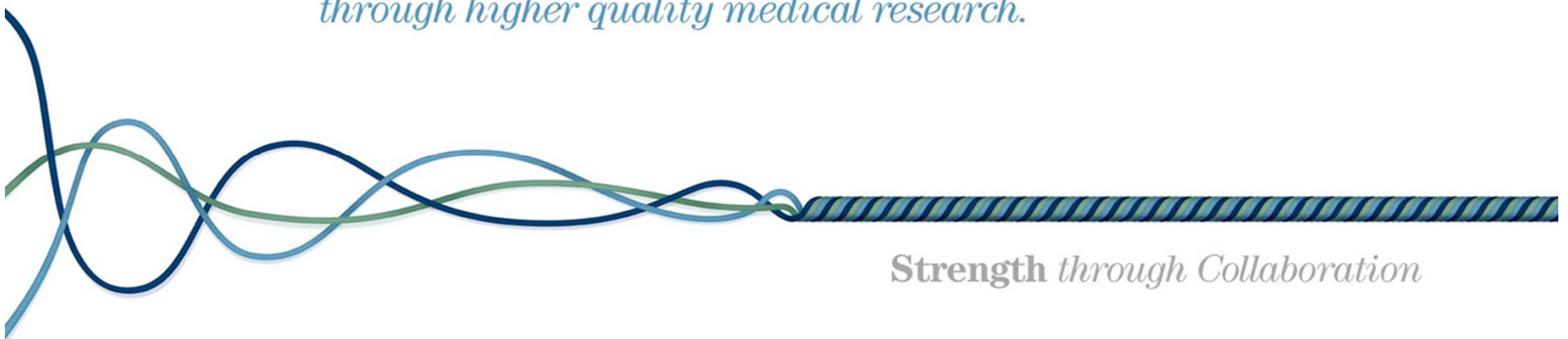




CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

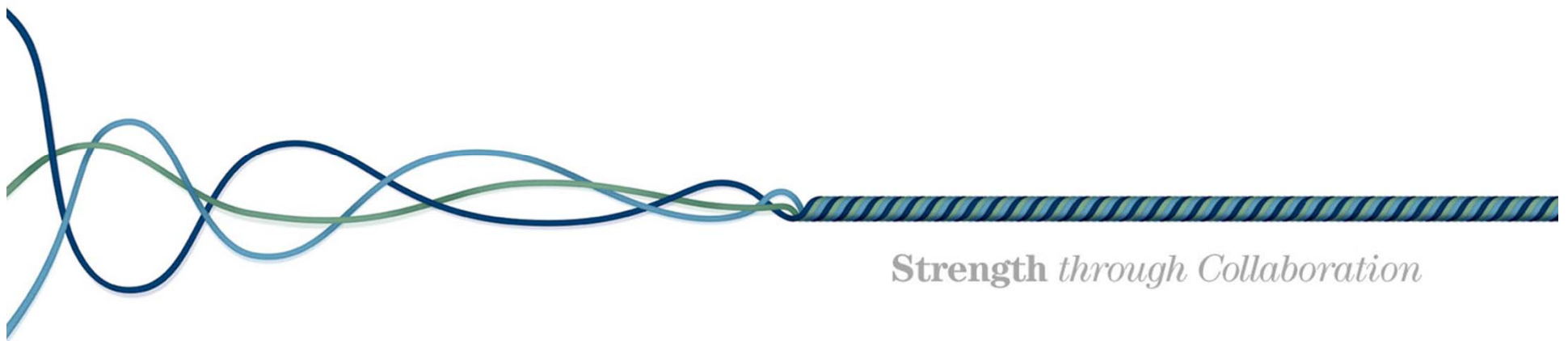
*The CDISC vision is to inform patient care & safety
through higher quality medical research.*



Strength *through Collaboration*

SDTMIG v3.3 Batch 2 Upcoming Public Review

Presented by Fred Wood



Strength through Collaboration

SDTMIG v3.3 Batch 2?

What

This package constitutes **Batch 2 for the planned SDTMIG v3.3**. It is planned to be available for a public 30-day review next week.

Why Batches

Given the volume of revised content and new concepts and domains, the SDS Team is dividing materials targeted for inclusion in SDTMIGs into manageable batches for public review. This was the process for SDTMIG v3.2.

