What's new in SDTM 3.1.2 ?

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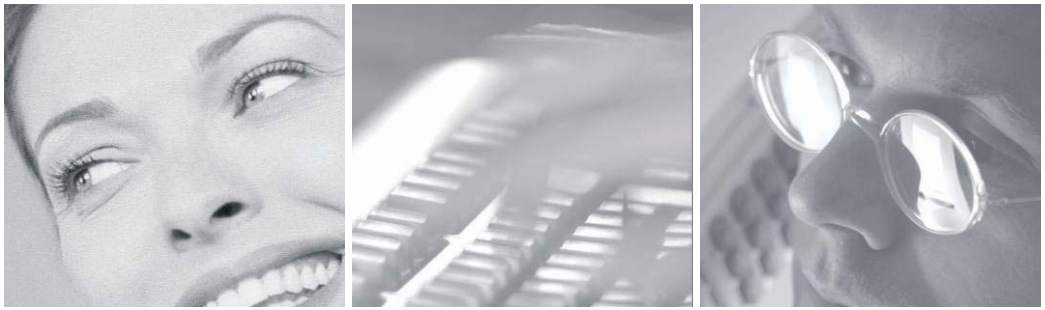

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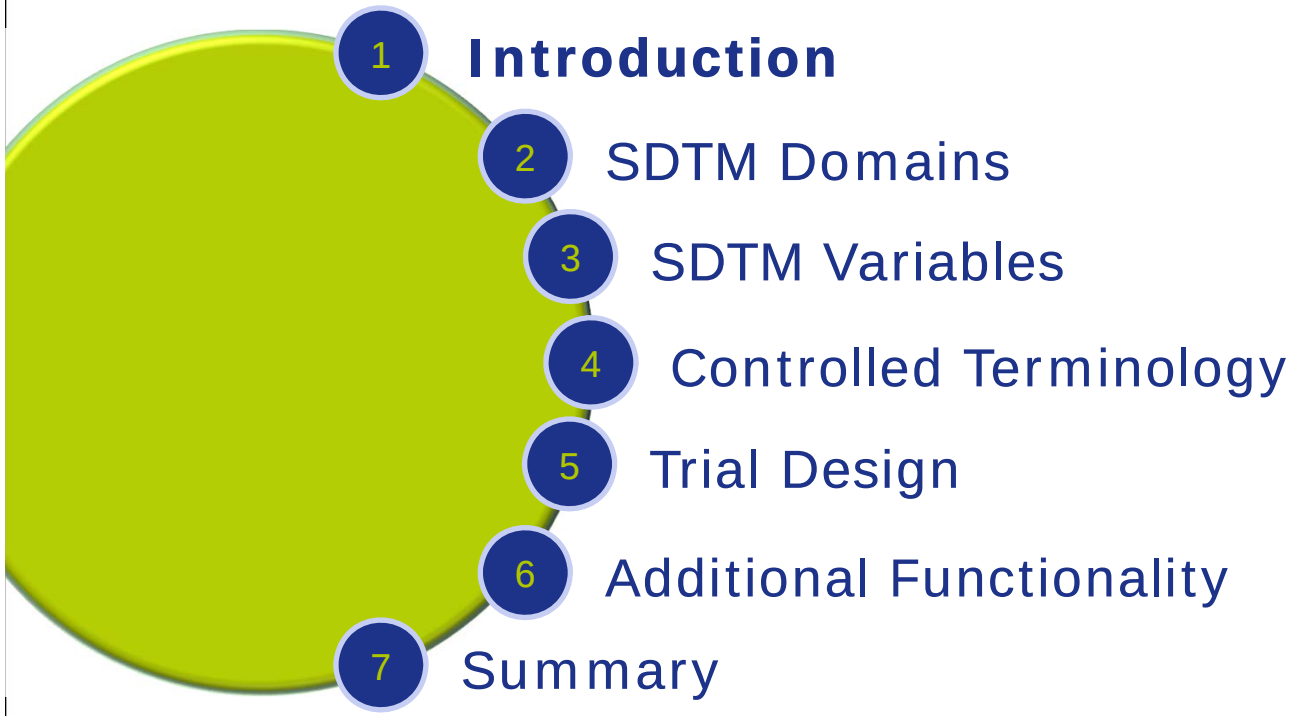
Overview



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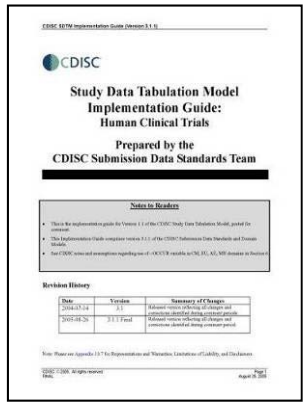
SDTM

- **S**tudy **D**ata **T**abulation **M**odel
- AIM :
  - Define a global standard for study data tabulations
  - Standardise regulatory submissions
  - Currently, de facto standard between the CROs and sponsors
- Focus on study data tabulation content
- Requested by FDA for all submissions


CDISC

Study Data Tabulation Model
Implementation Guide:
Human Clinical Trials

Prepared by the
CDISC Submission Data Standards Team

Notes to Readers

Revision History

(http://www.cdisc.org/models/sdtm/v1.1/index.html)

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SDTM Adoption By FDA

- Expected to be « required for FDA submission » within 2 years
  - Only CDER and CBER
  - CDRH interest is rising, CDISC SDTM team has formed a medical devices subteam
- FDA CDER:
  - Requesting sponsors to submit in SDTM format
  - Encouraging sponsors to submit in ADaM format
- FDA is reporting > 70% SDTM based submissions
- Continuous FDA pilot projects

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Introduction

- New releases:
  - SDTM IG 3.1.2 (298 pages)
  - SDTM 1.2
- SDTM IG 3.1.2:
  - Additional guidance
  - More examples
  - Minor and major changes to the model

(http://www.cdisc.org/standards/index.html)

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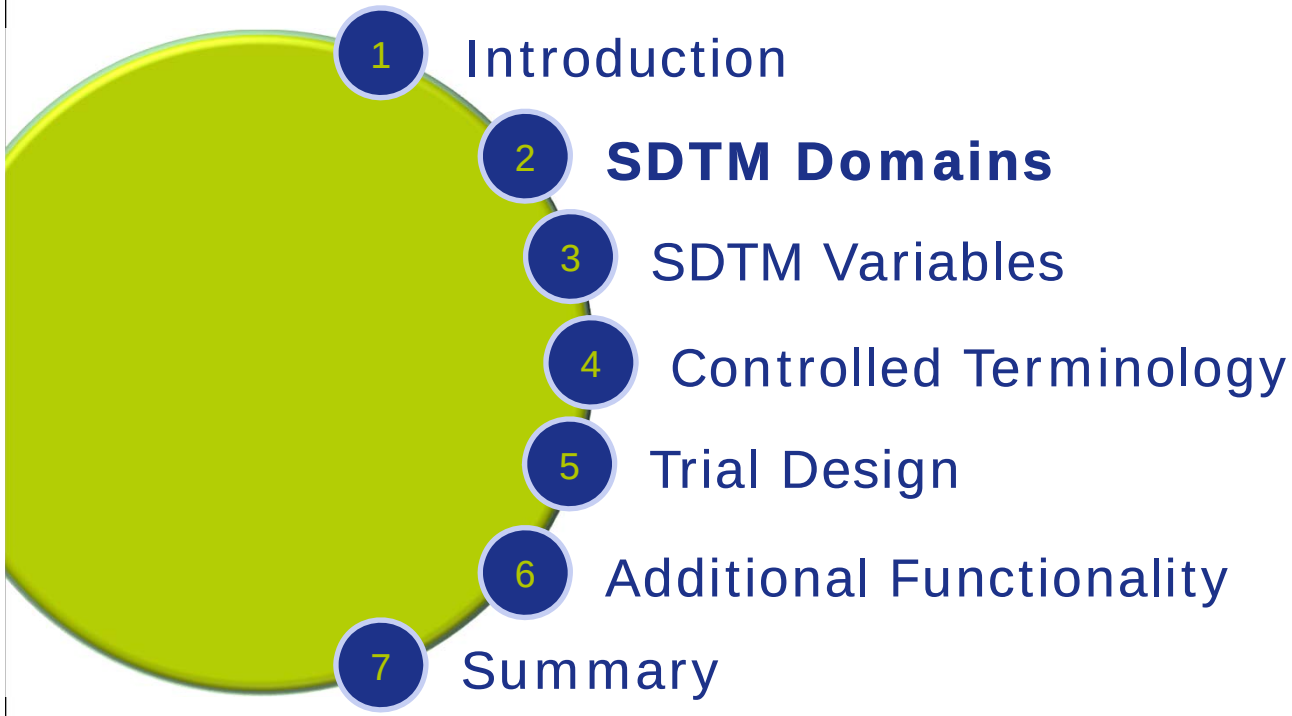
Overview



