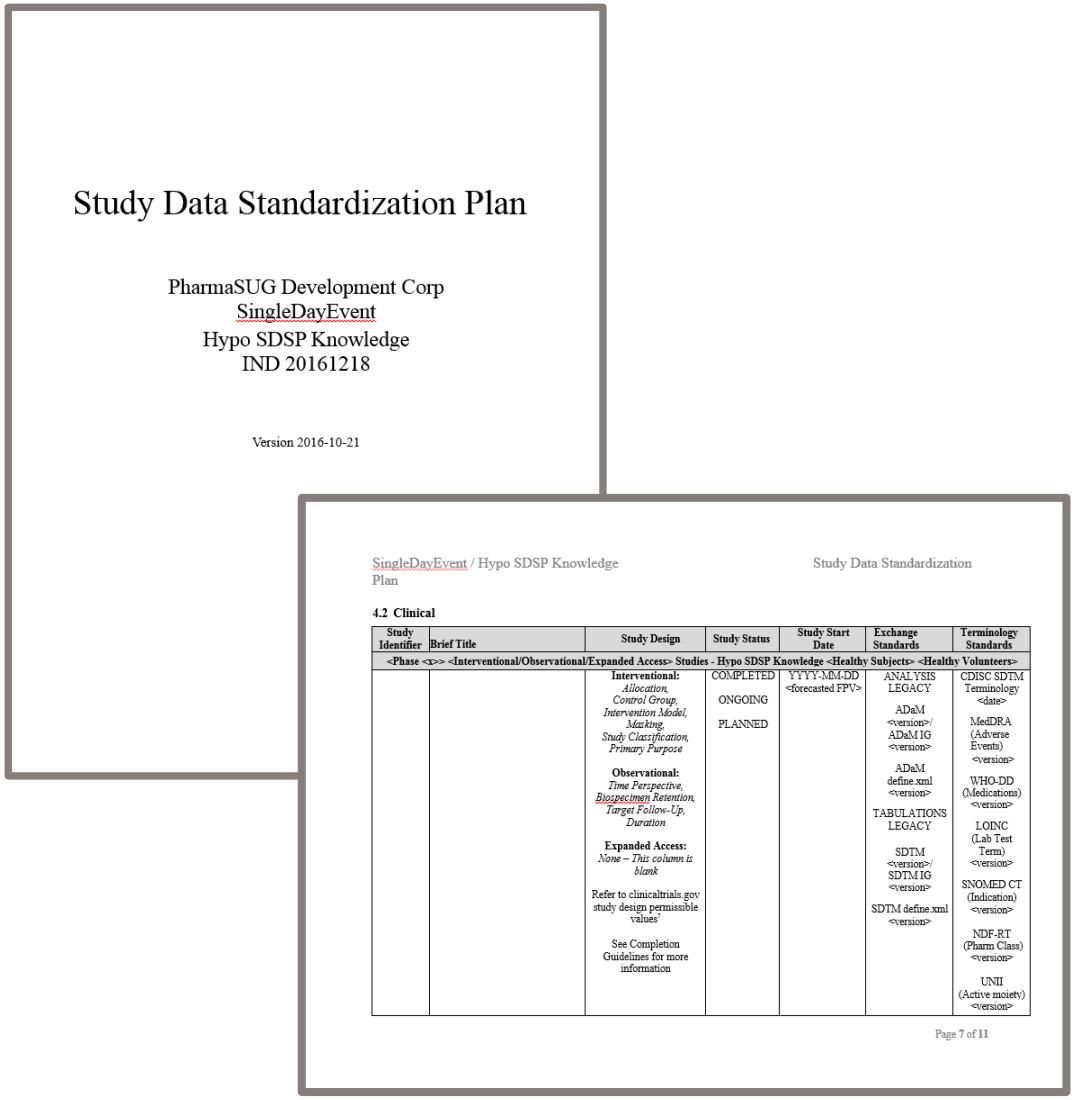
The Study Data Standardization Plan as a Strategic Tool for Analysis & Reporting

PharmaSUG Single Day Event – San Diego
October 21, 2016

David C. Izard

Agenda

- Hypothetical submission preparation steps
- History of SDSP
- FDA expectations
- Content plan
- Proactive development
- About those submission preparation steps…