Batch 1 Refresher (~April 2014)

- AG
- CV
- FT
- RE

Agenda

- Study Data Tabulation Model v1.5 – Rolling Copy
 - New Variables and Tables
- Section 6.1 (Interventions)
 - All Interventions Index – Revised to include a decision tree for when to use all intervention domains.
- Section 6.3 (Findings)
 - CC Domain – A new domain for Clinical Classifications, for named instruments used as serves as a surrogates for, or ranking of, disease status or other physiological or biological status.
 - NV Domain – Nervous System Findings domain
 - OE Domain – Ophthalmic Examinations domain
 - TU and TR Domains – broadened scope
- Section 8 (Relationships)
 - Alternative method for submitting Non-Standard Values to a Parent Domain
- Disease Milestones (Various sections of the SDTM and SDTMIG)
 - New variables and domains to support the Disease Milestones concept
 - Package was part of the TAUG for Diabetes (September 11, 2014)

SDTM Rolling Copy: Overview

- The SDTM Governance Team made a decision that a version of the SDTM will be published with any new release of an SDTM-based implementation guide
 - SDTMIG
 - SENDIG
 - SDTM-PGx (Pharmacogenomics)
 - SDTM-AP (Associated Persons)
 - SDTMIG-MD (Medical Devices)
- This will ensure alignment of new domains and concepts in each IGs with the SDTM at the time of publication.
- The version sent out for this review is considered SDTM v1.5 Draft 1, a PDF that clearly shows all changes.

SDTM Rolling Copy: Snapshot

--STRESU	Standard Units	Char	Variable Qualifier of -STRESC and -STRESN	Standardized units used for --STRESC and --STRESN. Example: mol/L.
--STNRLO	Normal Range Lower Limit-Standard Units	Num	Variable Qualifier of -STRESC and -STRESN	Lower end of normal range or reference range for standardized results (e.g., --STRESC, --STRESN) represented in standardized units (--STRESU).
--STNRHI	Normal Range Upper Limit-Standard Units	Num	Variable Qualifier of -STRESC and -STRESN	Upper end of normal range or reference range for standardized results (e.g., --STRESC, --STRESN) represented in standardized units (--STRESU).
--STNRC	Normal Range for Character Results	Char	Variable Qualifier of -STRESC	Normal range or reference range for results stored in --STRESC that are character in ordinal or categorical scale. Example: Negative to Trace.
--NRIND	Normal/Reference Range Indicator	Char	Variable Qualifier of -ORRES	Used to indicate the value is outside the normal range or reference range. May be defined by --ORNRLLO and --ORNRHI or other objective criteria. Examples: Y, N; HIGH, LOW; NORMAL; ABNORMAL.
--ORREF	Reference Result in Original Units	Char	Variable Qualifier of -ORRES	Reference value for the result or finding as originally received or collected. --ORREF uses the same units as --ORRES, if applicable.
--STREFC	Reference Result in Standard Format	Char	Variable Qualifier of -STRESC	Reference value for the result or finding copied or derived from -ORRES in a standard format.
--STREFN	Numeric Reference Result in Std Units	Num	Variable Qualifier of -STRESN	Reference value for continuous or numeric results or findings in standard format or in standard units. --STREFN uses the same units as --STRESN, if applicable.
--RESCAT	Result Category	Char	Variable Qualifier of -ORRES	Used to categorize the result of a finding. Example: MALIGNANT or BENIGN for tumor findings. RESISTANCE VARIANT for genetic variation.
--CHRON	Chronicity of Finding	Char	Variable Qualifier of -STRESC	Characterization of the duration of a biological process resulting in a particular finding. Multiple terms are not allowed for this variable. Examples: ACUTE, CHRONIC, SUBACUTE.
--DISTR	Distribution Pattern of Finding	Char	Variable Qualifier of -STRESC	Description of the distribution pattern of a finding within the examined area. Examples: FOCAL, MULTIFOCAL, DIFFUSE, FOCAL MULTIFOCAL.