1. Introduction
2. **SDTM Domains**
3. SDTM Variables
4. Controlled Terminology
5. Trial Design
6. Additional Functionality
7. Summary

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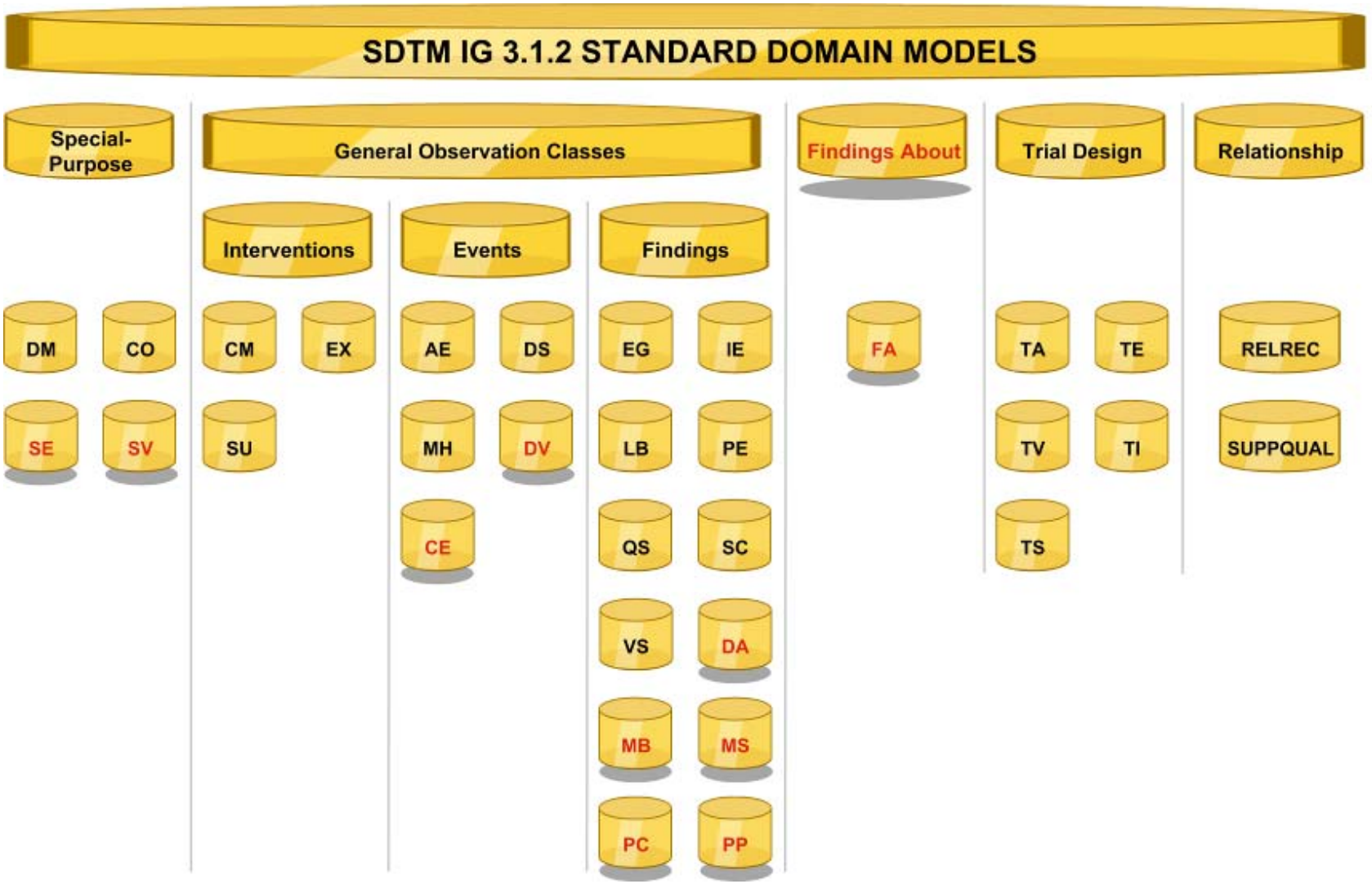
SDTM Standard Domain Models



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New Published Domains

- PC = Pharmacokinetic Concentrations
- PP = Pharmacokinetic Parameters

- DA = Drug Accountability
- DV = Protocol Deviations

- MB = Microbiological Specimen
- MS = Microbiological Susceptibility

- CE = Clinical Events
- FA = Findings About Events/Interventions

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PC & PP: Pharmacokinetics

- Pharmacokinetic Concentrations: Data about concentrations of analytes as a function of time
- Pharmacokinetic Parameters: Data describing parameters of time-concentration curve
- PP derived from PC
  - Records are related via RELREC
  - However often not all concentrations are used for calculation of a parameter
  - Need to indicate which PC data is used to calculate which PP parameter

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PC & PP: Pharmacokinetics

- PC

STUDYID	DOMAIN	USUBJID	PCSEQ	PCGRPID	PCTESTCD	PCTEST	PCCAT	PCORRES	PCORRESU	PCTPT	PCTPTNUM
XYZ	PC	18	1	**DRGX**	DRUG X	Study drug	ANALYTE	9	ug/mL	5 min	1
XYZ	PC	18	2	**DRGX**	DRUG X	Study drug	ANALYTE	20	ug/mL	25 min	2
XYZ	PC	18	3	**DRGX**	DRUG X	Study drug	ANALYTE	31	ug/mL	50 min	3
XYZ	PC	18	4	EXCLUDE	DRUG X	Study drug	ANALYTE	20	ug/mL	100 min	4

- PP

STUDYID	DOMAIN	USUBJID	PPSEQ	PPGRPID	PPTESTCD	PPTEST	PPCAT	PPORRES	PPORRESU
XYZ	PP	18	1	ALL	TMAX	Time to Max effect	DRUG X	1.04	h
XYZ	PP	18	2	ALL	CMAX	Max effect Concentration	DRUG X	38.5	mg/L
XYZ	PP	18	3	**SOME**	THALF	Half-life of 1st exp phase	DRUG X	0.42	h

- TMAX and CMAX use ALL PC concentrations
- THALF does not use PCTPT = 100 min
- RELREC

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
XYZ	PP	18	PPGRPID	ALL		1
XYZ	PC	18	PCGRPID	DRGX		1
XYZ	PC	18	PCGRPID	EXCLUDE		1
XYZ	PP	18	PPGRPID	**SOME**		2
XYZ	PC	18	PCGRPID	**DRGX**		2

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Clinical Events

- Clinical events of interest

- Not classified as Adverse Events
  - Stated in Protocol
  - Disease under study, ‘Signs and Symptoms’