Study Data Standardization Plan

PharmaSUG Development Corp
SingleDayEvent
Hypo SDSP Knowledge
IND 20161218

Version 2016-10-21

SingleDayEvent / Hypo SDSP Knowledge Plan — Study Data Standardization

4.2 Clinical

Study Identifier	Brief Title	Study Design	Study Status	Study Start Date	Exchange Standards	Terminology Standards
<Phase <x>> <Interventional/Observational/Expanded Access> Studies - Hypo SDSP Knowledge <Healthy Subjects> <Healthy Volunteers>						
		Interventional: *Allocation, Control Group, Intervention Model, Masking, Study Classification, Primary Purpose* **Observational:** *Time Perspective, Biospecimen Retention, Target Follow-Up, Duration* **Expanded Access:** *None – This column is blank* Refer to clinicaltrials.gov study design permissible values' See Completion Guidelines for more information	COMPLETED ONGOING PLANNED	YYYY-MM-DD <forecasted FPV>	ANALYSIS LEGACY ADaM <version>/ ADaM IG <version> ADaM define.xml <version> TABULATIONS LEGACY SDTM <version>/ SDTM IG <version> SDTM define.xml <version>	CDISC SDTM Terminology <date> MedDRA (Adverse Events) <version> WHO-DD (Medications) <version> LOINC (Lab Test Term) <version> SNOMED CT (Indication) <version> NDF-RT (Pharm Class) <version> UNII (Active moiety) <version>

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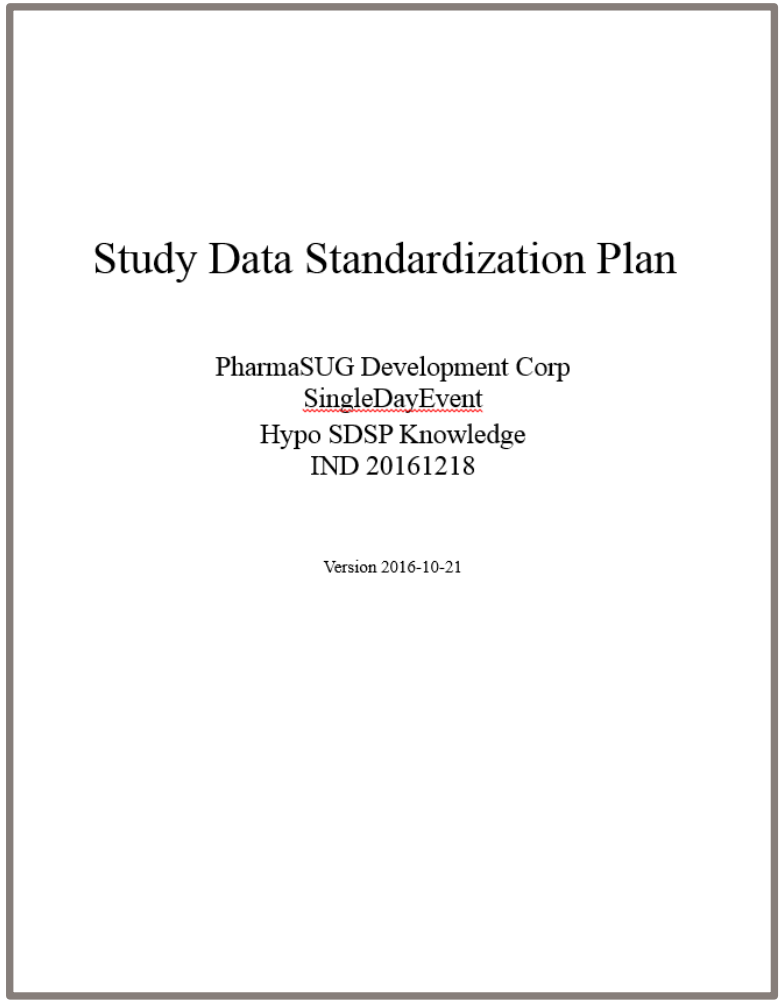
Hypothetical Submission Preparation Steps

- Integrated Analysis Plan (ISS SAP a/o ISE SAP) Development
  - "We need to combine AEs across all studies… What to you mean I need to up-version my dictionary terms before I perform this analysis?"
  - "What are all the studies we are considering for the NDA?"

