subjects
2. Treatment assignment
3. Discontinuations
4. Study Population
5. Inclusion and Exclusion criteria
6. Adverse Events
7. Important Protocol deviations
8. Efficacy Population
9. Concomitant Medications
10. Safety monitoring

Part 02 :Individual subject Listings by site

Figure C: Example of By Site, by Listing Option A

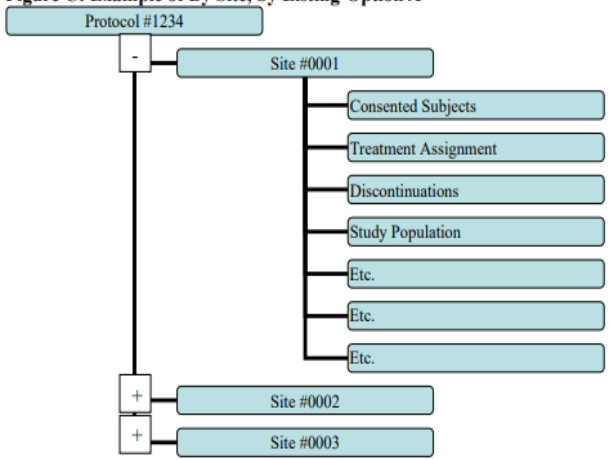
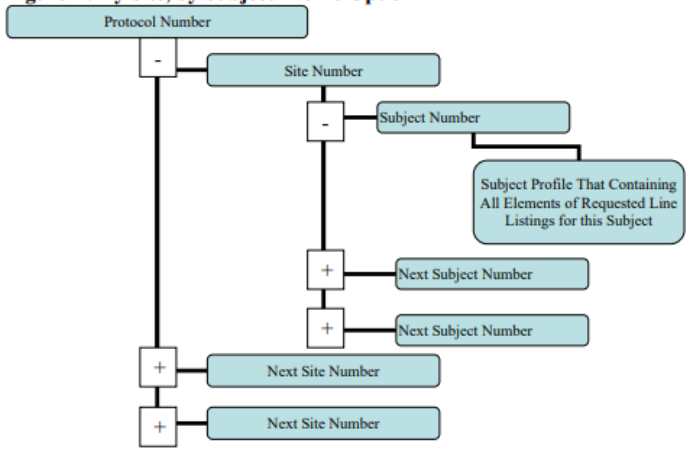


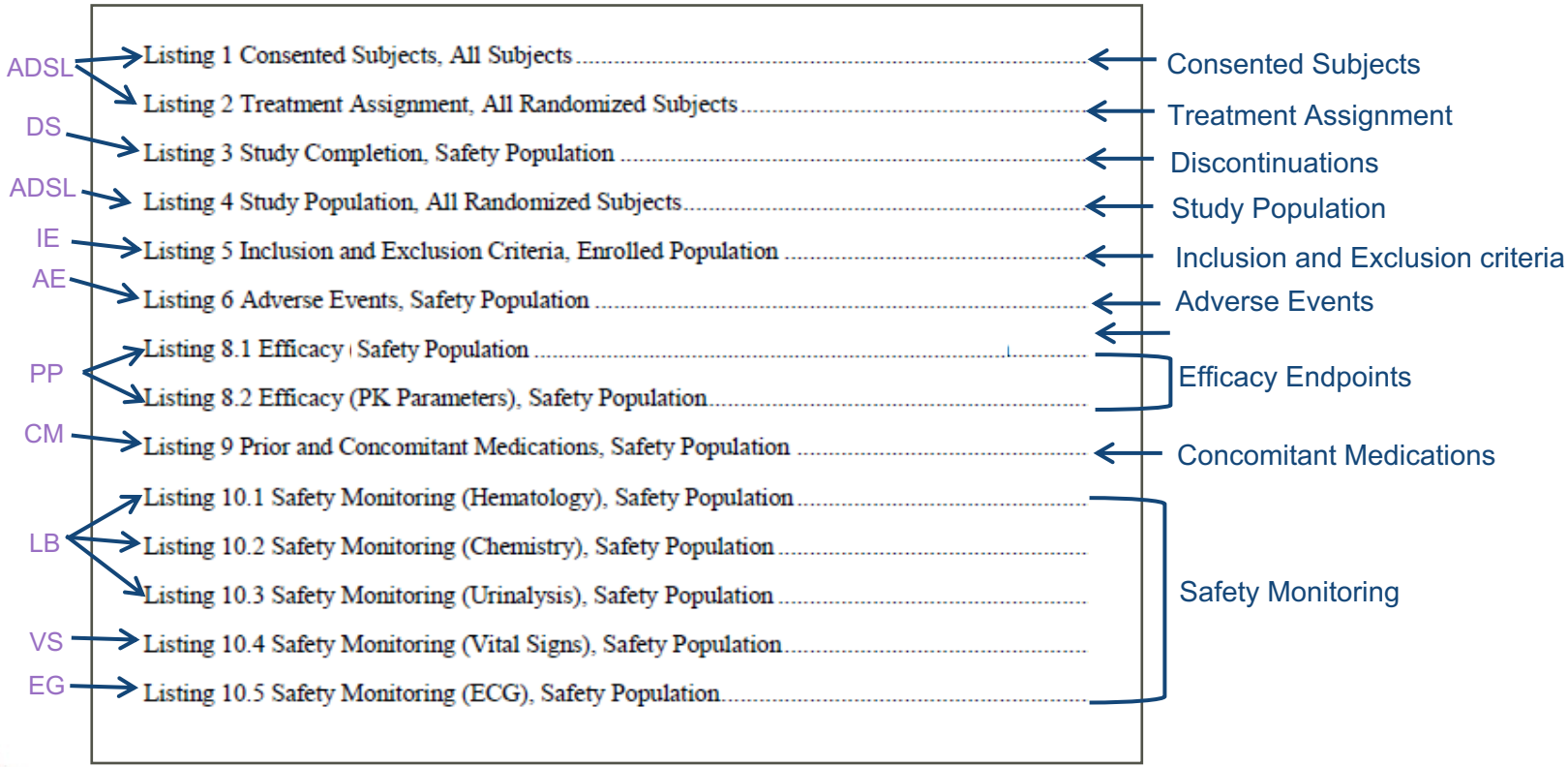
Figure B: By Site, by Subject Profile Option B



