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SDSP: Sponsor and FDA Liaison

Bhanumathi Bayatapalli and Shefalica Chand, Seattle Genetics, Inc., Bothell WA

ABSTRACT

The discussion between a sponsor and FDA on data standards for statistical programming deliverables in an electronic submission should start at the early stages of product development and continue along the way to filing. This discussion will involve data standards, structures, and versions to be used for each study submitted with an NDA or BLA. The Study Data Standardization Plan (SDSP) is used as a tool to communicate with FDA on these aspects. Sponsors and applicants are encouraged to utilize established FDA-sponsor meetings (e.g., pre-IND, end of phase 2, Type B/C) to share and discuss the SDSP.

INTRODUCTION

The US Food and Drug Administration (FDA) encourages early and ongoing discussions with sponsors concerning the use of data standards in the form of a Study Data Standardization Plan (SDSP). The SDSP establishes and documents a plan for describing the data standardization approach for clinical and nonclinical studies within a development program and assists FDA in identifying potential data standardization issues.

Providing an SDSP as early as possible in a clinical development program guarantees that the FDA reviewers acknowledge and welcome the data standards utilized by the sponsor for each study and pooled analysis. The information included in this document is in accordance with the Study Data Technical Conformance Guide and the published Data Standards Catalog.

In future correspondence with FDA, the SDSP should be revised as the development program expands and further studies are anticipated.

Each time a study is launched, changes to the SDSP are not required to be shared with FDA. The cover letter that follows a study data submission will identify the degree to which the most recent version of the SDSP was implemented. Additionally, the SDSP appendix for the FDA Center for Biologics Evaluation and Research (CBER) should be issued to the review office no later than the End-of-Phase 2 (EOP2) meeting for clinical studies that will be sent to CBER.

This paper will share a simple yet comprehensive step-by-step guideline on developing and maintaining the SDSP. We will also discuss the PhUSE SDSP template for oncology trials and how it can be efficiently utilized for writing sponsor specific SDSP documents.

SDSP COMMUNICATION/MEETINGS WITH FDA AND SUBMISSION ACTIVITIES

The SDSP should be made accessible to the FDA at critical decision-making meetings and submission activities.

- EOP 2 Meeting
- Type C Meeting
- Pre NDA/BLA meeting

Prior to submission, critical decisions related to data standards and versions should be agreed upon with FDA.

After submission, the SDSP should be updated and maintained as needed (i.e. adding new studies/pooled analysis) per FDA request.

It could be advantageous for the sponsor or the agency to reevaluate selected versions of the standards in order to improve Integrated Summary of Safety (ISS) and Integrated Summary of Efficacy (ISE) review.

At the very least, sponsors should run the most recent validation rule sets (e.g., Pinnacle 21) against all data, irrespective of when the Clinical Study Report (CSR) was submitted. Shortly after submission, the FDA will determine compliance and data quality while utilizing the most up-to-date rule sets.

SDSP TEAM:

Input is required across the functional teams to submit to FDA, for example: Biostatistics, Statistical Programming, Data Management, Regulatory Affairs, and Regulatory Publishing.

SDSP TEMPLATE:

Follow the PHUSE SDSP completion guidelines to create an SDSP.

1. Header and Footer: A sponsor-specific header and footer needs to be displayed. Extended Headers and/or Footers are allowed as per Sponsor SOPs.
2. Sponsor Cover Page
3. The sponsor needs to maintain the Revision History.

Revision History		
Version	**Summary of Major Change(s) and Impact**	**Revision Date**
1.0	First Approved version of Study Data Standardization Plan	yyyy-mm-dd
1.1	<Changes>	

The SDSP will have various details related to the sponsor, product, submission-specific information, versions, standards being used, etc. Mainly it has 6 sections: 1) Introduction 2) Sponsor Information; 3) Production Information; 4) List of Standards for Non-clinical, Clinical and Pooled Studies; 5) Non-Conformance to Supported Standards Justification; 6) FDA Data Standards Discussions, and SDSP CBER Appendix (if applicable).

Sponsor Information:

Name of Product	< Name of the Product >
Indication	< Indication >
IND	< IND Number >
Sponsor Name	< Sponsor Name >
Sponsor Contact	< Sponsor Contact >
Sponsor Contact Email	<Sponsor Contact Email >

Product Information:

This is a required and free text section. The description related to the product under development, its intended indication(s), and patient populations, are captured here by the sponsor.

