

A Dive Into CDISC Therapeutic Area User Guides



Johannes Ulander & Niels Both
Standardisation and Harmonisation Specialists

AGENDA

-  Therapeutic Area Standards
-  Medical History Implementation
 -  Diagnosis
 -  Symptoms
 -  Dates in MHSTDTC
-  Conclusions and Discussion



Therapeutic Area User Guides (TAUGs)

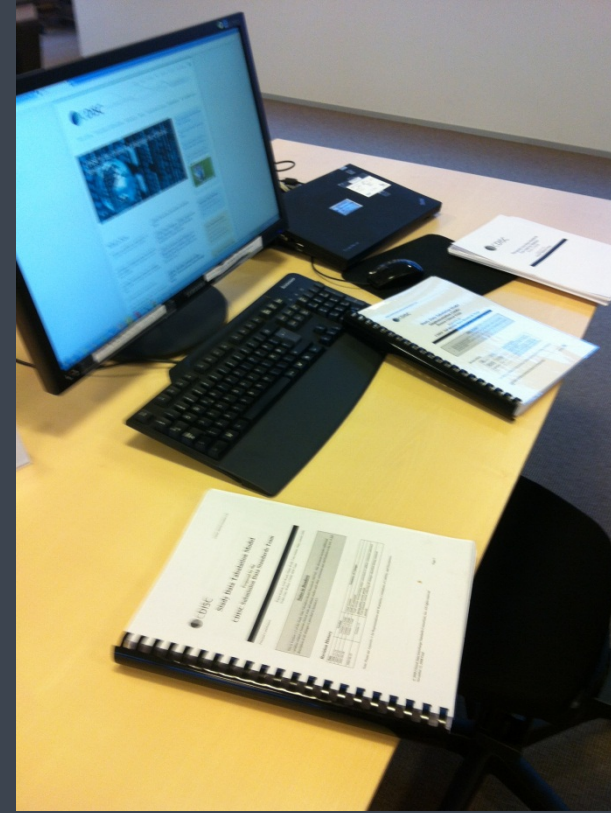
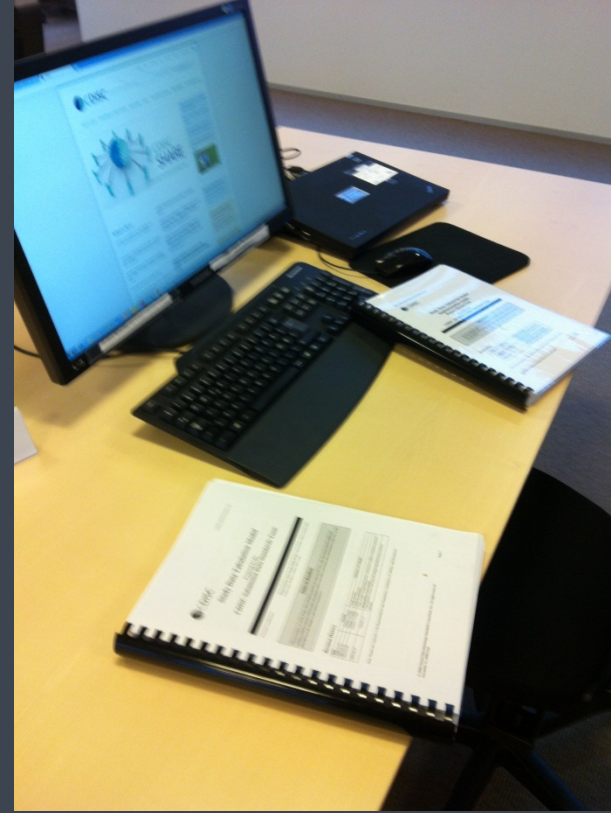
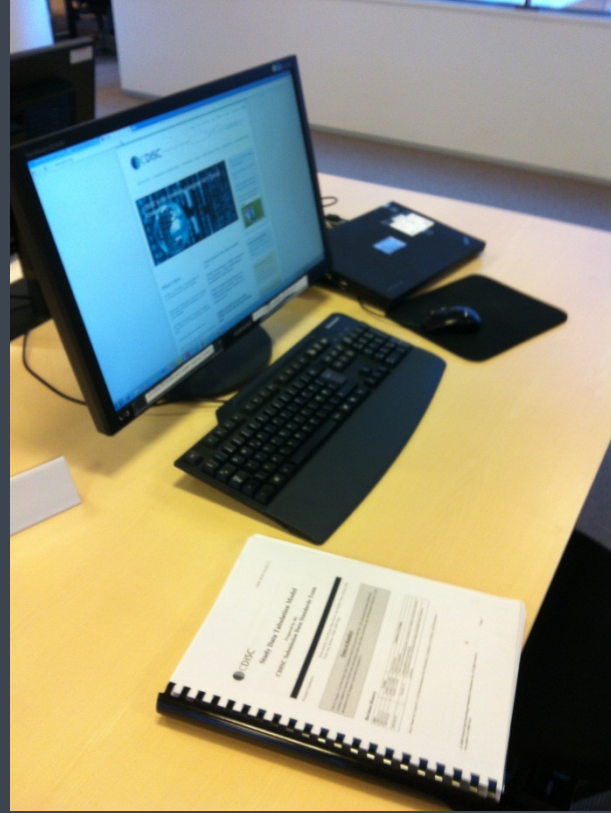
Program Overview – September 2015						
Therapeutic Area	Organization/PM	Stage 0 Charter Approval	Stage 1 Check of Concepts Completed	Stage 3a Posted for Internal Review	Stage 3b Posted for Public Review	*Stage 3c **Projected Publication
Traumatic Brain Injury v1	CDISC Amy Palmer	Oct 13	Sep 14	Mar	Jul	Q415
Breast Cancer v1	CDISC John Owen	Oct 14	Oct 14	Mar	Oct	Q415

