

SA06: PHUSE Bioresearch Monitoring Data Reviewers Guide

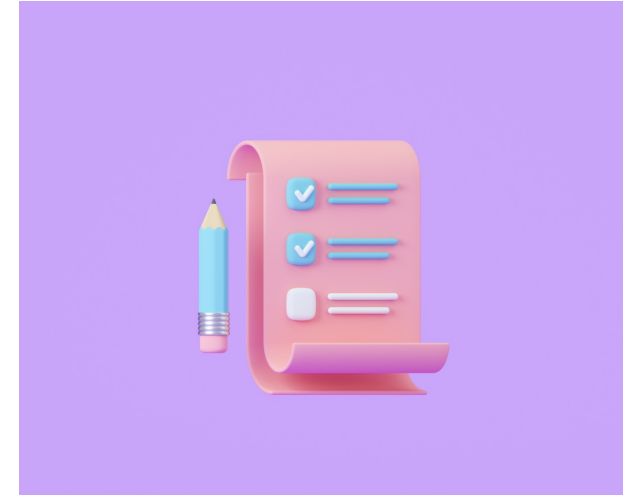
November 16, 2022

Jack Field, AstraZeneca

Steve Fitzpatrick, Novartis

Agenda

- BIMO Background
- PHUSE BDRG Project Introduction
- PHUSE BDRG Scope And Contents
- PHUSE BDRG Template
- PHUSE BDRG Completion Guideline & Examples
- Key Points
- Updates Based On Latest TCG
- PHUSE BIMO FAQ Project
- Resources, Thank You & Q&A



BIMO Background

- OSI ensures CDER-regulated drugs and biologics have reliable evidence of safety and effectiveness
- The OSI oversees BIMO to ensure protection of rights, safety and welfare of clinical trial participants
- In 2018, in support of site inspections, the OSI developed the first BIMO TCG
- BIMO deliverables are required for each major study in NDAs, BLAs and NDA/BLA supplemental applications containing clinical data

Acronyms!