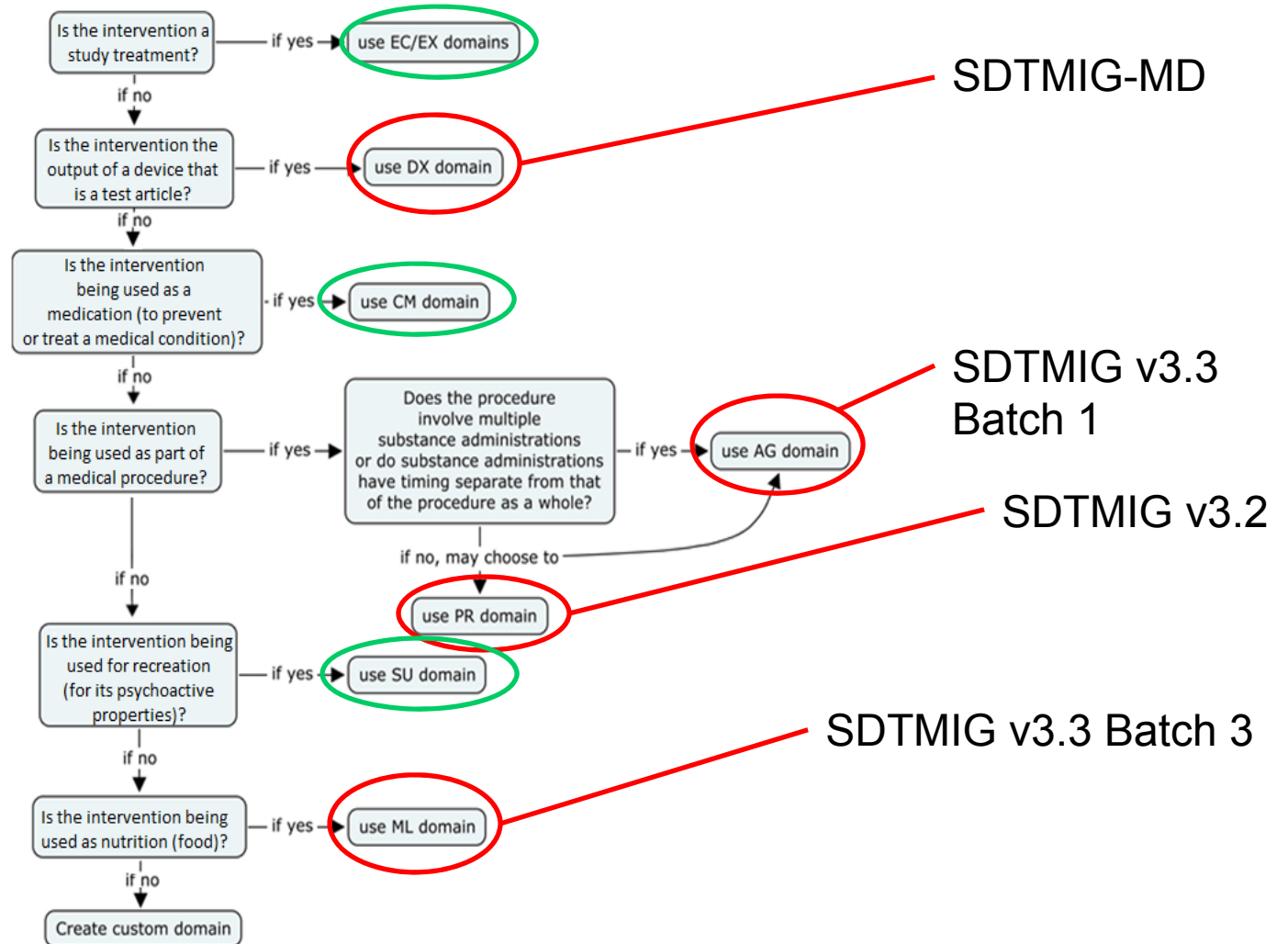
SDTM Rolling Copy: What's New (1)

- New General-Observation-Class Variables
 - Events
 - --EVAL (Evaluator)
 - --EVALID (Evaluator Identifier)
 - --ACPTFL (Accepted Record Flag)
 - Findings
 - --NSPCES
 - --NSTRN
 - --ORREF (Reference Result in Original Units)
 - --STREFC (Reference Result in Standard Format)
 - --STREFN (Numeric Reference Result in Std Units)
 - --CHRON (Chronicity of Finding)
 - --DISTR (Distribution Pattern of Finding)
 - --REPNUM (Repetition Number)
 - Identifiers
 - FOCID (Focus of Study-Specific Interest)
 - --RECID (Invariant Record Identifier)

SDTM Rolling Copy: What's New (1)

- Concept of Domain-Specific Variables
 - --EGBEATNO
 - --EGLEAD
- New Domains
 - Table 2.2.10, Subject Milestones
 - Table 3.6, Trial Milestones
- Proposed Deletions
 - --STRF, --ENRF