Pipeline of TAUG releases or updates						
	2011	2012	2013	2014	2015	2016
#TAUGs	1	4	7	9	12	10

CV Imaging v1	CDISC/DCRI Amy Palmer	May	Jul	Oct	Dec	Q216
Prostate Cancer v1	CDISC John Owen	Oct				Q316
Major Depressive Disorder	CDISC Amy Palmer	Oct				Q316
General Anxiety Disorder v1	CDISC Amy Palmer					
Bi-polar Disorder v1	CDISC Amy Palmer					

Stage 0 – Scoping, Stage 1 – Concept Modeling, Stage 2 – Standards Development, Stage 3a – Internal Review, Stage 3b – Public Review, Stage 3c – Publication

September 8, 2015 Key | Stage completed | Stage ongoing | All months reflect when stage is, or is projected to be, completed.





Therapeutic Area User Guides (TAUGs)

- Alzheimer's
- Asthma
- Cardiovascular
- Diabetes
- Dyslipidemia (Draft)
- Multiple Sclerosis
- Pain
- Parkinson's Disease
- Polycystic Kidney Disease
- Schizophrenia (Draft)
- Tuberculosis
- Virology





Origin of domains in TAUGs

The origin of the 53 domains used in TAUGS are distributed across:

- 1 SDTMIG v3.2
- 2 SDTMIG Medical Devices v1.0 (SDTMIG-MD v1.0)
- 3 SDTMIG Associated Persons v1.0 (SDTMIG-AP v1.0)
- 4 Draft domains proposed (TAUG Draft domains not yet in any SDTMIG)

1 SDTMIG 3.2	2 SDTMIG-MD v1.0	4 TAUG Draft domains not yet in any SDTMIG
AE IS RP	DE Device Events	AG Procedure Agents PB Pgx Biological State
CE LB SC	DI Device Identifier	BE Biospecimen Events PF Pharmacogenomics Findings
CM MB SR	DO Device Options	BS Biospecimen PG Pharmacogenomics
DD MH SU	DR Device Subject Relationship	ED Education Details QT ECG QT Correction Model Data
DM MI TA	DU Device In-Use	ML Meals SB Subject Biological State
DS MO TE	3 SDTMIG-AP v1.0	NV Nervous Systems Findings UR Urinary System
EG MS TR	APBS	OE Ophthalmic Exams VR Viral Resistance
EX PR TS	APDD	
FA QS TU	APDM	
HO RE VS	APMH	

Table 1. Origin of TAUG domains



Why focus on Medical History?