- Examples:
  - Nausea, headache, …
  - Rash event

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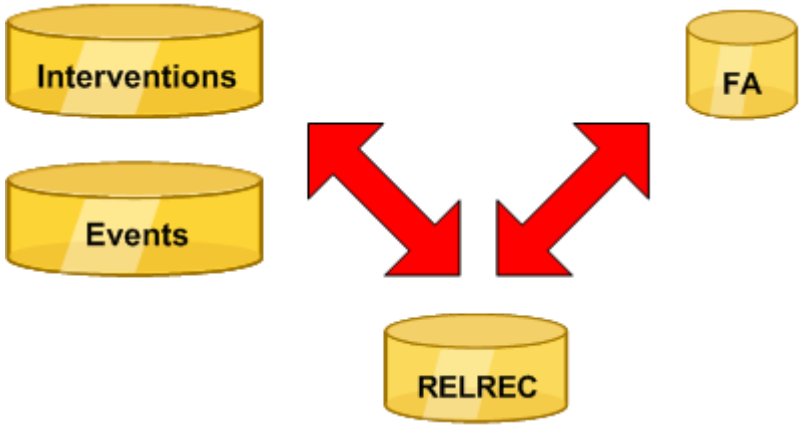
Findings About

- Solution for problems SUPPQUAL cannot handle
  - Additional information with different timing
  - To represent each measurement with its unit
- Only in combination with Events, Interventions
- Linked via RELREC
- New variable: --OBJ



SDTM IG 3.1.2 section 6.4.1

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When to use Findings About

- Data that do not describe an Event or Intervention as a whole
  - different timing
  - snapshots over time
- Data that indicate the occurrence of related symptoms
  - E.g. Migraine <-> related symptoms: nausea, headache
- Data for which no Event or Intervention record has been collected or created
  - Details of condition collected, condition itself not collected
- Data that indicate the occurrence of pre-specified AE's
  - AE: AE's that did occur
  - FA: Presp. AE's that did not occur
- Data having qualifiers that can be represented in Findings variables
  - Units and methods

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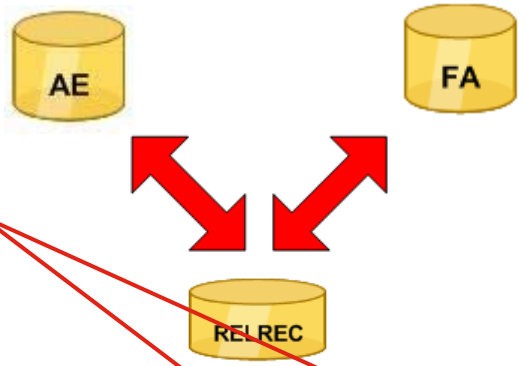
Use case 1: Data that do not describe an event or intervention as a whole

ADVERSE EVENTS					
Event name: AETERM					Watery Stools
When did the event start?					Jan 5, 2006 AESTDTC
When did the event end?					Jan 11, 2006 AEENDTC
At each visit, record severity of the Adverse Event (L = Mild, M = Moderate, H = Severe)					
Visit	1	2	3	4	
Severity	L	M	H	L	FAORRES where FATESTCD = "SEV"



- AE

STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	AEDECOD	AESEV	AESTDTC	AEENDTC
XXX	AE	123	1	Watery Stools	Diarrhea	SEVERE	2006-01-05	2006-01-11

- FAAE

STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FAORRES	VISIT	FADTC
XXX	FA	123	1	SEV	Severity/Intensity	Diarrhea	MILD	1	2006-01-06
XXX	FA	123	2	SEV	Severity/Intensity	Diarrhea	MODERATE	2	2006-01-07
XXX	FA	123	3	SEV	Severity/Intensity	Diarrhea	SEVERE	3	2006-01-08
XXX	FA	123	4	SEV	Severity/Intensity	Diarrhea	MODERATE	4	2006-01-11

- RELREC

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
XXX	AE	123	AESEQ	1		1
XXX	FA	123	FASEQ	1		1
XXX	FA	123	FASEQ	2		1
XXX	FA	123	FASEQ	3		1
XXX	FA	213	FASEQ	4		1

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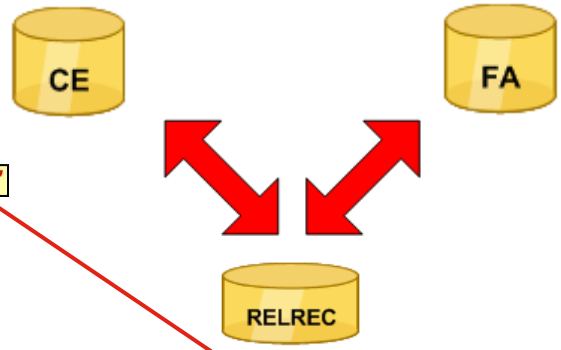
Use case 2: Data that indicate the occurrence of related symptoms

Migraine Symptoms Diary	CETERM	
Migraine Reference Number	90567	
When did the migraine start	DD-MM-YYYY HH:MM	16-05-2007 10:30
Answer the following 5 minutes BEFORE dosing	FATPT	
Severity of Migraine	○ Mild ○ Moderate ✔ Severe	FAORRES where FATESTCD = "SEV"
Associated Symptoms:		
Sensitivity to light	○ No ✔ Yes	
Sensitivity to sound	FAOBJ ✔ No ○ Yes	FAORRES where FATESTCD = "OCCUR"
Nausea	○ No ✔ Yes	
Aura	○ No ✔ Yes	

CESTDTC



- CE

STUDYID	DOMAIN	USUBJID	CESEQ	CESPID	CETERM	CEDECOD	CESTDTC
ABC	CE	ABC-123	1	90567	Migraine	Migraine	2007-05-16T10:30

- FACE

Row	STUDYID	DOMAIN	USUBJID	FASEQ	FASPID	FATESTCD	FATEST	FAOBJ	FACAT
1	ABC	FA	ABC-123	1	90567	SEV	Severity/Intensity	Migraine	MIGRAINE SYMPTOMS
2	ABC	FA	ABC-123	2	90567	OCCUR	Occurrence	Sensitivity To Light	MIGRAINE SYMPTOMS
3	ABC	FA	ABC-123	3	90567	OCCUR	Occurrence	Sensitivity To Sound	MIGRAINE SYMPTOMS
4	ABC	FA	ABC-123	4	90567	OCCUR	Occurrence	Nausea	MIGRAINE SYMPTOMS
5	ABC	FA	ABC-123	6	90567	OCCUR	Occurrence	Aura	MIGRAINE SYMPTOMS

Row	FAORRES	FASTRESC	FADTC	FATPT	FAELTM	FATPTREF
1 (cont'd)	SEVERE	SEVERE	2007-05-16	5M PRE-DOSE	-PT5M	DOSING
2 (cont'd)	Y	Y	2007-05-16	5M PRE-DOSE	-PT5M	DOSING
3 (cont'd)	N	N	2007-05-16	5M PRE-DOSE	-PT5M	DOSING
4 (cont'd)	Y	Y	2007-05-16	5M PRE-DOSE	-PT5M	DOSING
5 (cont'd)	Y	Y	2007-05-16	5M PRE-DOSE	-PT5M	DOSING

- RELREC

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
ABC	CE		CESPID		ONE	1
ABC	FA		FASPID		MANY	1