SDTMIG Interventions Index: Added Decision Tree



Clinical Classifications (CC) Domain: Overview

- For named instruments whose output is an ordinal or categorical score that serves as a surrogate for, or ranking of, disease status or other physiological or biological status
- Falls under Clinical Outcome Assessments (COA)
 - Modeled and maintained in the same manner as Questionnaires (QS) and Functional Tests (FT, SDTM v3.3 Batch 1)
 - CT developed for CCTEST and CCTESTCD
- May be single scores or composites within or across domains.
Examples:
 - Child-Pugh
 - NYHA Class

Clinical Classifications (CC) Domain: Child-Pugh Example

Controlled Terminology for CCTESTCD and CCTEST

STUDYID	DOMAIN	USUBJID	CCSEQ	CCGRPID	CCLNKID	CCTESTCD	CCTEST	CCCAT
ABC123	CC	100456	1		CPH1	CPS0101	CPS01-Bilirubin	CHILD-PUGH SCORE
ABC123	CC	100456	2		CPH2	CPS0102	CPS01-Serum Albumin	CHILD-PUGH SCORE
ABC123	CC	100456	3		CPH3	CPS0103	CPS01-PT INR	CHILD-PUGH SCORE
ABC123	CC	100456	4		CPH4	CPS0104	CPS01-Ascites	CHILD-PUGH SCORE
ABC123	CC	100456	5	1		CPS0105	CPS01-WH Hepatic Encephalopathy	CHILD-PUGH SCORE
ABC123	CC	100456	6			CPS0106	CPS01-Child-Pugh Score	CHILD-PUGH SCORE
ABC123	CC	100456	7			CPS0107	CPS01-Child-Pugh Class	CHILD-PUGH SCORE

CCORRES	CCORRESU	CCSTRESC	CCSTRESN	VISITNUM	CCDTC
2-3	mg/dL	2	2	3	2014-04-23
2.8-3.5	g/dL	2	2	3	2014-04-23
<1.7		1	1	3	2014-04-23
Moderate to Severe Grade I-II (or suppressed with medication)		3	3	3	2014-04-23
10		2	2	3	2014-04-23
C		10	10	3	2014-04-23
		SEVERE		3	2014-04-23

Link to corresponding records in LB through RELREC

Range within instrument in which subject's lab value falls

Corresponding score

Nervous System Findings (NV) Domain

- First introduced as part of the TA User Guide for Multiple Sclerosis
- Results of tests from a neurological examination or procedure that measures active processes
- Examples:
 - Measurement of glucose metabolism
 - Uptake of fluorodeoxyglucose via PET/CT, expressed as an uptake ratio
 - Visual evoked potential (VEP)
 - Brain responses to visual stimuli, as assessed via an EEG

Ophthalmologic Examinations (OE) Domain

- First introduced as part of the TA User Guide for Multiple Sclerosis
- Findings from physiological ophthalmic examinations
 - Morphological ophthalmic examinations should be represented in the MO domain
- New Identifier Variable, FOCID will contain:
 - OD (Oculus Dexter, Right Eye)
 - OS (Oculus Sinister, Left Eye)
 - OU: (Oculus Uterque, Both Eyes)
- Tests modeled include the following:
 - Intraocular Pressure (mm)
 - Burning Sensation, Grade
 - Itching, Grade
 - Foreign Body Sensation, Grade
 - Watering, Grade
 - Dryness, Grade
 - Sensitivity to Light, Grade

TU and TR Domains

- The scope broadened to accommodate use outside oncology setting.
 - Allow domains to represent data for other types of lesions
 - Not limited to tumors.
- Changes to currently published material are minimal
 - Domain names updated to include “Tumor/Lesion”
 - Additional examples added
 - Cardiovascular lesions (TAUG-CV)
 - Cysts for Polycystic Kidney Disease

Submitting Non-Standard Variables: Overview

- Section 8.4 (Relating Non-Standard Variables Values to a Parent Domain) Revised
 - Incorporates content submitted as part of the publicly reviewed “SDS Proposal for Alternate Handling of Supplemental Qualifiers” (SDTMIG v3.2, Batch 2).
- Provides an alternative method for submitting NSVs in parent domain.
- Doesn't change the nature of the non-standard data submitted
- Complete metadata must be provided for each NSV
 - Variable lengths set to the appropriate length, as with all standard character variables
 - Roles to be used:
 - Non-Standard Identifier
 - Non-Standard Qualifier
 - Non-Standard Timing
- NSVs would be ordered after the standard variables, and ordered by Role