- Briefing Packages for Pre-IND / EOP2 / PreNDA meetings
  - "The FDA needs to know how we plan on presenting the data – give me a list of studies as well as our integrations strategy, and let me know if there are any issues we need to raise the agency at this point in time…"
  - "We made an agreement at the EOP2 meeting that we didn't need to integrate our Healthy Volunteer Phase 1 studies with the Phase 2 & 3 studies when we prepared our integrated analysis as part of the formal NDA – where was that documented? Who did we talk to? What specifically did they say?"

Study Data Standardization Plan

- A plan for the use of FDA endorsed data standards in the development of your product
- Goals of Study Data Standardization Plan
  - Get sponsors thinking about standardization at the point a program / research phase / study is conceived, designed & implemented
  - Foster early communication with the FDA regarding the organization and presentation of data and related assets
  - Provide a resource FDA can use as a reference when executing their product review


Study Data Standardization Plan

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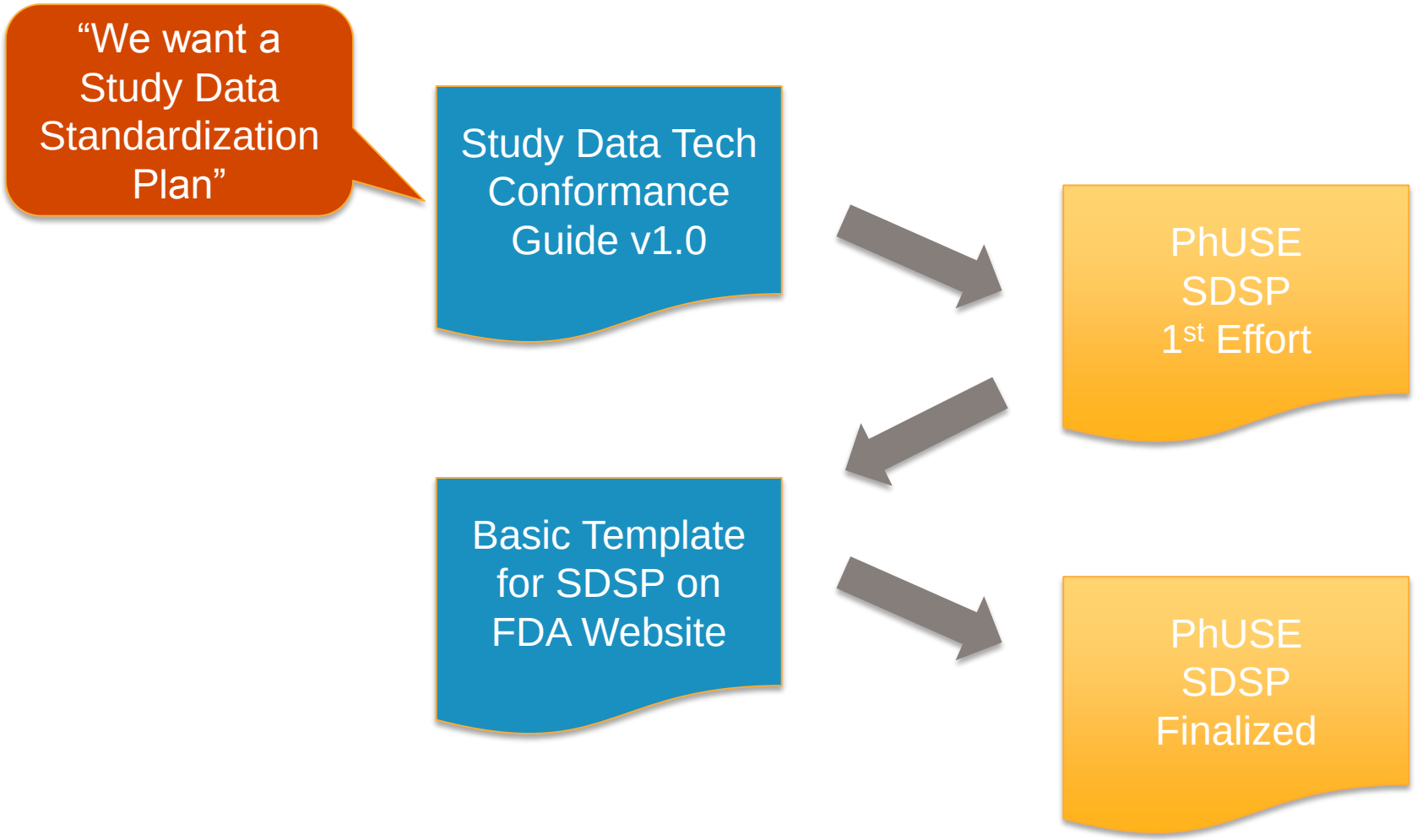
Brief History of Study Data Standardization Plan