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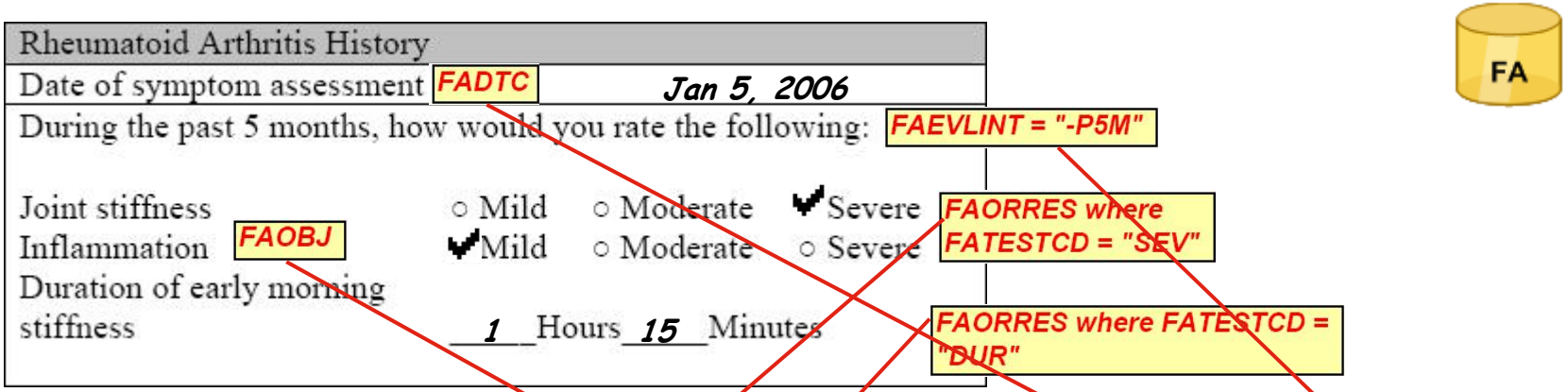
Use case 3: Data for which no Event or Intervention record has been collected or created

- Rheumatoid arthritis Event is not created
- Rheumatoid arthritis details are collected
- No RELREC



- FA

DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FACAT	FAORRES	FADTC	FAEVLINT
FA	123	1	SEV	Severity/ Intensity	Joint Stiffness	RHEUMATOID ARTHRITIS HISTORY	SEVERE	2006-01-05	-P5M
FA	123	2	SEV	Severity/ Intensity	Inflammation	RHEUMATOID ARTHRITIS HISTORY	MILD	2006-01-05	-P5M
FA	123	3	DUR	Duration	Early Morning Stiffness	RHEUMATOID ARTHRITIS HISTORY	PT1H15M	2006-01-05	-P5M

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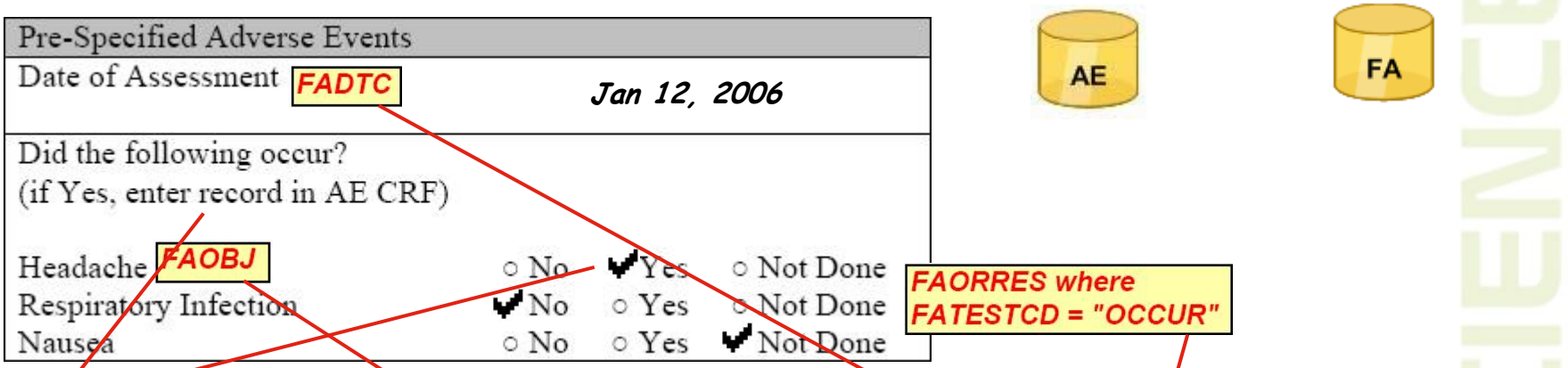
Use case 4: Data that indicate the occurrence of pre-specified Adverse Events

- SDTM Rule: AE can only contain Adverse Events that did occur
- No RELREC (no relationship collected in CRF)



- AE (collected in AE CRF)

STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	AESEV	AEPRESP	AESTDTC	AEENDTC
YYY	AE	12	1	Headache	MILD	Y	2006-01-05	2006-01-11

- FAAE

STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FAORRES	FASTRESC	FASTAT	FADTC
YYY	FA	12	1	OCCUR	Occurrence	Headache	Y	Y		2006-01-12
YYY	FA	12	2	OCCUR	Occurrence	Respiratory Infection	N	N		2006-01-12
YYY	FA	12	3	OCCUR	Occurrence	Nausea			NOT DONE	2006-01-12

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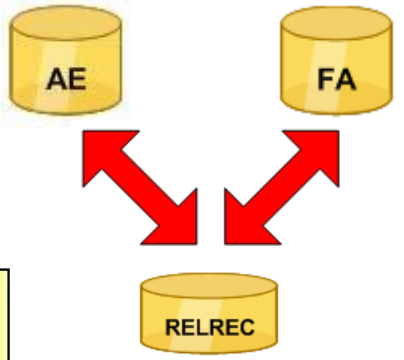
Use case 5: Data having qualifiers that can be represented in Findings variables

Injection Site Rash assessment		
Date of assessment	FADTC	Jan 8, 2006
Associated AE reference number	FASPID	5
Rash Size	FAORRES / FAORRESU where FATESTCD = "SIZE"	1.5 ○ cm ✔ in
Lesion Type & Count		
Macules	FAOBJ	○ 0 ○ 1 to 300 ✔ > 300
Vesicles		✔ 0 ○ 1 to 300 ○ > 300
Scars		○ 0 ✔ 1 to 300 ○ > 300

FAORRES where FATESTCD = "COUNT"



- AE (collected on AE CRF)

STUDYID	DOMAIN	USUBJID	AESEQ	AESPID	AETERM	AELOC	AESEV	AESTDTC
ZZZ	AE	123	1	5	Injection Site Rash	LEFT ARM	SEVERE	2006-01-05

- FAAE

STUDYID	DOMAIN	USUBJID	FASEQ	FASPID	FATESTCD	FATEST	FAOBJ	FAORRES	FAORRESU	FADTC
ZZZ	FA	123	1	5	SIZE	Size	Injection Site Rash	1.5	IN	2006-01-08
ZZZ	FA	123	2	5	COUNT	Count	Macules	> 300		2006-01-08
ZZZ	FA	123	3	5	COUNT	Count	Vesicles	0		2006-01-08
ZZZ	FA	123	4	5	COUNT	Count	Scars	1 to 300		2006-01-08

- RELREC

STUDYID	ROMAIN	USUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
ZZZ	AE	123	AESPID		ONE	1
ZZZ	FA	123	FAPID		MANY	1

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SDTM Domain Metadata

Logical keys have changed

Sponsor defined sorting keys allowed

Table 3.2.1. SDTM Submission Dataset-Definition Metadata Example

Dataset	Description	Class	Structure	Purpose	Keys	Location
SU	Substance Use	Interventions	One record per substance type per reported occurrence per subject	Tabulation	STUDYID, USUBJID, SUTRT, SUSTDTC	su.xpt
AE	Adverse Events	Events	One record per adverse event per subject	Tabulation	STUDYID, USUBJID, AEDECOD, AESTDTC	ae.xpt
DS	Disposition	Events	One record per disposition status or protocol milestone per subject	Tabulation	STUDYID, USUBJID, DSDECOD, DSSTDTC	ds.xpt
MH	Medical History	Events	One record per medical history event per subject	Tabulation	STUDYID, USUBJID, MHDECOD	mh.xpt
DV	Protocol Deviations	Events	One record per protocol deviation per subject	Tabulation	STUDYID, USUBJID, DVTERM, DVSTDTC	dv.xpt
CE	Clinical Events	Events	One record per event per subject	Tabulation	STUDYID, USUBJID, CETERM, CESTDTC	ce.xpt