Submitting Non-Standard Variables: Example

Existing Method Using SUPPHO

ho.xpt

STUDYID	DOMAIN	USUBJID	HOSEQ	HOTERM	HOSTDTC	HOENDTC	HODUR
1999001	HO	0001	1	Hospitalization	2004-01-05	2004-01-12	P1W

suppho.xpt

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1999001	HO	0001	HOSEQ	1	HOAERPFL	AE Reported This Episode	Y	CRF	
1999001	HO	0001	HOSEQ	1	HOMEDSFL	Meds Prescribed	Y	CRF	
1999001	HO	0001	HOSEQ	1	HOPROCFL	Procedures Performed	Y	CRF	
1999001	HO	0001	HOSEQ	1	HOPROVNM	Provider Name	General Hosp	CRF	
1999001	HO	0001	HOSEQ	1	HOSPUFL	Any Time in Spec. Unit	Y	CRF	
1999001	HO	0001	HOSEQ	1	HOSPUTYP	Specialized Unit Type	ICU	CRF	
1999001	HO	0001	HOSEQ	1	HORLCNDF	Visit Related to Study Med Cond.	Y	CRF	

New Method Including Non-Standard Variables in Parent (HO) Domain

ho.xpt

STUDYID	DOMAIN	USUBJID	HOSEQ	HOTERM	HOSTDTC	HOENDTC	HODUR	HOAERPFL	HOMEDSFL
1999001	HO	0001	1	Hospitalization	2004-01-05	2004-01-12	P1W	Y	Y

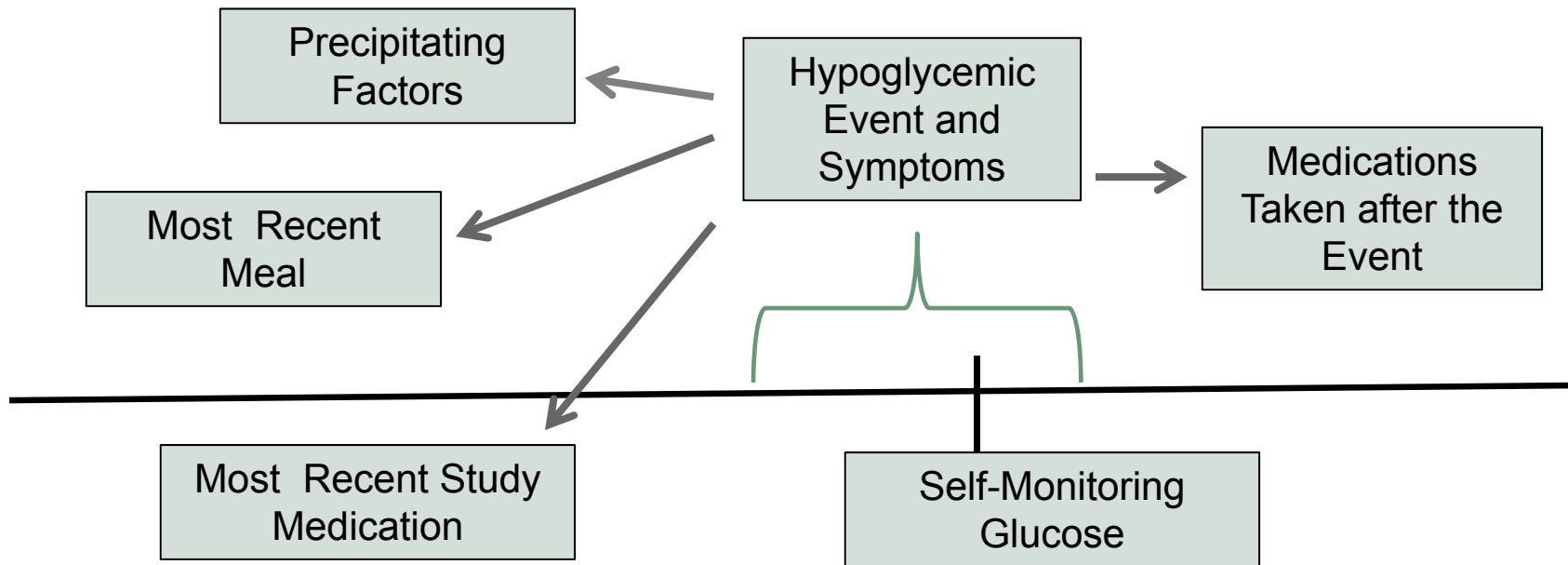
HOPROCFL	HOPROVNM	HOSPUFL	HOSPUTYP	HORLCNDF
Y	General Hosp	Y	ICU	Y