OSI = Office of Scientific Investigations

CDER = Center for Drug Evaluation and Research

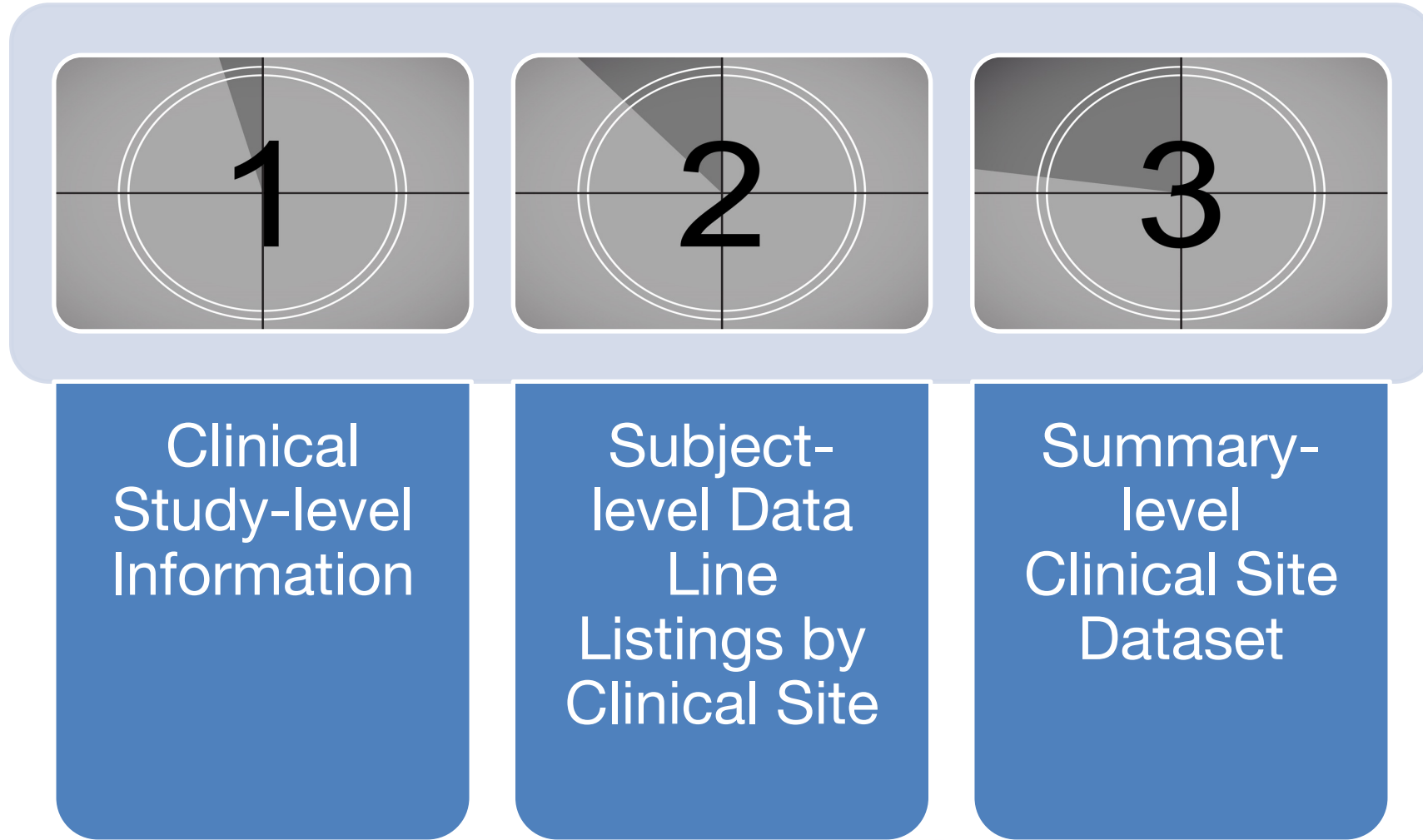
BIMO = Bioresearch Monitoring

TCG = Technical Conformance Guide

NDA = New Drug Application

BLA = Biologics License Application

BIMO – Easy As 1, 2, 3?



PHUSE BDRG Project Introduction

Problem Statement - BIMO Data Reviewer's Guide (BDRG):

- Although mentioned in the TCG, there is no formal FDA Guidance concerning a reviewer's guide
- Since there is a lack of clarity, each sponsor has defined their own approach for communication of their interpretation of the BIMO Technical Conformance Guide and BIMO deliverables
- This could result in Information Requests from the agency for Sponsors to provide additional clarification surrounding BIMO submission content
- This could result in a delay in the approval process



PHUSE BDRG Project Introduction

Solution Proposed - BIMO Data Reviewer's Guide (BDRG):



- Standardize the way to report the BIMO reporting requirements
- Form a team of representatives from FDA CDER, FDA CBER, PHUSE Leads, Subject Matter Experts across pharma industry supporting BIMO applications
- The PHUSE BIMO Data Reviewer's Guide Project is born!
- Developed a Standardized BIMO Data Reviewer's Guide Package published in June 2022 (Template, Completion Guidelines and Examples) to communicate the sponsors interpretation of the Bioresearch Monitoring Technical Conformance Guide

PHUSE BDRG Scope And Contents

- BIMO Data Reviewer's Guide (BDRG): a comprehensive suite of documents to fully describe the BIMO application to FDA reviewers
- Aim to have the BDRG look and feel like other PHUSE reviewer's guides
- Every attempt to minimise duplicate information from other submission documents
- No hyperlinks to other documents found in the electronic common technical document (eCTD) for consistency with other reviewer's guides



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PHUSE BDRG Template

Bioresearch Monitoring (BIMO) Data Reviewer's Guide

10 required sections in the BDRG

1 optional section in the BDRG

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>

.....

BDRG Template Version # DD-MMM-YYYY
BDRG Published Date # DD-MMM-YYYY

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- 10. eCTD Folder Structure skeleton for BIMO Items in MODULE 5
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PHUSE BDRG Template

1. Introduction

Purpose, Acronyms, Guidance, Metadata

2. Study Description

List of studies

3. Part I Request for Clinical Study-Level Information

List of sites, Entities contact info, Protocol, aCRF



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PHUSE BDRG Template

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

Listings, Efficacy endpoints, Safety monitoring

5. Part III Summary-Level Clinical Site Dataset

Treatment variables, Endpoint summary

6. External Datasets and Sources

External data sources



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PHUSE BDRG Template

7. Site Specific Matters

Site concerns, Subjects transferred between sites,
Identical site ID

8. Site Summary

Summary table for each major (i.e., pivotal) study

9. Conformance Summary for Part III Clinical Site Dataset

Conformance inputs, Issues summary

10. eCTD Folder Structure skeleton for BIMO Items in M5

A view of how the BIMO package fits into M5,
naming conventions

Appendix

Any other useful, supplemental info

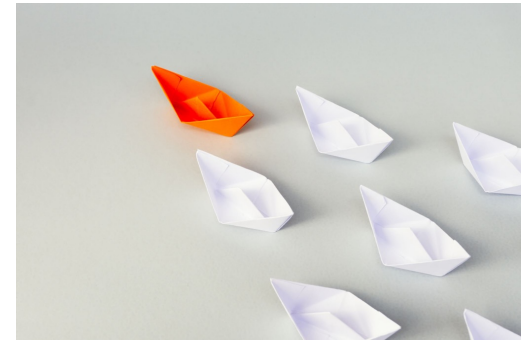
PHUSE BDRG Completion Guideline & Examples