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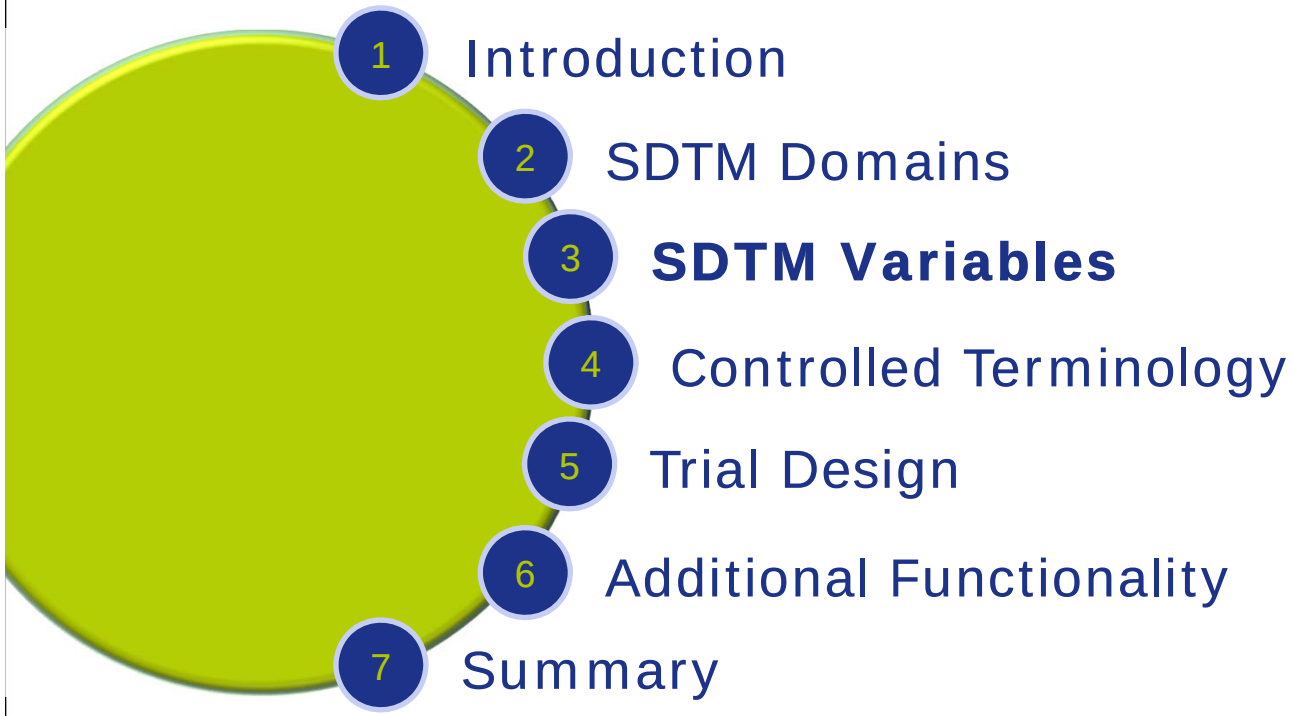
Overview



1. Introduction
2. SDTM Domains
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--PRESP

- Technique for pre-specified Events or Interventions

Situation	Value of --PRESP	Value of --OCCUR	Value of --STAT
Spontaneously reported event occurred			
Pre-specified event occurred	Y	Y	
Pre-specified event did not occur	Y	N	
Pre-specified event has no response	Y		NOT DONE

- Example:

MEDICAL HISTORY	
Conditions of interest:	**MHOCCUR**
Diabetes **MHTERM**	□ yes ✔ no
Gastrointestinal disease	□ yes □ no
Hypertension	✔ yes □ no
If other significant medical history, specify:	
Migraines	
Nose bleeds	

STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHPRESP	MHOCCUR	MHSTAT
ABC	MH	001	1	DIABETES	Y	N	
ABC	MH	001	2	GASTROINTESTINAL DISEASE	Y		NOT DONE
ABC	MH	001	3	HYPERTENSION	Y	Y	
ABC	MH	001	4	MIGRAINES			
ABC	MH	001	5	NOSE BLEEDS			

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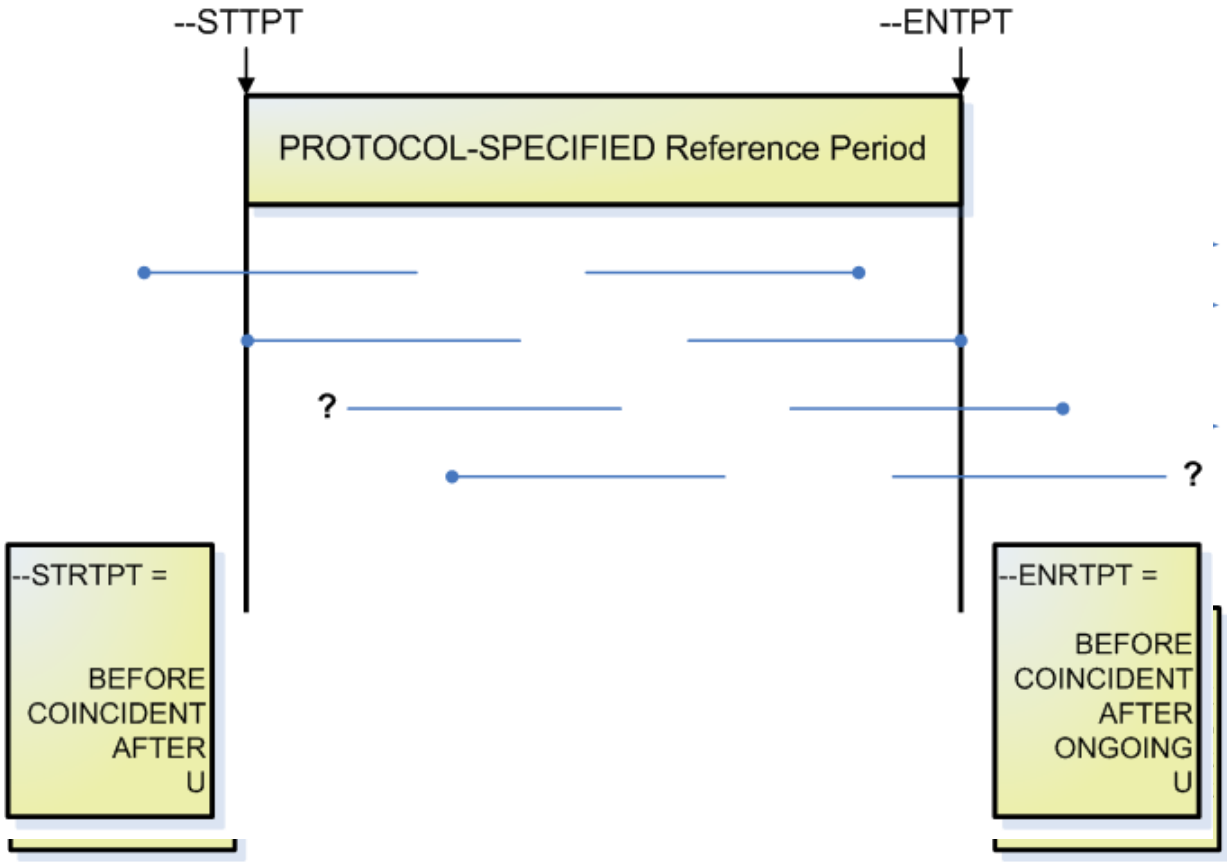
--STTPT, --STRTPT, --ENTPT, --ENRTPT