Disease Milestones Variables and Related Domains (1): Overview

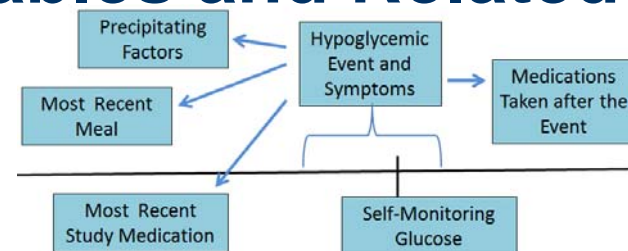
Additions include the following:

- New Timing Variables
 - SDTM Table 2.2.5
 - SDTMIG Section 4.1.4 (Actual and Relative Time Assumptions) added discussion
- New Trial Milestones Dataset
 - SDTM Section 3
 - SDTMIG Section 7
- New Subject Milestones Dataset
 - SDTM Section 2
 - SDTMIG Section 5
- The Disease Milestones package was part of the TAUG for Diabetes (released on September 11, 2014)

Disease Milestones Variables and Related Domains (2): Hypoglycemic Event Example



Disease Milestones Variables and Related Domains (3): The Data



STUDYID	DOMAIN	USUBJID	CESEQ	CETERM	CECAT	CEPRES	CEOCCUR	CESTDTC	MIDS	MIDSREL	MIDSRTC
XYZ	CE	XYZ-001-001	1	HYPOGLYCEMIA	HYPOGLYCEMIA			2013-09-01T11:00	HYPO 1		2013-09-01T11:00
XYZ	CE	XYZ-001-001	2	SWEATING	HYPOGLYCEMIA	Y	Y		HYPO 1	DURING	2013-09-01T11:00

STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FAORRES	MIDS	MIDSREL
XYZ	FA	XYZ-001-001	2	POSSCAUS	Possible cause identified	HYPOGLYCEMIC EVENT	Y	HYPO 1	PRIOR TO EVENT
XYZ	FA	XYZ-001-001	3	MEALCAUS	Missed or delayed meal a possible cause	HYPOGLYCEMIC EVENT	Y	HYPO 1	PRIOR TO EVENT
XYZ	FA	XYZ-001-001	4	PACAUS	Physical activity a possible cause	HYPOGLYCEMIC EVENT	N	HYPO 1	PRIOR TO EVENT

STUDYID	DOMAIN	USUBJID	MLSEQ	MLTRT	MIDS	MIDSREL	MIDSRTC
XYZ	ML	XYZ-001-001	1	EVENING MEAL	HYPO 1	LAST MEAL PRIOR TO	2013-09-01T11:00

STUDYID	DOMAIN	USUBJID	EXSEQ	EXTRT	EXCAT	EXDOSE	EXDOSU	EXSTDTC	MIDS	MIDSREL	MIDSRTC
XYZ	EX	XYZ-001-001	1	DRUG A	HIGHLIGHTED DOSE	10	mg	2013-09-01T07:00	HYPO 1	LAST INTERVENTION PRIOR TO	2013-09-01T11:00

STUDYID	DOMAIN	USUBJID	CMSEQ	CMTRT	CMCAT	CMSCAT	COMPRES	CMOCCUR	MIDS	MIDSREL	MIDSRTC
XYZ	CM	XYZ-001-001	1	HYPOGLYCEMIC TREATMENTS	HYPOGLYCEMIC TREATMENTS		Y	Y	HYPO 1	IMMEDIATELY AFTER THE EVENT	2013-09-01T11:00
XYZ	CM	XYZ-001-001	4	GLUCOSE TABLETS	HYPOGLYCEMIC TREATMENTS	MEDICATION	Y	Y	HYPO 4	IMMEDIATELY AFTER THE EVENT	2013-09-01T11:00

STUDYID	DOMAIN	USUBJID	LBSEQ	LBTEST	LBSTRESN	LBSTRESU	LBSPEC	LBRTC	MIDS	MIDSREL	MIDSRTC
XYZ	LB	XYZ-001-001	1	GLUCOSE	3.33	mmol/L	BLOOD	2013-09-01T11:15	HYPO 1	DURING	2013-09-01T11:00