LB NV APDM
DU CE
APDD OE VS ML
RE ED DR HO MI
MS AE
FA MH PR EG
SC DE SB RP QS TU PB APBS
BS SU SR EX TR CM
DD TS TE PG VR TA
DI UR DM MO PF
QT DS MB APMH AG



Domains Sorted by Level of Use

#TAUG	Domain	Alz	Asth	CV	Diab	Infl	MS	Pain	PD	PKD	QT	TB	Vir
9	DI	X	X	X	X	X	X		X	X	X		
9	FA		X	X	X	X	X	X	X	X		X	
9	MH	X	X	X	X		X	X	X	X		X	
7	CE			X	X	X	X		X	X		X	
7	LB	X	X	X	X	X				X		X	
6	CM		X		X	X			X	X		X	
6	MO	X		X			X		X	X		X	
5	DU	X	X				X		X			X	
5	PR	X		X		X			X	X			
4	HO		X	X		X				X			
4	PF	X				X				X			X



What is Medical History?

- Diagnosis
- Symptoms
- Method of diagnosis
- Family History



Medical History is Mapped to...



Diagnosis → Medical History – MH

Symptoms → MH or Findings About – FAMH

Method of diagnosis → DI (Device In-Use)

Family History → APMH (or FAMH)



MHCAT

	MHCAT	MHSCAT	SUPPMH.MHSSCAT	Related categories
Alzheimer	PRIMARY DIAGNOSIS			
	GENERAL			
Asthma	Asthma Related			
Diabetes	DIABETES	COMPLICATIONS OF DIABETES		
Dyslipidemia	Hypercholesterolemia			
	Cardiovascular Risk Factors			
Multiple Sclerosis	PRIMARY DIAGNOSIS	ONSET COURSE		
	GENERAL	INITIAL SYMPTOMS		
Pain	PRIMARY DIAGNOSIS			
Parkinson's Disease	NULL	DIAGNOSTIC CRITERIA	Ambulatory/Axial Difficulties	Family History of PD (APMH)
	PRIMARY DIAGNOSIS	INITIAL MOTOR SYMPTOMS		MEDICAL HISTORY (FACAT)
	PARKINSON'S DISEASE (for symptoms)	DEVELOPING MOTOR SYMPTOMS		
	INFECTION HISTORY			
Polycystic Kidney Disease	PRIMARY DIAGNOSIS			PRIMARY DIAGNOSIS (APMH)
	PKD (for symptoms)			ADPKD Manifestation (APMH)
Schizophrenia	GENERAL			FAMILY MEDICAL HISTORY (APMH)
	SCHIZOPHRENIA			
Tuberculosis	STUDY INDICATION			
	RISK FACTORS			
	COMORBID CONDITION			
	GENERAL			
	TB SYMPTOMS			
Cardiovascular				
Influenza				
QT Studies				
Virology				



MHCAT

	MHCAT	MHSCAT	SUPPMH.MHSSCAT	Related categories
Alzheimer	PRIMARY DIAGNOSIS			
	GENERAL			
Asthma	Asthma Related			
Diabetes	DIABETES	COMPLICATIONS OF DIABETES		
Dyslipidemia	Hypercholesterolemia			
	Cardiovascular Risk Factors			
Multiple Sclerosis	PRIMARY DIAGNOSIS	ONSET COURSE		
	GENERAL	INITIAL SYMPTOMS		
Pain	PRIMARY DIAGNOSIS			
Parkinson's Disease	NULL	DIAGNOSTIC CRITERIA	Ambulatory/Axial Difficulties	Family History of PD (APMH)
	PRIMARY DIAGNOSIS	INITIAL MOTOR SYMPTOMS		MEDICAL HISTORY (FACAT)
	PARKINSON'S DISEASE (for symptoms)	DEVELOPING MOTOR SYMPTOMS		
	INFECTION HISTORY			
Polycystic Kidney Disease	PRIMARY DIAGNOSIS			PRIMARY DIAGNOSIS (APMH)
	PKD (for symptoms)			ADPKD Manifestation (APMH)
Schizophrenia	GENERAL			FAMILY MEDICAL HISTORY (APMH)
	SCHIZOPHRENIA			
Tuberculosis	STUDY INDICATION			
	RISK FACTORS			
	COMORBID CONDITION			
	GENERAL			
	TB SYMPTOMS			
Cardiovascular				
Influenza				
QT Studies				
Virology				



MHCAAT for Diagnosis

4 approaches are used across TAUGs:

1. MHCAAT = PRIMARY DIAGNOSIS
2. MHCAAT = STUDY INDICATION
3. MHCAAT = *Disease*
4. FA approach, FAOBJ = MHCAAT/MHTERM



MHCAT for Diagnosis: Approaches 1-3

1.