Option 1: Recommended when we create listings based on data for TLFs/CSR
Option 2: Recommended when we decide to use patient profile

Part 02 :Individual subject Listings by site

CDISC Domains



Part 02 :Individual subject listings by site

Table of contents

Part 02 :Individual subject Listings by site

Base dataset used is ADSL →

Site 001: Listing 1
Consented Subjects
All Subjects

USUBJID

Subject Number	Treatment Group	Randomization Flag	Randomization Number	Date of Informed Consent	Reason for Screen Failure	Other Reason for Screen Failure
001-901	TRT01A	No		11JAN2021	Breif Smell Identification Test	DCSREASP
001-902		No		13JAN2021	Contraband	
001-903		No		13JAN2021	Contraband	
001-904	AB	Yes	101	13JAN2021/15:22		
001-905	BA	Yes	102	13JAN2021/15:40	DCSREAS	
001-906	BA	Yes	104	13JAN2021/15:58		
001-907	AB	Yes	103	13JAN2021/15:59		
001-908		No		13JAN2021	Vitals - Blood Pressure	
001-909	BA	Yes	105	13JAN2021/16:20		
001-910		No		15JAN2021	Positive UDS - Cotinine	
001-911		No		15JAN2021	Breif Smell Identification Test	
001-912		No		15JAN2021	Vitals - Blood Pressure	
001-913	AB	Yes	106	15JAN2021/14:58		
001-914	BA	Yes	107	15JAN2021/15:00		
001-915		No		15JAN2021	Breif Smell Identification Test	

RANDFL

RFICDT

For requirements of each listing refer to Bioresearch Monitoring Technical Conformance Guide

Part 03: Clinsite.xpt

- As per “Appendix 3: Clinical Site Data Elements Summary Listing” in the Bioresearch Monitoring Technical Conformance Guide there are 41 variables to be mapped to this dataset

- We have categorised into 5 groups for making understanding easier.

1.Investigator/Site

- Investigator last name
- Investigator first name
- Investigator Middle Initial
- Investigator Phone number
- Investigator Fax number
- Investigator mail address
- Country
- State
- City
- Postal
- Street

2.Sponsor

- Sponsor Count
- Sponsor name
- IND Number
- Under IND
- NDA Number
- BLA Number
- Supplement Number
- Financial Disclosure Amount

3.Subject

- Description of Planned Treatment Arm
- Description of Planned cohort
- Number of subject discont study
- Number of subject discont study treatment
- Number of subjects screened
- Number of subjects in Safety population
- Number of subjects in Efficacy population

4.Study

- Study Identifier
- Title
- Study Site Identifier
- Number of non-serious adverse events
- Number of serious adverse events
- Number of important protocol deviations
- Number of non-important protocol deviations