Disease Milestones Variables and Related Domains (4): TM and SM Examples

Trial Milestones (tm.xpt)

STUDYID	DOMAIN	TMSEQ	MIDSTYPE	MIDSDEF	MIDSRPT
ABC	TM	1	HYPOGLYCEMIC EVENT	Hypoglycemic Event, the occurrence of a blood glucose concentration below the specified (by study) level of hypoglycemia	Y

Subject Milestones (sm.xpt)

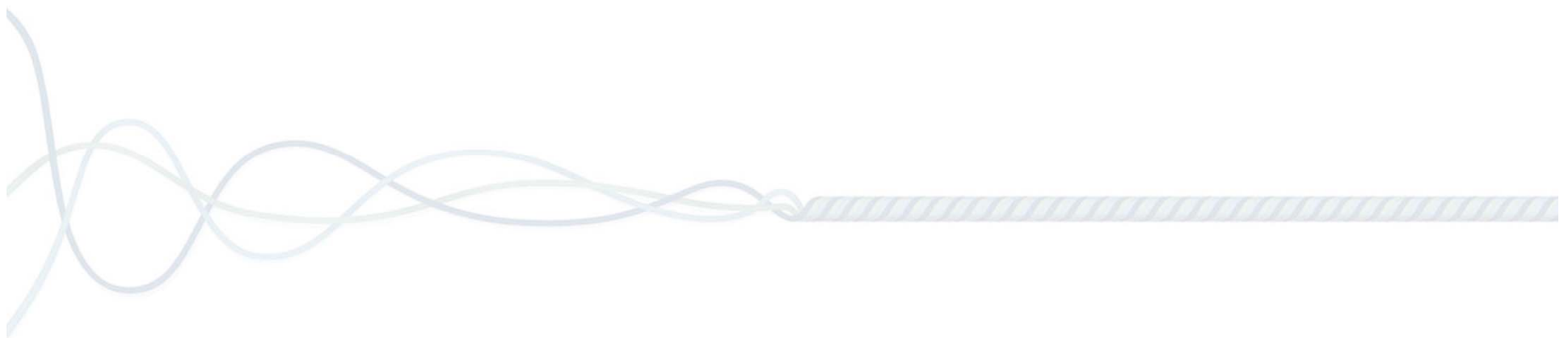
STUDYID	DOMAIN	USUBJID	SMSEQ	MIDS	MIDSTYPE	SMSTDTC	SMSTDY	SMENDTC	SMENDY
ABC	SM	ABC-1001	2	HYPO 1	HYPOGLYCEMIC EVENT	2013-09-01T11:00	25	2013-09-01T11:00	25
ABC	SM	ABC-1001	3	HYPO 2	HYPOGLYCEMIC EVENT	2013-09-24T08:48	50	2013-09-24T08:48	50