- SDTM IG 3.1.1: Reference time points in DM
- SDTM IG 3.1.2: Protocol-specified reference period per domain



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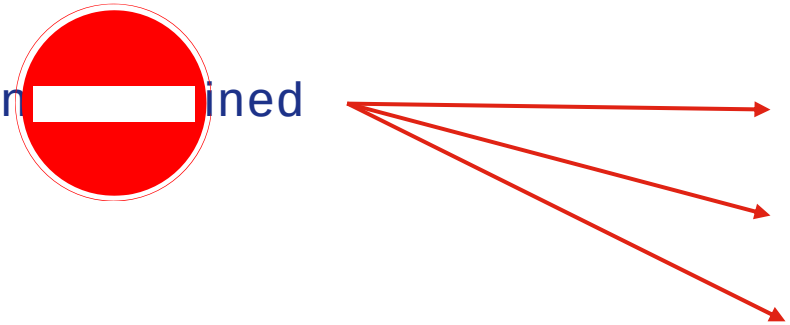
Origin of Variables

- Metadata documented in define.xml

- SDTM IG 3.1.1
  - CRF
  - Derived
  - Spon ined



- SDTM IG 3.1.2
  - CRF
  - Derived
  - eDT
  - Assigned
  - Protocol

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Origin of Variables

- CRF
  - Paper or electronic
- Derived
  - Calculated from other SDTM variables
- eDT: electronic Data Transfer
- Assigned
  - Individual judgement, adjudicator
  - Default values: DOMAIN, --TESTCD
- Protocol
  - Trial Design

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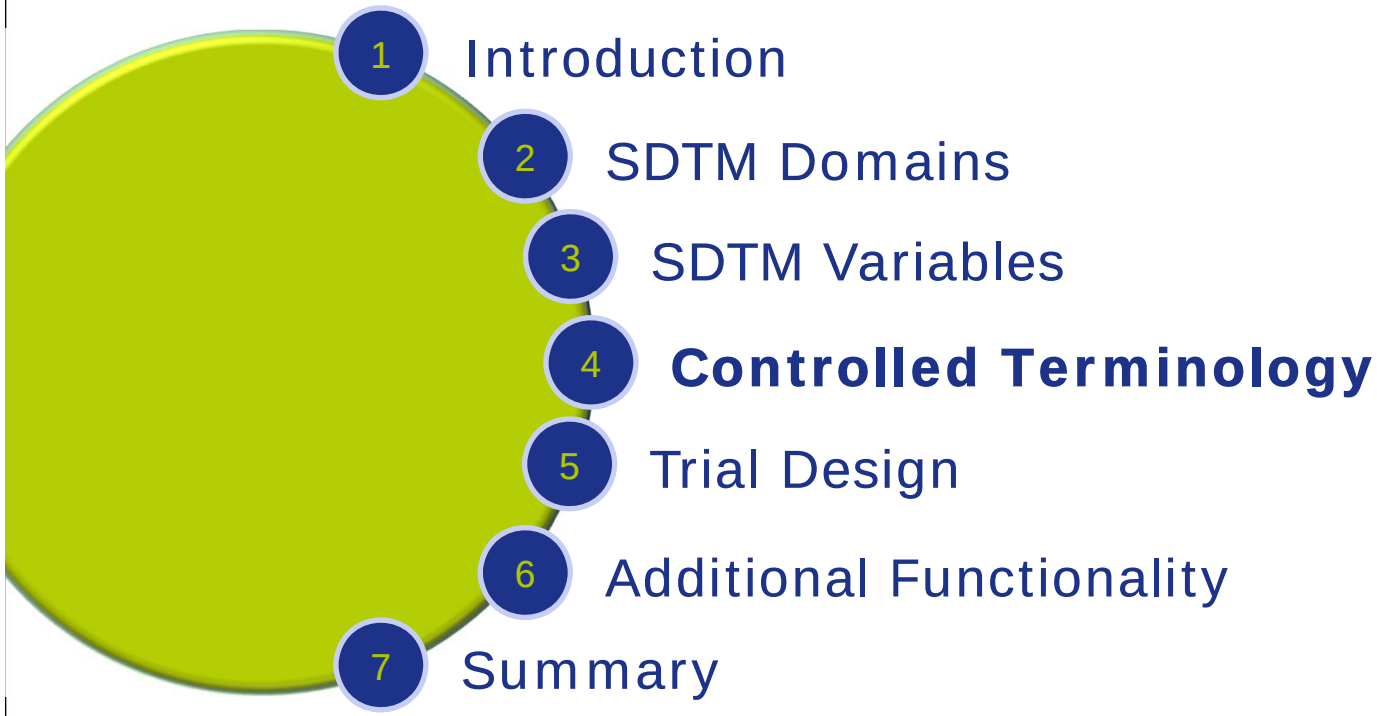
Overview



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Controlled Terminology

Indicates which CDISC codelist should be used

Indicates variable may be subject to sponsor CT

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role			
BRTHDTC	Date/Time of Birth	Char	ISO 8601	Record Qualifier	Date/time of birth of the subject.		
AGE	Age	Num		Record Qualifier	Age expressed in AGEU. May be derived from RFSTDTC and BRTHDTC, but BRTHDTC may not be available in all cases (due to subject privacy concerns).	Exp	
AGEU	Age Units	Char	(AGEU)	Variable Qualifier	Units associated with AGE.	Exp	
SEX	Sex	Char	(SEX)	Record Qualifier	Sex of the subject	Req	
RACE	Race	Char	(RACE)	Record Qualifier	Race of the sub Ethnicity Data regarding the co (http://www.fd regarding RACE.		
ETHNIC	Ethnicity	Char	(ETHNIC)	Record Qualifier	The ethnicity of the subject. Sponsors should refer to "Collection of Race and Ethnicity Data in Clinical Trials" (FDA, September 2005) for guidance regarding the collection of ethnicity (http://www.fda.gov/cder/guidance/5656fnl.htm).	Perm	
ARMCD	Planned Arm Code	Char	*	Record Qualifier	ARMCD is limited to 20 characters and does not have special character restrictions. The maximum length of ARMCD is longer than for other "short" variables to accommodate the kind of values that are likely to be needed for crossover trials. For example, if ARMCD values for a seven-period crossover were constructed using two-character abbreviations for each treatment and separating hyphens, the length of ARMCD values would be 20.	Req	SDTMIG 4.1.2.1
ARM	Description of Planned Arm	Char	*	Synonym Qualifier	Name of the Arm to which the subject was assigned.	Req	SDTMIG 4.1.2.1, SDTMIG 4.1.2.4
COUNTRY	Country	Char	(COUNTRY) ISO 3166	Record Qualifier	Country of the investigational site in which the subject participated in the trial.	Req	
DMDTC	Date/Time of Collection	Char	ISO 8601	Timing	Date/time of demographic data collection.	Perm	SDTM 2.2.5, SDTMIG 4.1.4.1
DMDY	Study Day of Collection	Num		Timing	Study day of collection measured as integer days.	Perm	SDTM 2.2.5, SDTMIG 4.1.4.1