- **Completion Guideline**

- Comprehensive Instructions on how to populate the BDRG Template
- Possible scenarios, deviations

- **Three Examples covering various options and scenarios**

- A Single pivotal study
- Multiple pivotal studies
- Studies with safety, time to event endpoints and PK endpoints
- Additional listings, splitting logic
- Many different options/scenarios mentioned in the Completion Guidelines are laid out in the examples to provide clarity



Key Points

- **The BIMO TCG and the BDRG mentions FDA CDER. What about submissions to FDA CBER?**
 - At this time, the BIMO TCG and PHUSE BDRG are CDER initiated guidance
 - However, we have CDER and CBER representation on our PHUSE BIMO initiative team
 - It is recommended that you discuss BIMO needs for CBER at your pre-submission meetings.
- **Why is the Conformance section of the BDRG Template mandatory when there are no official validation rules nor rejection criteria for BIMO?**
 - This is a perfect section to describe deviations from the BIMO TCG
 - Additional details are included in the Completion Guidelines

Key Points

- **This looks like quite a bit of additional work... is the BDRG mandatory?**
 - BIMO TCG v3.0 lists the BDRG as optional...
 - ... however, like the SDTM and ADaM TCGs, there is a non-binding reference to a reviewer's guide in the BIMO TCG
 - The FDA were key stakeholders in the PHUSE BDRG Project
- **Are you expecting us to duplicate tables in the body of the BDRG? See table 3.1, 3.2 (Part I item A and B)**
 - The rationale is to provide the reviewer with the metadata of what is presented in the Part I Clinical Study Information
 - No record level information is expected in these tables in the BDRG

Updates Based on Latest TCG

- **BIMO TCG v3.0 was released 11th August 2022 – after BDRG went live!**
 - BIMO Review Guide renamed to BIMO Data Review Guide
 - TRTEFFR renamed to TRTEFFR1
 - EFFPOP, TRTEFFR2, CENSOR2 variables added
 - TRTEFFS no longer requested
 - Geopolitical Entities, Names and Code (GENC) replaces ISO codes for COUNTRY
- **What does this mean for the PHUSE BDRG Template/Guidelines/Examples**
 - Minimal impact on BDRG Template and Completion Guidelines
 - Some examples will need to be updated based on the latest TCG
 - How does EFFPOP in Part III CLINSITE dataset impact the Part II efficacy listings?
 - BDRG should be used for the submission (PHUSE BDRG is referenced as bdrg.pdf)



PHUSE BIMO FAQ Project

- **PHUSE BIMO FAQ Project**

- There were hundreds of questions from project team and the public over the course of the PHUSE BDRG Project
- The team addressed questions specifically related to the BDRG but there were many remaining general BIMO questions
- There is a user need to address these and any other questions that come up in the early implementation stage
- PHUSE team has offered to host an FAQ forum



- **Who can join?**

- The team is looking for active members keen to share BIMO experience
- Reach out to Katie Warren if you are interested in joining the project



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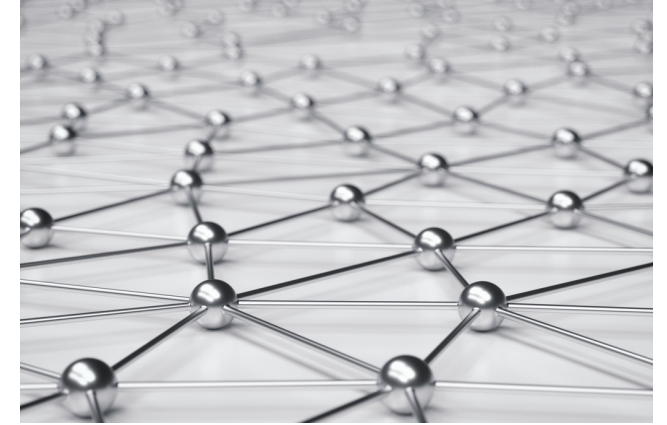
Resources

Available at a portal (PHUSE Advanced Hub) near you...

PHUSE BDRG Publication

Bioresearch Monitoring Technical Conformance Guide

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



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Thank You

- **Leads**
 - Katie Warren: PHUSE Project Manager
 - Julie Maynard (Janssen R&D): Project Team Lead
 - Sopan Dharma Kaith (Cytel Inc.): Project Team Lead
- **Team Members (all listed on the Advanced Hub)**
 - 50 members representing >24 organisations including active team members from the FDA CDER and CBER divisions
- **PHUSE Steering Committee**
- **Industry Public Reviewers**
- **All our attendees for participating in today's presentation and taking this information back to your organizations**



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Jack Field, jack.field@astrazeneca.com

Steve Fitzpatrick, steve.fitzpatrick@novartis.com