Disease

PRIMARY DIAGNOSIS

mh.xpt								
Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHDECOD	MHCAT	MHSTDTC
1	ABC123	MH	AD01-101	1	Mild Cognitive Impairment		PRIMARY DIAGNOSIS	
2	ABC123	MH	AD01-101	2	Blind Left Eye	Blindness unilateral	GENERAL	1999-07-07
3	ABC123	MH	AD01-101	3	Traumatic Brain Injury	Traumatic brain injury	GENERAL	2005-03-28
4	ABC123	MH	AD01-102	1	Alzheimer's Disease		PRIMARY DIAGNOSIS	

2.

Disease

STUDY INDICATION

mh.xpt							
Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHDECOD	MHCAT
1	ABC	MH	ABC-01-101	1	PULMONARY TUBERCULOSIS	Pulmonary tuberculosis	STUDY INDICATION
2	ABC	MH	ABC-01-101	2	COPD	Chronic obstructive pulmonary disease	COMORBID CONDITION
3	ABC	MH	ABC-01-101	3	TYPE II DIABETES	Type 2 diabetes mellitus	RISK FACTORS

3.

Specific Type

Disease

mh.xpt										
Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHCAT	MHPRESP	MHOCCUR	MHDTC	MHSTDTC
1	XYZ	MH	XYZ-001-001	1	TYPE 1 DIABETES	DIABETES		Y	2010-09-26	2010-03-25
2	XYZ	MH	XYZ-001-002	1	TYPE 2 DIABETES	DIABETES		Y	2010-10-26	2010-04-25



MHCAT for Diagnosis: Approach 4

Since MH is too general, put specifics in FA

famh.xpt

Row	STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FACAT	FAORRES	FAORRESC	FATPT	FADTC
1	ABC123	FA	456	1	SEV	Severity	Asthma	Asthma History	MODERATE PERSISTENT	MODERATE PERSISTENT	Diagnosis	2013-05-24

famh.xpt

Row	STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FACAT	FAORRES	FAORRESC	FADTC
1	ABC123	FA	456	1	DIAGDTC	Date of Diagnosis	Asthma	Asthma History	1992	1992	2013-05-24
2	ABC123	FA	456	2	SUBTYPE	Subtype	Asthma	Asthma History	Exercise induced	Exercise induced	2013-05-24



3 ways to capture symptoms

MS

mh.xpt

Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHGRPID	MHTERM	MHDECOD	MHCAT	MHSCAT	MHSTDTC
1	ABC123	MH	MS01-101	1	1	RRMS	Relapsing Remitting Multiple Sclerosis	PRIMARY DIAGNOSIS	ONSET COURSE	1999-03
2	ABC123	MH	MS01-101	2	1	Double Vision	Diplopia	PRIMARY DIAGNOSIS	INITIAL SYMPTOMS	1999-02
3	ABC123	MH	MS01-101	3	1	Tingling	Paresthesia	PRIMARY DIAGNOSIS	INITIAL SYMPTOMS	1998-12
4	ABC123	MH	MS01-101	4		SPMS	Secondary Progressive Multiple Sclerosis	PRIMARY DIAGNOSIS	CURRENT COURSE	2008-11

Alzheimer's

suppmh.xpt

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1	ABC123	MH	AD01-101	MHSEQ	1	MHOSDTC	Onset of Symptoms Date	1999-05	CRF	MOTHER
2	ABC123	MH	AD01-102	MHSEQ	1	MHOSDTC	Onset of Symptoms Date	2000-02	CRF	FATHER
3	ABC123	MH	AD01-103	MHSEQ	1	MHOSDTC	Onset of Symptoms Date	1998	CRF	STUDY SUBJECT