List of Studies and Standards:

This is where the sponsor lists the data standards versions that are planned to be followed for the studies, in reference to the values provided in the PhUSE template.

Section 4.1: Non-Clinical Studies from SDSP Template

This section summarizes studies relevant non-human subjects. Leave this section as blank in SDSP, if sponsor does not have non-clinical studies or <To be populated at later stage>.

Study Identifier	Brief Title	Study Type	Study Status	Study Start Date	Exchange Standards	Terminology Standards
If value is unknown, specify TBD	Specify title for the study	If value is unknown, leave blank or specify TBD	COMPLETED/ ONGOING/ PLANNED	yyyy-mm-dd <(forecasted Protocol sign)> TBD	LEGACY/ SEND IG v/ SDTM v/ TBD SDTM IG v/TBD Define.xml v/TBD No Electronic Data	Sponsor Defined Terminology CDISC SEND Terminology <date> <TBD> NONE

Section 4.2 Clinical Studies Section from SDSP Template

This section summarizes studies with human subjects. All studies within the relevant (IND)s should be listed. Each study should be grouped by Phase/Type of Study/Indication. Sort by study identifier within each group of studies. This section will be updated for Planned, Started, or Completed throughout the development of the Compound/Product. Post-marketing studies are not expected to be included in the SDSP.

Study Identifier	Brief Title	Study Design	Study Status	Study Start Date	Exchange Standards	Terminology Standards
<Phase <x>> <Interventional/Observational/Expanded Access> Studies - <indication or Healthy Subjects or Healthy						
If value is unknown, specify/ TBD	Specify title for the study. May come from protocol	If values are unknown, leave blank or specify/ TBD	COMPLETED/ ONGOING/ PLANNED	yyyy-mm-dd <(forecasted Informed Consent)>/ TBD	1. SDTM v/TBD 2. SDTM IG v/TBD 3. SDTM define.xml v/TBD 4. ADaM v/TBD 5. ADaM IG v/TBD 6. ADaM define.xml v/TBD	1.CDISC SDTM Terminology<date> 2.MedDRA v/ TBD 3.WHO-DD v/ TBD 4.LOINC 5.SNOMED CT 6.NDF-RT (Pharm Class) <version><TBD> UNII (Active moiety) <version>/TBD>

Section 4.3: Pooled Studies from SDSP Template

This section summarizes list of studies to be pooled. If the Sponsor does not have the list of such studies yet, then provide the first line as "The compound has no planned, ongoing, or completed at this time." Do not remove the table below.

Data Pool Identifier	Data Pool (List of Studies)	Pool Status	Pool Description	Exchange Standards	Terminology Standards
		CURRENT PLANNED	ISS <any additional information, such as certain domains> ISE <any additional information, such as certain domains>	1.ADaM v/<version> 2.ADaM IG v/TBD 3.ADaM define.xml v/TBD *4. Up-version<ed>* *<yyyy-mm-dd>/* *<TBD>*	1.MedDRA v/ TBD a. Initial <TBD> b. Final <TBD> 2.WHO Global/ TBD (Pharm Class) <version> 3.UNII (Active moiety) <version> *4. Up-version<MedDRA><yyyy-mm-dd>*

Section 5: Non-Conformance to Supported Standards Justification

Sponsor should clarify any discrepancies between the expected vs. the actually provided standard in this section:

Study Identifier	Expected Standard	Provided Standard	Justification for Non-Conformance to Standards (including Exception Information)

Section 6: FDA Data Standards Discussions from SDSP Templates

If the Sponsor gets directions from FDA in writing or in meetings, these can be noted in the table below, which provides a few examples.

Date of Discussion	Meeting Identifier	Form of Discussion	Result/Agreement
yyyy-mm-dd	32-368-5942	Email	FDA agreed that studies in SDTM 1.1/ SDTM IG 3.1.1 can remain in this version for submission. Studies include: ABC-TC-002 and ABC-AML-001.
yyyy-mm-dd	32-659-4884	Type C Meeting	FDA agreed draft Oncology domains used in ABC-TC-003 can be submitted. FDA agreed that draft Breast Cancer Standards can be used in ABC-OVB-002 & ABC-OVB-003.

CBER APPENDIX:

For submissions specifically destined for CBER, this document should be submitted well in advance of any licensing application (i.e., no later than the EOP 2 meeting) to CBER. It covers all sections shown below.