Sponsor

Protocol/CDISC domains

5.Endpoints

- Primary Endpoint
- Primary Endpoint Type

- Treatment Efficacy Result for SAFPOP
- Treatment Efficacy Result for EFFPOP

- Censored Observations in SAFPOP
- Censored Observations in EFFPOP

"continuous"
"discrete"
"time to event"
"other"

Summary statistic for Primary endpoint by treatment arm per site

Total number of censored observations in SAFPOP. If not applicable leave blank

SAFPOP

EFFPOP

ENDPOINT	ENDPTYPE	TRTEFFR1	TRTEFFR2	CENSOR1	CENSOR2
Percent Responders	Binary	0.48	0.58	.	.
Change from Baseline	Continuous	0.74	0.76	.	.
Percent Responders	Binary	0.14	0.12	.	.
Change from Baseline	Continuous	0.14	0.16	.	.
Percent Responders	Binary	0.48	0.44	.	.

Multiple endpoints

SAP/Protocol

Efficacy datasets (e.g.: ADEFF)

ADTTE

Part 03: Define.xml

Created using Pinnacle 21 specification

Integrated studies:

- Integrate ADaM domains. Add their metadata.
- Add metadata of clinsite along with the integrated domains in ADaM define

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
[redacted]	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 ISTAT 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	BIMO	One record per study per site per arm	BIMO	STUDYID, SITEID, ARM		clinsite.xpt

Non-Integrated studies:

- Create Clinsite .xpt
- Add metadata of clinsite in a separate define
- No need to combine with ADaM

Datasets

Dataset	Description	Class	Structure	Purpose	Keys	Documentation	Location
CLINSITE	Clinical Site Data Elements Summary	BIMO	One record per study per site per arm per primary endpoint		STUDYID, SITEID, ARM, ENDPOINT		clinsite.xpt

Part 04: Reviewer's guide

- Created using PHUSE Template
- The information presented is related to sites

m5 folder Structure

Figure 2: Place Clinical Study-Level Information and Subject-Level Line Listings by Clinical Site in the M5 Folder

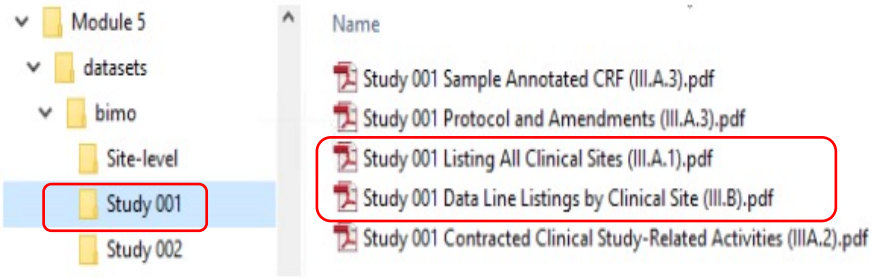
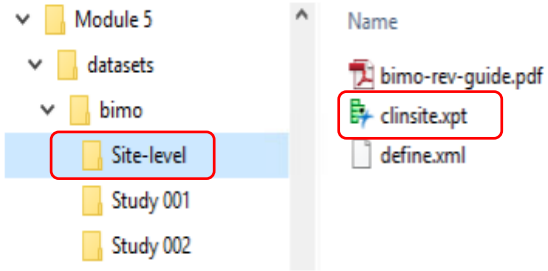
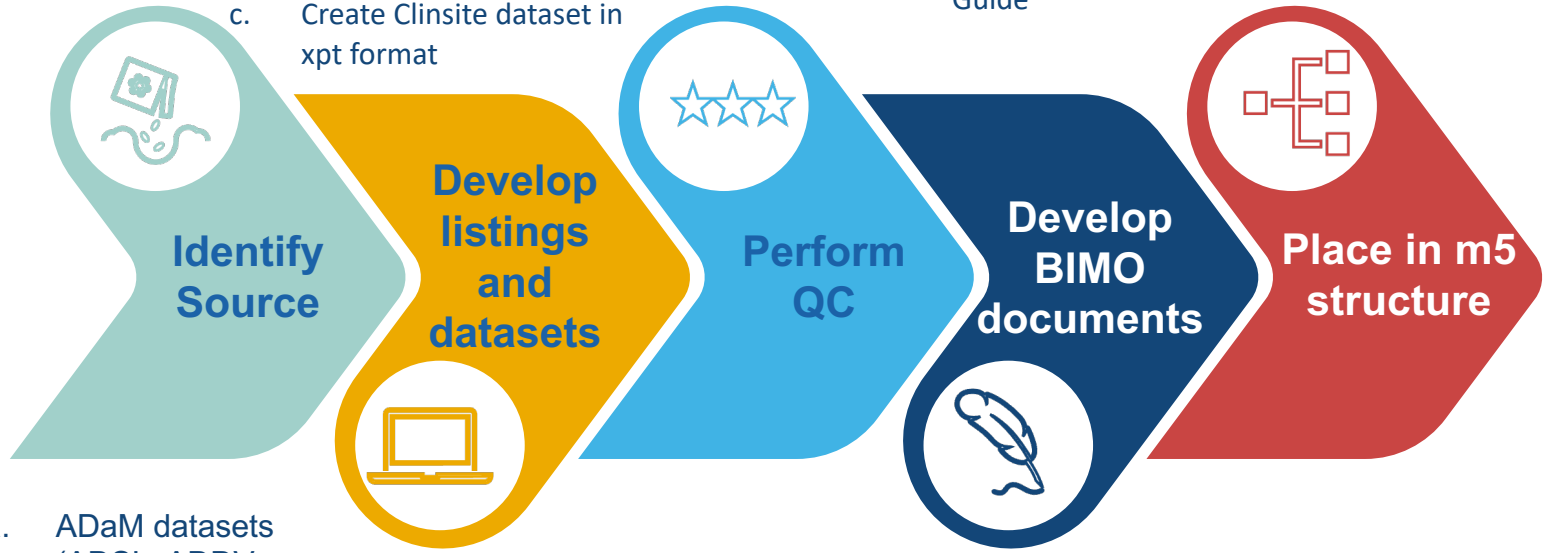