** Indicates variable may be subject to controlled terminology. (Parenthesis indicates CDISC/NCI codelist code value)*

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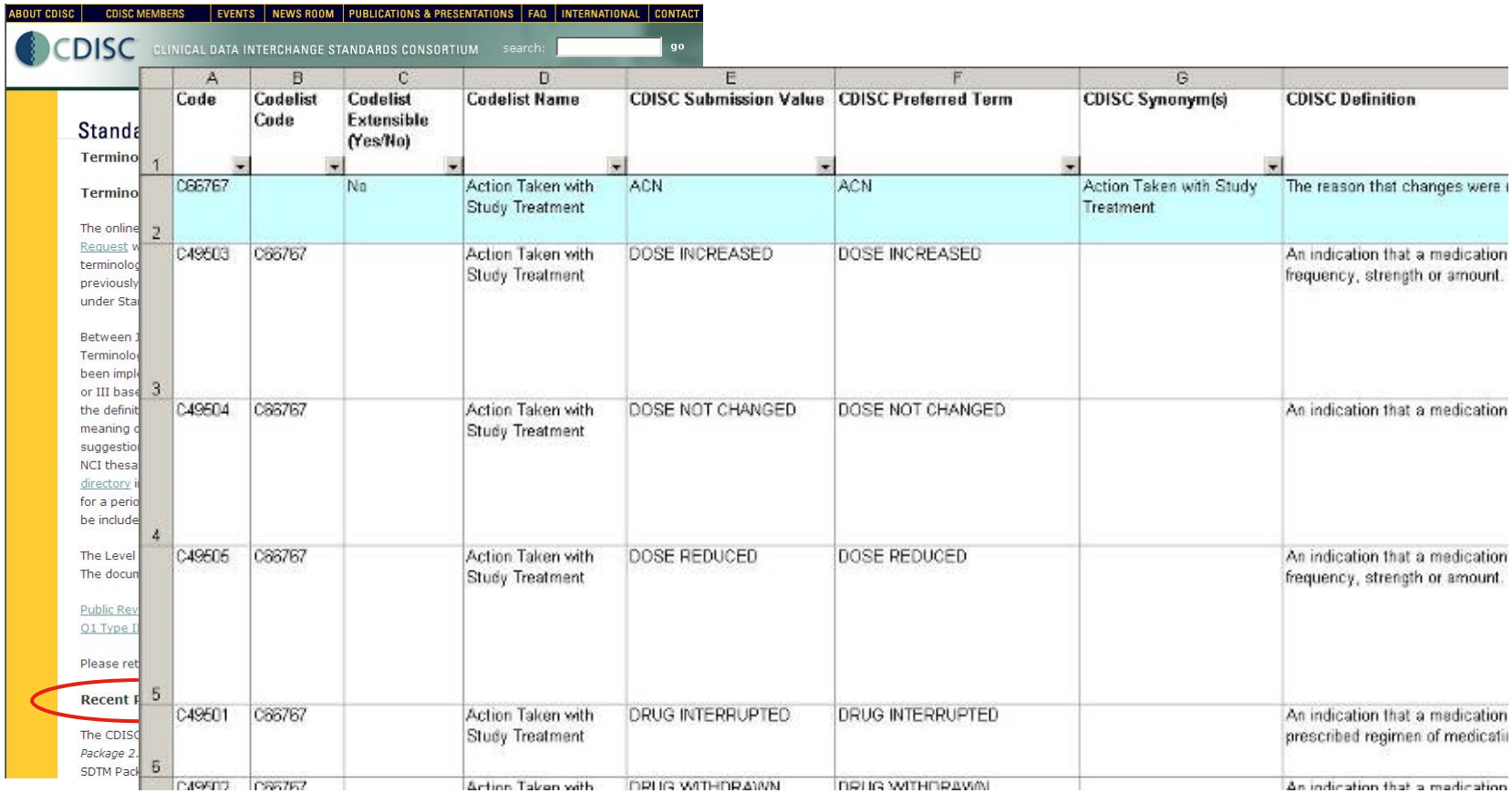
Controlled Terminology

- CDISC CT: September 2008 (http://www.cdisc.org/standards/terminology/index.html)



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CDISC CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM search: go

	A	B	C	D	E	F	G	
1	Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Preferred Term	CDISC Synonym(s)	CDISC Definition
2	C66767		No	Action Taken with Study Treatment	ACN	ACN	Action Taken with Study Treatment	The reason that changes were
3	C49503	C66767		Action Taken with Study Treatment	DOSE INCREASED	DOSE INCREASED		An indication that a medication frequency, strength or amount.
4	C49504	C66767		Action Taken with Study Treatment	DOSE NOT CHANGED	DOSE NOT CHANGED		An indication that a medication
5	C49505	C66767		Action Taken with Study Treatment	DOSE REDUCED	DOSE REDUCED		An indication that a medication frequency, strength or amount.
6	C49501	C66767		Action Taken with Study Treatment	DRUG INTERRUPTED	DRUG INTERRUPTED		An indication that a medication prescribed regimen of medicati
	C49502	C66767		Action Taken with	DRUG WITHDRAWN	DRUG WITHDRAWN		An indication that a medication

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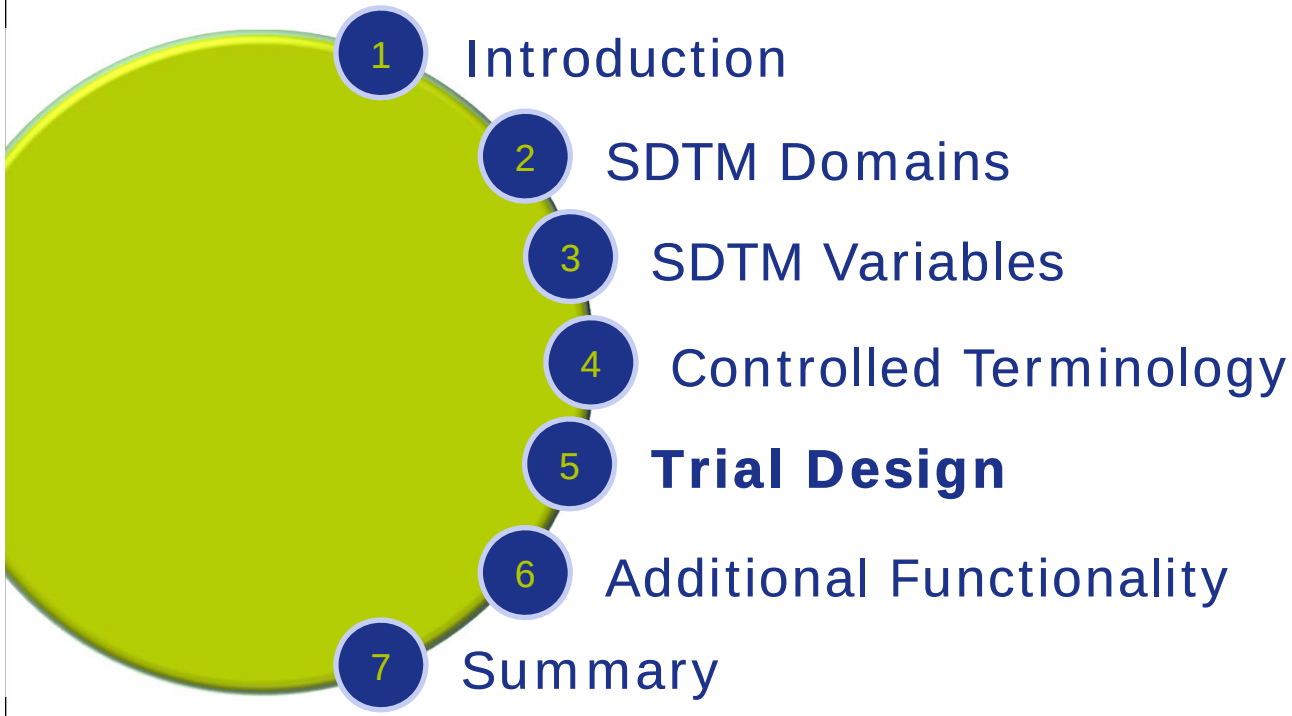
Overview