1. SDTM DATASETS

List all the proposed SDTM datasets used/planned for each clinical study in the submission.

SDTM IG Version: 3.2			
STUDY ID: xx-xx	**TITLE: <>**		
DOMAIN	**Select Domains to be Submitted X**	**Variables to be Utilized (Besides Those Required) Indicate Exp, Perm**	**Additional Comments**
Trial Design			
TA (Trial Arms)	<X>		
TE (Trial Elements)	<X>		
TI (Trial Inclusion/ Exclusion Criteria)	<X>		
TS (Trial Summary)	<X>		
TV (Trial Visits)	<X>		
Special Purpose			
CO (Comments)	<X>		
DM (Demographics)	<X>		
SE (Subject Elements)	<X>		
SV (Subject Visits)	<X>		
Interventions			
CM (Concomitant Medications)	<X>		
EX (Exposure)	<X>		
<Other datasets as applicable>	<X>		
Events			
AE (Adverse Events)	<X>		
DS (Disposition)	<X>		
<Other datasets as applicable>	<X>		

SDTM IG Version: 3.2			
STUDY ID: xx-xx	**TITLE: <>**		
DOMAIN	**Select Domains to be Submitted X**	**Variables to be Utilized (Besides Those Required) Indicate Exp, Perm**	**Additional Comments**
Findings			
DA (Drug Accountability)	<X>		
EG (ECG Test Results)	<X>		
<Other datasets as applicable>	<X>		
Findings About			
FA (Findings About)	<X>		
SR (Skin Response)	<X>		
Relationships			
RELREC (Related Records)	<X>		
SUPP<xx> (Supplemental Qualifiers)	<X>		
Custom			
<**DOMAIN NAME**> <(Domain Long Name)>	<X>		

2. SUPPLEMENTAL QUALIFIERS

List each SUPPQUAL variable in an individual row and it should match what is indicated in SDTM Datasets section of CBER Appendix.

SDTM IG Version: 3.2			
STUDY ID:	**TITLE:**		
Supplemental Qualifier Domain	**Qualifier Variable Name (QNAM)**	**Qualifier Variable Label (QLABEL)**	**Corresponding CRF Question or Derivation Information**

3. ADAM DATASETS

List all ADaM datasets used/planned for each clinical study (if analysis is planned to be performed on the individual study).

ADaM IG Version: 1.1			
STUDY ID:xx-xx	**TITLE: < >**		
TYPE	**DOMAIN**	**Select Domains to be Submitted X**	**Comments**
ADSL (Subject Level Analysis Dataset)	ADSL	<X>	
BDS (Basic Data Structure)	**ADLB**	<X>	
	ADVS	<X>	
	<Other datasets applicable>	<X>	
OCCDS (Occurrence Data Structure)	**ADAE**	<X>	
	<Other datasets applicable>	<X>	

4. ISS AND ISE

The following table summarizes the Integrated Summary of Safety and Integrated Summary of Efficacy using ADaM (ISS and ISE).

List all ADaM domains that will be used in the submission.

Dataset Label	**Efficacy**	**Safety**	**Other***	**Included Studies**	**Phase**	**Contributing Datasets**
ADSL (Analysis Dataset – Subject Level)		<X>		xx-xx xx-xy xx-xz	<1/1b> <2> <3>	SDTM.DM; SDTM.EX; SDTM.DS; SDTM.VS; etc.

*Other: endpoints not part of safety and efficacy (e.g., immunogenicity)

Final SDSP should be submitted in PDF format. It contains the updated Table of Contents, document header, and content version date. Hyperlinks need to be created between section 4 and 5; 5 and 6.

ACKNOWLEDGMENTS

We would like to thank our teams for their support and valuable suggestions and comments.

REFERENCES

PhUSE CSS Deliverables – SDSP Completion Guidelines, SDSP Template, SDSP Sponsor Implementation.

https://www.phuse.eu/css-deliverables

Study Data Technical Conformance Guide

https://www.fda.gov/media/131872/download

FDA Data Standard Catalog
https://www.fda.gov/media/85137/download

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the authors at:

Bhanumathi Bayatapalli
Seattle Genetics, Inc.
21823 - 30th Drive S.E.
Bothell, WA 98021
bbayatapalli@seagen.com

Shefalica Chand
Seattle Genetics, Inc.
21823 - 30th Drive S.E.
Bothell, WA 98021
schand@seagen.com