Figure 2: Place the Site-Level Dataset Define File and BIMO Data Reviewer's Guide in the M5 Folder



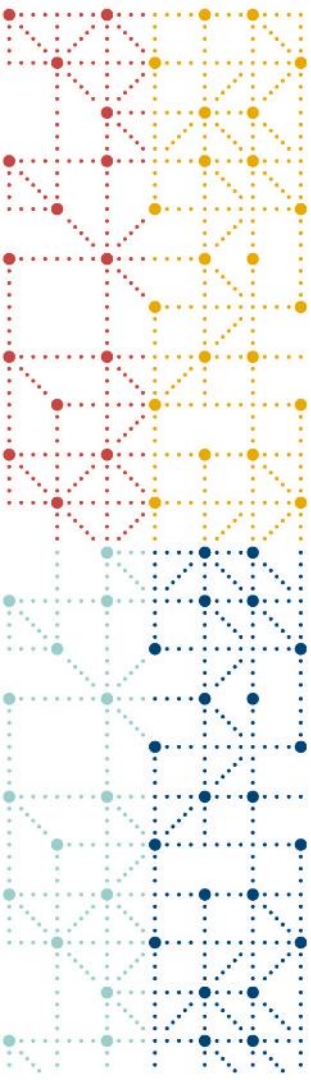
a. Create list of clinical sites as pdf document
b. Choose the option to present the by site listing and develop them as pdfs
c. Create Clinsite dataset in xpt format

a. Define.xml
b. BIMO Reviewer's Guide



a. ADaM datasets (ADSL, ADDV, ADAE, efficacy datasets, SDTM datasets)
b. Site related info

a. Manual checks done against CSR listings/patient profiles
b. Independent programming and quality check for Clinsite dataset.



Challenges

Uncommon variables in each study when 2 studies involved

- Variables can be merged
- Information carrying variables related to data presented in listing can alone be retained

No Validation using Pinnacle 21

- Manual reviews
- Independent Programming

Purpose column is blank

Datasets

Dataset	Description	Class	Structure	Purpose	Keys	Documentation	Location
CLINSITE	Clinical Site Data Elements Summary	BIMO	One record per study per site per arm per primary endpoint		STUDYID, SITEID, ARM, ENDPOINT		clinsite.xpt

Update Purpose = “BIMO” in text file manually

Using GENC codelist

GENC Name (FDA Standard)	GENC 2 Letter Code	GENC 3 Letter Code (FDA Standard)	GENC Number	NCIt Subset Code	NCIt Subset Name
AFGHANISTAN	AF	AFG	004	C124085	Geopolitical Entities, Names and Codes Terminology
AKROTIRI	QZ	XQZ	900	C124085	Geopolitical Entities, Names and Codes Terminology

STATE

COUNTRY

2 letter code for COUNTRY

Unabbreviated name for STATE




Thoughts, Opinions & Questions

Thank You!