Pain

fa.xpt

ROW	STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FSTEST	FAOBJ	FAORRES	FASTRESC
1	STUDY01	FA	2324-P0001	1	SYMPDTC	Onset of Symptom Date	FIBROMYALGIA	2000-05	2000-05
2	STUDY01	FA	2324-P0002	1	SYMPDTC	Onset of Symptom Date	FIBROMYALGIA	2001-10	2001-10
3	STUDY01	FA	2324-P0003	1	SYMPDTC	Onset of Symptom Date	FIBROMYALGIA	2010-07	2010-07



Parkinsons TAUG is the most complete

mh.xpt

ROW	STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHDECOD	MHCAT	MHSCAT	MHPRESP	MHOCCUR	MHDTG	MHSTDTC
1	STUDY01	MH	2324-P0001	1	Parkinson's disease		PRIMARY DIAGNOSIS				2006-01-12	2001-05
2	STUDY01	MH	2324-P0001	2	Blind Left Eye	Blindness unilateral						1999-07-07
3	STUDY01	MH	2324-P0001	3	Traumatic Brain Injury	Traumatic brain injury						2005-03-28
4	STUDY01	MH	2324-P0001	4	4-6 Hz Rest Tremor		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	Y	2006-01-12	
5	STUDY01	MH	2324-P0001	5	Bradykinesia		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	Y	2006-01-12	
6	STUDY01	MH	2324-P0001	6	Rigidity		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	N	2006-01-12	
7	STUDY01	MH	2324-P0001	7	Asymmetric Onset		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	Y	2006-01-12	
8	STUDY01	MH	2324-P0001	8	Substantial Response to Dopaminergic Therapy		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	N	2006-01-12	
9	STUDY01	MH	2324-P0001	9	Tremor (including internal tremor)		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	N	2006-01-12	
10	STUDY01	MH	2324-P0001	10	Stiffness		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	Y	2006-01-12	
11	STUDY01	MH	2324-P0001	11	Change in facial expression		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	N	2006-01-12	
12	STUDY01	MH	2324-P0001	12	Disturbances of dexterity		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	Y	2006-01-12	

suppmh.xpt

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
STUDY01	MH	2324-P0001	MHSEQ	1	MHOSDTC	Onset of Symptoms Date	1999-05	CRF	
STUDY01	MH	2324-P0001	MHSEQ	4	MHAGE1	Age at MH Event	5 YEARS	CRF	
STUDY01	MH	2324-P0001	MHSEQ	4	HOSPFL1	Hospitalized at MH Event	Y	CRF	
STUDY01	MH	2324-P0001	MHSEQ	16	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	17	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	18	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	19	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	20	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	



Parkinsons TAUG is the most complete

mh.xpt

ROW	STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHDECOD	MHCAT	MHSCAT	MHPRESP	MHOCCUR	MHDTC	MHSDTC
1	STUDY01	MH	2324-P0001	1	Parkinson's disease		PRIMARY DIAGNOSIS				2006-01-12	2001-05
2	STUDY01	MH	2324-P0001	2	Blind Left Eye	Blindness lateral						1999-07-07
3	STUDY01	MH	2324-P0001	3	Traumatic Brain Injury	Traumatic brain injury						2005-03-28
4	STUDY01	MH	2324-P0001	4	4-6 Hz Rest Tremor		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	Y	2006-01-12	
5	STUDY01	MH	2324-P0001	5	Bradykinesia		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	Y	2006-01-12	
6	STUDY01	MH	2324-P0001	6	Rigidity		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	N	2006-01-12	
7	STUDY01	MH	2324-P0001	7	Asymmetric Onset		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	Y	2006-01-12	
8	STUDY01	MH	2324-P0001	8	Substantial Response to Dopaminergic Therapy		PARKINSON'S DISEASE	DIAGNOSTIC CRITERIA	Y	N	2006-01-12	
9	STUDY01	MH	2324-P0001	9	Tremor (including internal tremor)		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	N	2006-01-12	
10	STUDY01	MH	2324-P0001	10	Stiffness		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	Y	2006-01-12	
11	STUDY01	MH	2324-P0001	11	Change in facial expression		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	N	2006-01-12	
12	STUDY01	MH	2324-P0001	12	Disturbances of dexterity		PARKINSON'S DISEASE	INITIAL MOTOR SYMPTOMS	Y	Y	2006-01-12	