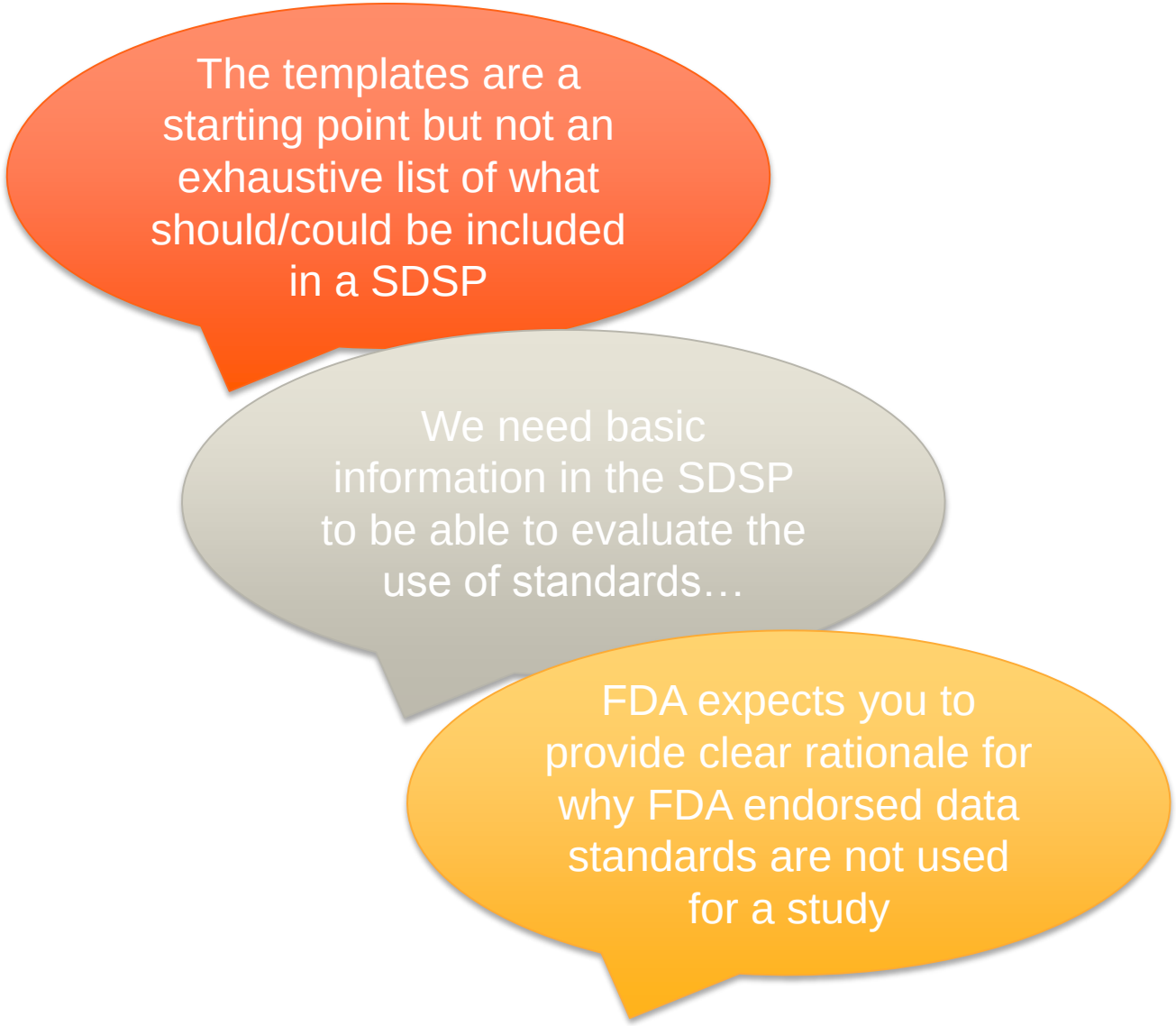
FDA Expectations

"For clinical and nonclinical studies, sponsors should include a plan (e.g., in the IND) describing the submission of standardized study data to FDA. The Study Data Standardization Plan (SDSP) assists FDA in identifying potential data standardization issues early in the development program."