Acknowledgements for Batch 2

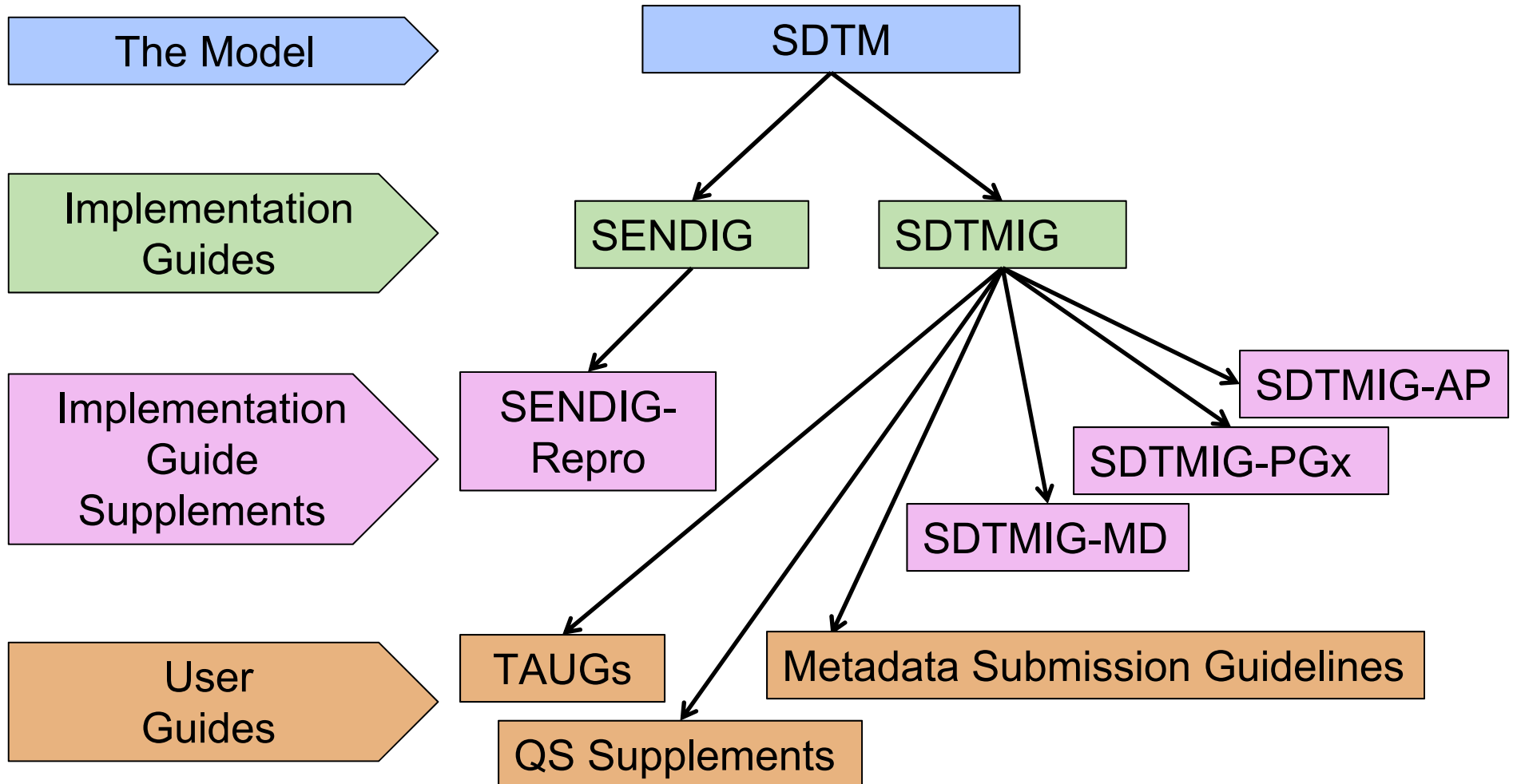
- SDS Leadership Team
- SDS Team
- Ophthalmology Subteam
- CFAST Representatives
 - CDISC
 - National Cancer Institute
 - Critical Path Institute
 - TransCelerate Biopharma Inc.

Please look for the posting of this package, and provide comments.

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SDTM, Implementation Guide, and User Guide Relationships



Therapeutic-Area Collaboration: Coalition for the Accelerating Standards and Therapies



- CDISC
- National Cancer Institute
- Critical Path Institute
- FDA
- National Institutes of Health
- TransCelerate Biopharma Inc.

Therapeutic-Area User Guides

TAUG	Status	Lead Organization(s)
Alzheimer's Disease v1	Final	C-Path's Coalition Against Major Diseases
Alzheimer's Disease v2	Provisional *	CFAST (C-Path and CDISC Leads)
Asthma v1	Provisional *	CFAST (CDISC Lead)
Pain v1	Provisional *	CDISC and the Analgesic Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION)
Parkinson's Disease v1	Provisional *	CDISC, National Institute of Neurological Disorders and Strokes (NINDS) and the Coalition Against Major Diseases (CAMD)
Polycystic Kidney Disease v1	Provisional *	CDISC and c-Path's Polycystic Kidney Disease Outcomes Consortium
Tuberculosis v1	Provisional *	C-Path's Critical Path to TB Drug Regimens (CPTR) and CDISC
Virology v1	Provisional *	CDISC SDS and Lab Teams
Diabetes	Provisional *	CFAST (TransCelerate Lead)
Multiple Sclerosis	Provisional *	C-Path

Therapeutic-Area User Guides

TAUG	Status	Lead Organization(s)
Cardiovascular Endpoints v1	Provisional *	CDISC, DCRI
QTc Prolongation	Public Review Complete	CFAST (TransCelerate Lead)
Influenza	Public Review Complete	C-Path
Traumatic Brain Injury	Under Dev	CDISC
Schizophrenia	Under Dev	CDISC, DCRI
Breast Cancer	Under Dev	TransCelerate
Dyslipidemia	Under Dev	TransCelerate
COPD	Under Dev	TransCelerate
Hepatitis C	Under Dev	CFAST (TransCelerate Lead)