suppmh.xpt

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	ONAM	OLABEL	QVAL	QORIG	QEVAL
STUDY01	MH	2324-P0001	MHSEQ	1	MHOSDTC	Onset of Symptoms Date	1999-05	CRF	
STUDY01	MH	2324-P0001	MHSEQ	4	MHAGE1	Age at MH Event	5 YEARS	CRF	
STUDY01	MH	2324-P0001	MHSEQ	4	HOSPFL1	Hospitalized at MH Event	Y	CRF	
STUDY01	MH	2324-P0001	MHSEQ	16	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	17	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	18	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	19	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	
STUDY01	MH	2324-P0001	MHSEQ	20	MHSSCAT	MH 2nd Sub-Category	Ambulatory/Axial Difficulties	CRF	



Date of Diagnosis vs. Onset of Symptoms

1.6 Known Issues

- Date of Diagnosis:** The SDTMIG does not provide advice on how to represent date of diagnosis of an event. Various solutions have been proposed, but this document treats the date of diagnosis of a medical history event as the value a supplemental qualifier with QNAM=MHDXDTC. Some users have simply mapped a collected “date of diagnosis” to MHSTDTC. Although date of diagnosis can reasonably be treated as the start of an event, this mapping alone does not provide the information that this particular start date is specifically the date of diagnosis.

1	Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHDECOD	MHCAT	MHSTDTC
	1	ABC123	MH	AD01-101	1	Mild Cognitive Impairment		PRIMARY DIAGNOSIS	2001-05

2	Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
	1	XYZ	MH	XYZ-001-001	MHSEQ	1	MHDXDTC	Date of Diagnosis	2010-03-25	CRF	INVESTIGATOR

3	Row	STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FACAT	FAORRES	FASTRESC	FADTC
	1	ABC123	FA	456	1	DIAGDTC	Date of Diagnosis	Asthma	Asthma History	1992	1992	2013-05-24



Schizophrenia TAUG has the final answer?

A peek into the new SDTM version:

- MHEVTYP is a draft variable in SDTM v1.5 used to specify the aspect of the medical condition or event by which its start date is defined, such as the diagnosis and/or onset of symptoms. This variable is expected to be included in SDTM v1.5.

SDTM v1.5 introduces MHEVTYP

mh.xpt

Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHGRPID	MHTERM	MHDECOD	MHCAT	MHEVTYP	MHSTDTC	MHENDTC
1	ABC123	MH	001-001	1		APPENDICITIS	Appendicitis	GENERAL		2006-05-04	2006-05-04
2	ABC123	MH	001-001	2	1	ANXIETY	Anxiety	SCHIZOPHRENIA	SYMPTOMS	2003	

Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHGRPID	MHTERM	MHDECOD	MHCAT	MHEVTYP	MHSTDTC	MHENDTC
3	ABC123	MH	001-001	3	1	AGITATION	Agitation	SCHIZOPHRENIA	SYMPTOMS	2003-11	2004-02-14
4	ABC123	MH	001-001	4	1	DISORGANIZED SCHIZOPHRENIA	Disorganized schizophrenia	SCHIZOPHRENIA	DIAGNOSIS	2004-01	
5	ABC123	MH	123-456	1		CATATONIC SCHIZOPHRENIA	Catatonic schizophrenia	SCHIZOPHRENIA	DIAGNOSIS	2008-06-06	
6	ABC123	MH	9999-789	1		SCHIZOPHRENIA	Schizophrenia	SCHIZOPHRENIA	DIAGNOSIS	2014-08-05	

Standards Hierarchy

Which standard is applicable in cases of ambiguity, such as:

- Should TAUGs released after Schizophrenia use MHEVTYP even though it has not been implemented in SDTM yet?
- Once the MHEVTYP is implemented in the SDTM, does it then supersede what is written in other TAUGs?
- Is it OK to submit draft TAUG domains before they are implemented in SDTMIG? Can they be used in other therapeutic areas?