FDA Expectations

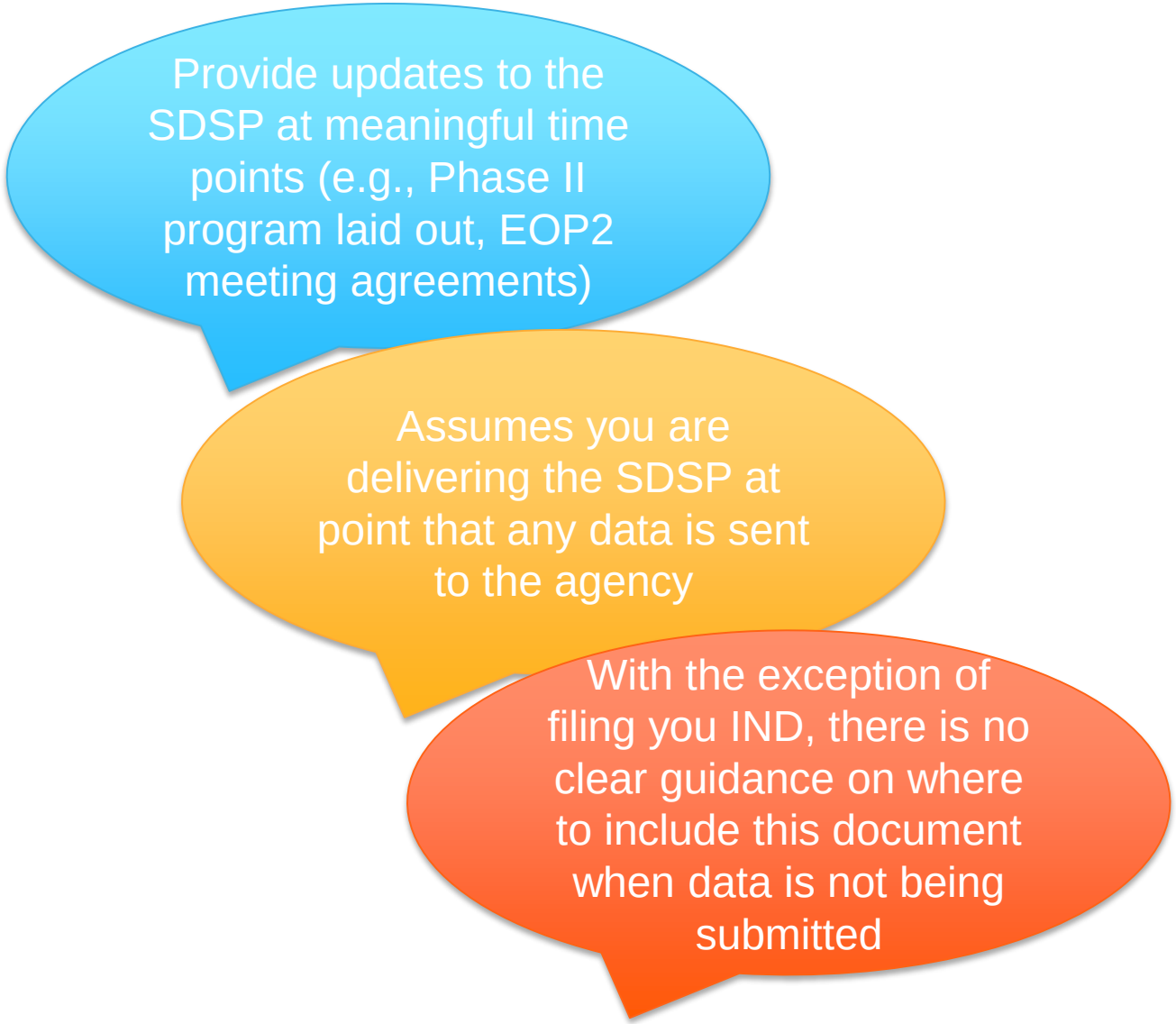
"The SDSP should include, but is not limited to, the following:

1. List of planned studies
2. Type of studies (e.g., Phase I, II or III)
3. Study designs (e.g., parallel, cross-over, open-label extension)
4. Planned data standards, formats and terminologies and their versions or a justification of studies that may not conform to the currently supported standards"



FDA Expectations

"The SDSP should be updated in subsequent communications with the FDA as the development program expands and additional studies are planned. Updates to the SDSP should not be communicated each time a study is started. The cover letter accompanying a study data submission should describe the extent to which the latest version of the SDSP is executed."