1. Introduction
2. SDTM Domains
3. SDTM Variables
4. Controlled Terminology
5. **Trial Design**
6. Additional Functionality
7. Summary

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Trial Design

- SE and SV are now Special-Purpose domains

- Some new variables
  - TIVERS: Inclusion/Exclusion criteria version number
  - TIRL: Inclusion/Exclusion Criterion Rule

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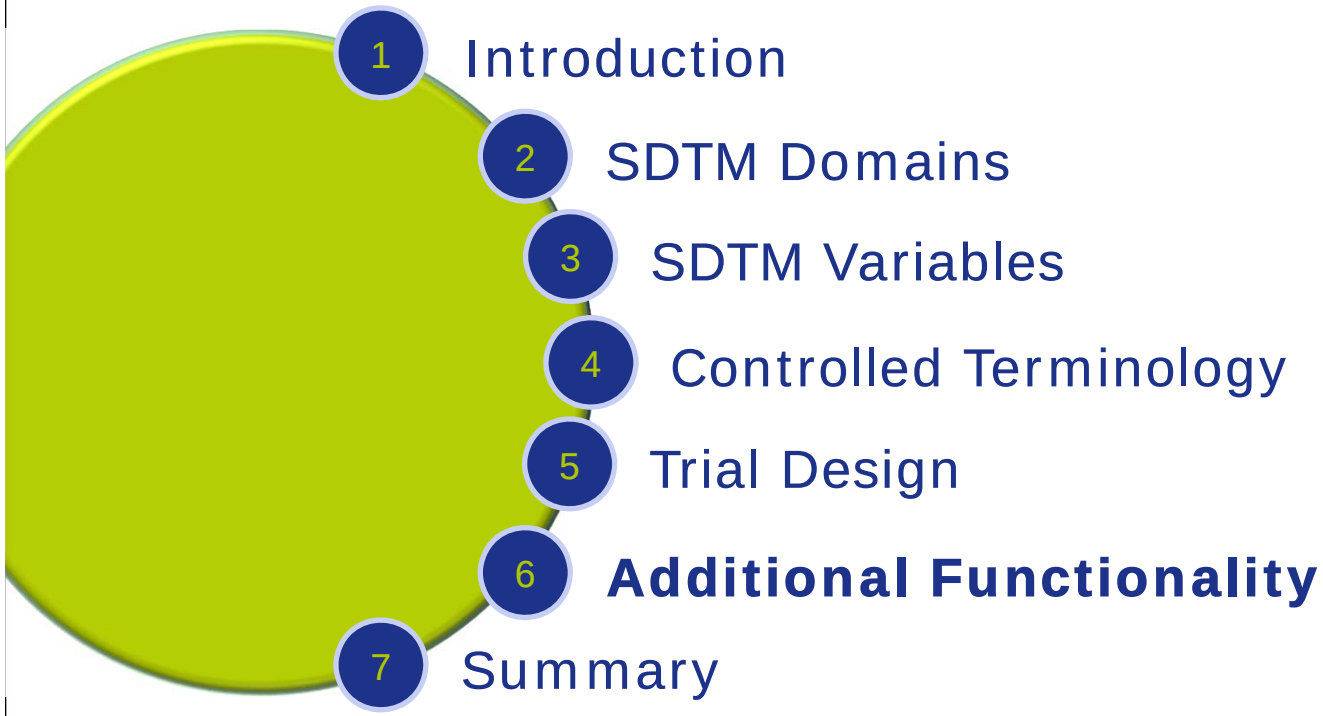
Overview



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Additional Functionality

- Splitting domains
  - 1 domain, multiple datasets
  - By --CAT or --OBJ
  - Examples:

    FAAE, FACE, FASU
    QSAD, QS36

- The value « multiple »
  - Only for non-result qualifiers
  - See example on next slide

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Additional Functionality

[DM]

Race	Check all that apply
American Indian or Alaska Native	✔
Asian	☐
Black or African American	✔
Native Hawaiian or Other Pacific Islander	☐
White	☐
Other, Specify: *Aborigine*	✔

RACE

Multiple values checked

Checked values go into QVAL

- DM

Row	STUDYID	DOMAIN	USUBJID	RACE
1	ABC	DM	001	MULTIPLE

- SUPPDM

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1	ABC	DM	001			RACE1	Race 1	AMERICAN INDIAN OR ALASKA NATIVE
2	ABC	DM	001			RACE2	Race 2	BLACK OR AFRICAN AMERICAN
3	ABC	DM	001			RACE3	Race 3	OTHER
4	ABC	DM	001			RACEOTH	Race, Other	ABORIGINE

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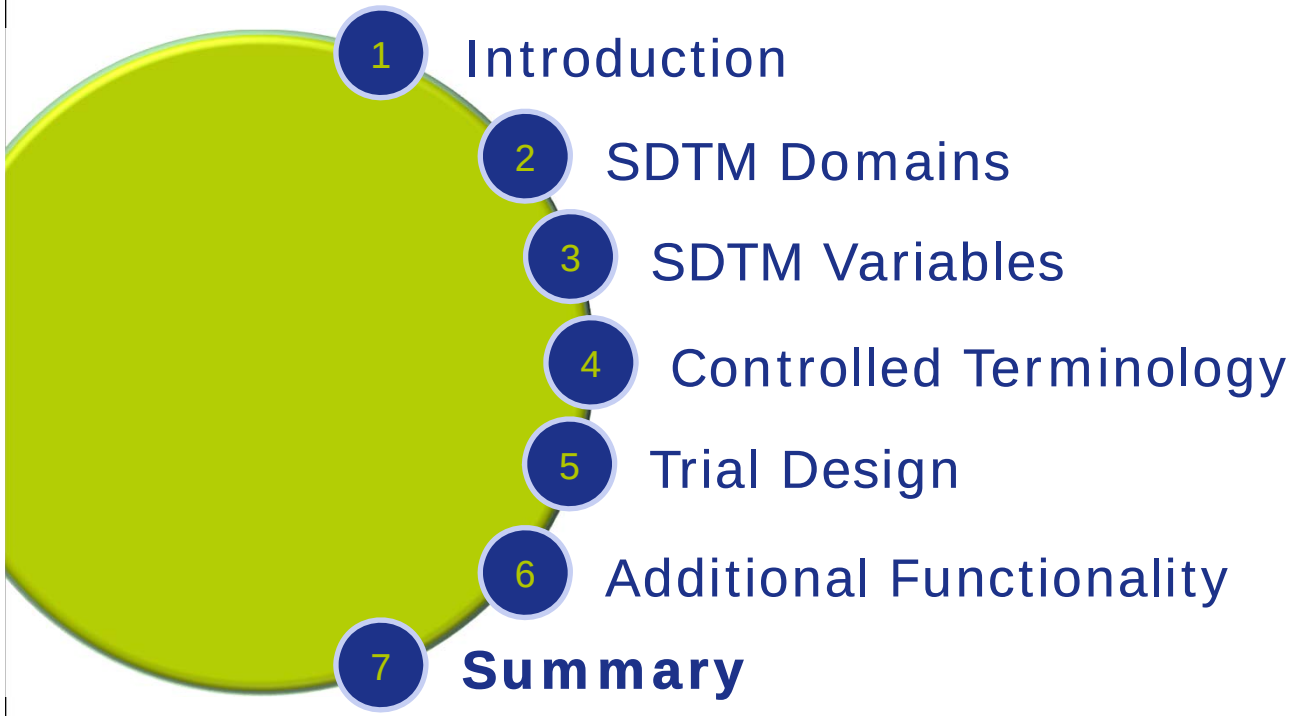
Overview



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Summary

SDTM 1.2 – SDTM IG 3.1.2

- Expanded model
- More functionality, usability
- More complex ?
- Correction of SDTM IG 3.1.1 errors
- Backward compatible
- Will become current FDA submission standard

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Questions ?

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