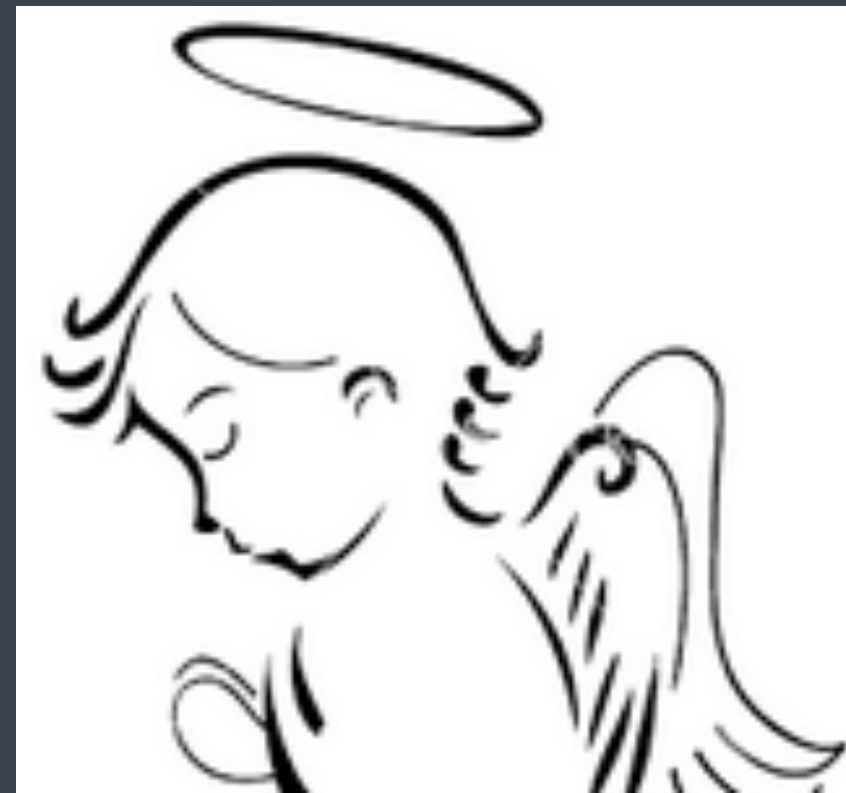


Conclusions & Recommendations

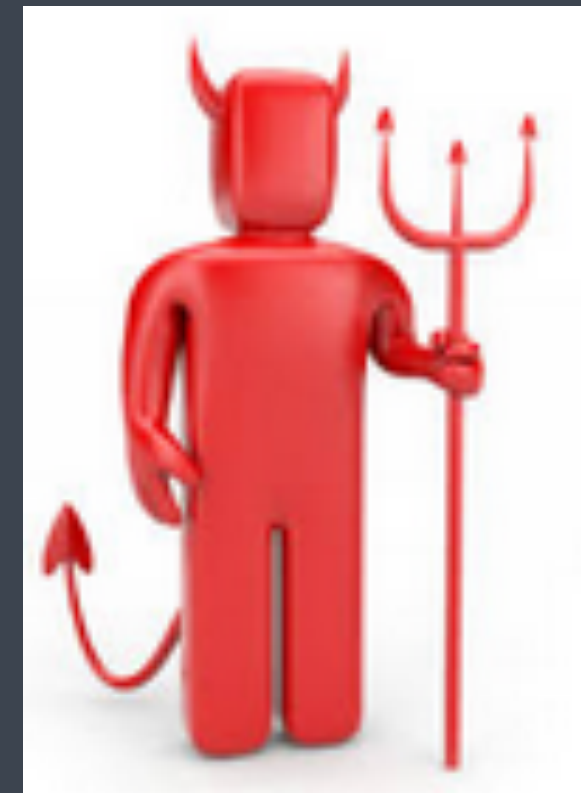
- We are happy to see how TAUG development is aiding in the work to extend and improve future versions of CDISC standards
- Future TAUG versions should reduce variation as much as possible
- Electronic Metadata Repositories (e.g. SHARE) and the use of “Research Concepts” can be utilised to improve this
- The standards hierarchy needs to be clarified



Thank you for listening



Johannes Ulander



Niels Both