Content Plan for Study Data Standardization Plan

Study Data Standardization Plan

Contents

Content Plan for Study Data Standardization Plan

SingleDayEvent Hypo SDSP Knowledge Study Data Standardization Plan

1. Introduction

1.1 Purpose

The purpose of the Study Data Standardization Plan (SDSP) is to establish and document a plan for describing the data standardization approach for studies within a development program. The Study Data Standardization Plan (Standardization Plan) assists FDA in identifying potential data standardization issues early in the development program[1].

1.2 Scope

The scope of this document is for use with FDA submissions only. After it has been approved for use, the scope could expand to be used with other regulatory agencies after the proper discussions.

The SDSP is intended to include historical, current, and planned information about the development of the compound and indication. Multiple plans are permissible within a compound. It will be updated and maintained throughout the development of the compound, as new studies are planned or as the data standardization strategy evolves.

Standards that are currently available in the Data Standards Catalog[2] are the basis for which standards are listed.

Content Plan for Study Data Standardization Plan

1.4 Definitions

Nonclinical	Planned Study	Study Start Date has not been achieved.
	Ongoing Study	Study Start Date has been achieved and the study is not completed.
	Completed Study	The final report has been signed by the study director. (Comparison Chart of FDA, Environmental Protection Agency (EPA), Organization for Economic Co-operation and Development (OECD)[3])
	Study Start Date	The date on which the protocol is signed by the study director. Also known as Study Initiation Date. (Comparison Chart of FDA, Environmental Protection Agency (EPA), Organization for Economic Co-operation and Development (OECD)[3]) (CDISC SEND Controlled Terminology, STSTDTC[5])
	No Electronic Data	Study data is not available electronically.

Clinical	Planned Study	Study Start Date has not been achieved.
	Ongoing Study	1 or more patients is enrolled in the clinical trial[4] and the study is not completed.
	Completed Study	The final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the prespecified protocol or was terminated.[4]
	Study Start Date	The earliest date of informed consent among any subject (Date/Time of Informed Consent, RFICDTC) that enrolled in the study. For studies conducted without informed consent (ie. emergency use) use the date of treatment. Dates for subjects who were screen failures are not included. (CDISC SDTM Controlled Terminology, SSTDTC[6])

Nonclinical & Clinical	Legacy Data	Study data that does not conform to the standards by the date of requirement specified in the published Data Standards Catalog[2].

Content Plan for Study Data Standardization Plan

2. General Sponsor Information

Name of Product	
Indication	
IND	
Sponsor Name	
Sponsor Contact	
Sponsor Contact Email	

Who you want to answer questions about this plan…

3. Product Information

Describe the product under development, its intended indication(s), and patient populations.

(Text here)

Content Plan for Study Data Standardization Plan

4.1 Nonclinical

Study Identifier	Brief Title	Study Type	Study Status	Study Start Date	Exchange Standards	Terminology Standards
		REPEAT DOSE TOXICITY PRIMARY PHARMACODYNAMICS PHARMACODYNAMIC DRUG INTERACTIONS PHARMACOKINETIC DRUG INTERACTIONS (Please see Completion Guidelines for more information)	COMPLETED ONGOING PLANNED	YYYY-MM-DD <forecasted FPV>	LEGACY SDTM <version>/ SEND IG <version> tumor.xpt define.xml <version> No Electronic Data	LEGACY CDISC SEND Terminology <date> NONE

Content Plan for Study Data Standardization Plan / Proactive Development

4.1 Nonclinical

Study Identifier	Brief Title	Study Type	Study Status	Study Start Date	Exchange Standards	Terminology Standards
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Forecasted Study Initiation Date

Many permutations possible here

Should be articulated in the protocol (typically no separate SAP for Pre-Clinical)

Note reference to "Legacy" terminology

Content Plan for Study Data Standardization Plan

4.2 Clinical

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Content Plan for Study Data Standardization Plan / Proactive Development

CHILTERN
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4.2 Clinical

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Maybe in your SAP, definitely known at the end of the study

Incorporate into your SAP

Be aware of Data Standards Catalog Date of Requirement

Content Plan for Study Data Standardization Plan

Data Pool Identifier	Data Pool (List of Studies)	Pool Description	Exchange Standards	Terminology Standards
		ISS <any additional information, such as certain domains> ISE <any additional information, such as certain domains>	ANALYSIS LEGACY ADaM <version>/ ADaM IG <version> ADaM define.xml <version> TABULATIONS LEGACY SDTM <version>/ SDTM IG <version> SDTM define.xml <version>	CDISC SDTM Terminology <date> MedDRA (Adverse Events) <version> WHO-DD (Medications) <version> LOINC (Lab Test Term) <version> SNOMED CT (Indication) <version> NDF-RT (Pharm Class) <version> UNII (Active moiety) <version>

Content Plan for Study Data Standardization Plan / Proactive Development

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Everything on this page should be considered and articulated in your Integrated ISS/ISE Statistical Analysis Plan

Pay close attention to the Data Standards Catalog

Date of Requirement **and** Date Support Ends

Content Plan for Study Data Standardization Plan

5. Non-Conformance to Supported Standards Justification

Study Identifier	Domain	Expected Standard	Provided Standard	Justification for Non-Conformance to Standards (including Exception Information)
		SDTM <version>/ SEND IG <version> SEND define.xml <version> SDTM <version>/ SDTM IG <version> SDTM define.xml <version> ADaM <version>/ ADaM IG <version> ADaM define.xml <version>		

Content Plan for Study Data Standardization Plan / Proactive Development

5. Non-Conformance to Supported Standards Justification

Study Identifier	Domain	Expected Standard	Provided Standard	Justification for Non-Conformance to Standards (including Exception Information)
	Added column **Adds clarity for expected versus provided standard** **Examples: "Medical History"** **"data definitions for legacy format data"**	SDTM <version>/ SEND IG <version> SEND define.xml <version> SDTM <version>/ SDTM IG <version> SDTM define.xml <version> ADaM <version>/ ADaM IG <version> ADaM define.xml <version>		

This is your opportunity to clearly rationalize why something other than FDA endorsed data standards are present in your submission

Content Plan for Study Data Standardization Plan

6. FDA Data Standards Discussions

Date of Discussion	Meeting Identifier	Form of Discussion	Result/Agreement
YYYY-MM-DD		Teleconference Face-to-face Email	(Text here)

Content Plan for Study Data Standardization Plan / Proactive Development

Lean on your Regulatory Affairs colleagues for support

It is a two way street – keep them informed as well!

6. FDA Data Standards Discussions

Date of Discussion	Meeting Identifier	Form of Discussion	Result/Agreement
YYYY-MM-DD		Teleconference Face-to-face Email	(Text here)

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- Integrated Analysis Plan (ISS SAP a/o ISE SAP) Development
  - "We need to combine AEs across all studies… What to you mean I need to up-version my dictionary terms before I perform this analysis?"
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If you have been maintaining your SDSP you know all of this…

- FDA Briefing Package for Pre-IND / EOP2 / PreNDA meetings
  - "The FDA needs to know how we plan on presenting the data – give me a list of studies as well as our integration strategy, and let me know if there are any issues we need to raise the agency at this point in time…"

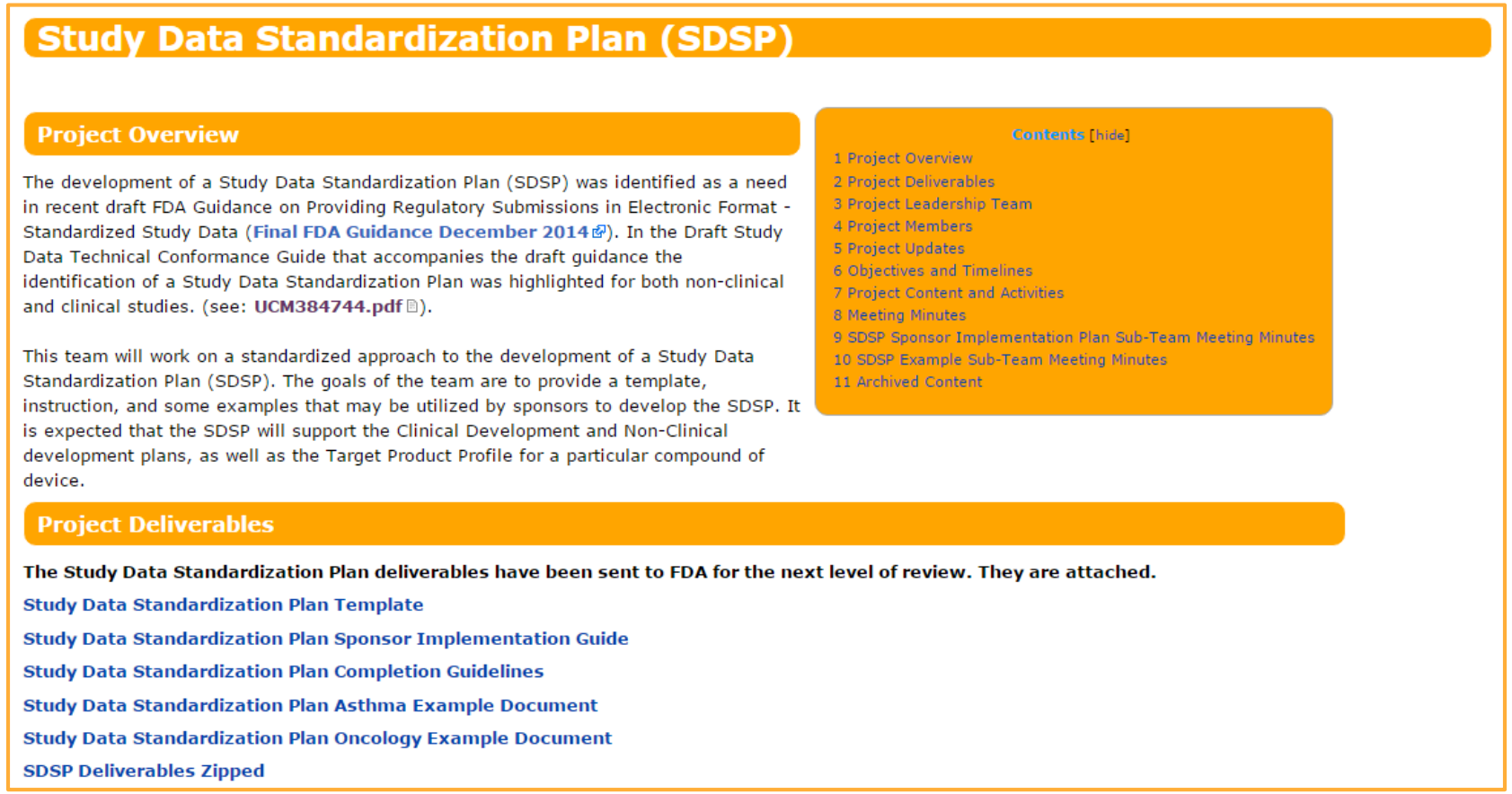
Here you go…

  - "We made an agreement at the EOP2 meeting that we didn't need to integrate our Healthy Volunteer Phase 1 studies with the Phase 2 & 3 studies when we prepared our integrated analysis as part of the formal NDA – where was that documented? Who did we talk to? What specifically did they say?"

No need to scramble, all of the information Regulatory Affairs needs is at your fingertips…

Resources – Study Data Standardization Plan

- At the following location on the PhUSE website…
  http://www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_(SDSP)
- …you will find the following information



Study Data Standardization Plan (SDSP)

Project Overview

The development of a Study Data Standardization Plan (SDSP) was identified as a need in recent draft FDA Guidance on Providing Regulatory Submissions in Electronic Format - Standardized Study Data (**Final FDA Guidance December 2014**). In the Draft Study Data Technical Conformance Guide that accompanies the draft guidance the identification of a Study Data Standardization Plan was highlighted for both non-clinical and clinical studies. (see: **UCM384744.pdf**).

This team will work on a standardized approach to the development of a Study Data Standardization Plan (SDSP). The goals of the team are to provide a template, instruction, and some examples that may be utilized by sponsors to develop the SDSP. It is expected that the SDSP will support the Clinical Development and Non-Clinical development plans, as well as the Target Product Profile for a particular compound of device.

Contents [hide]

Project Deliverables

The Study Data Standardization Plan deliverables have been sent to FDA for the next level of review. They are attached.

Study Data Standardization Plan Template

Study Data Standardization Plan Sponsor Implementation Guide

Study Data Standardization Plan Completion Guidelines

Study Data Standardization Plan Asthma Example Document

Study Data Standardization Plan Oncology Example Document

SDSP Deliverables Zipped

Questions? Thank you!

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