

Leverage of Therapeutic Area Data Standards User Guide for SDTM Mapping



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**DM aspect on practical hurdle for e-Data
Submission to PMDA, 2018 task force 1, Data
Science Expert Committee, JPMA**

Disclaimer

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Agenda

1. Introduction

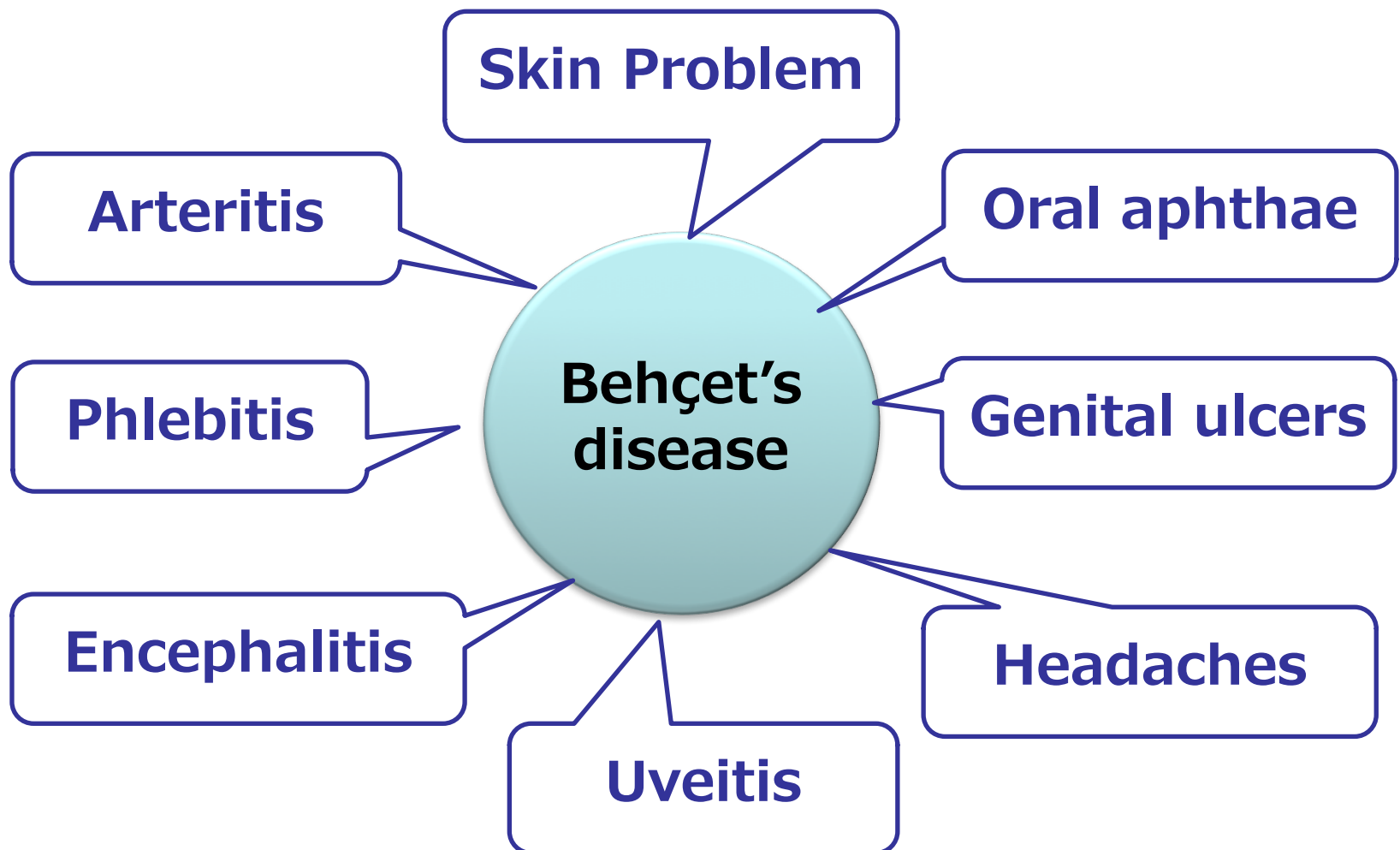
2. TAUG SDTM Mapping Index

3. Use Case in Actual Study

CASE1: Storage of EG data measured 3 times per point

CASE2: Mapping for Creatinine Clearance(CG Formula)

How to develop SDTM datasets for Behçet's disease study?



How to develop SDTM datasets for Behçet's disease study?

Purpose	TEST/Examination
Oral aphthae Y/N?	Physical Examination
Volumetric Brain Measurement	MRI
Diagnosis	Pathergy reaction
Joint Assessment (Swollen/Tender)	ACR Core set
HLA type (HLA-B51 Pos/Neg)	Laboratory test
Eye Assessment	RNFL(Retinal Nerve Fiber Layer) thickness

How to map
the test
results into
SDTM???

No good
example in
SDTM IG . .

How to develop SDTM datasets for Behçet's disease study?

Purpose	TEST/Examination	Reference guide	SDTM datasets
Oral aphthae Y/N?	Physical Examination	(SDTM IG)	
Volumetric Brain Measurement	MRI	TAUG for Alzheimer's Disease	PR MO
Diagnosis	Pathergy reaction	TAUG for Tuberculosis	FA
Joint Assessment (Swollen/Tender)	ACR Core set	TAUG for Rheumatoid Arthritis	MK
HLA type (HLA-B51)	Laboratory test	TAUG for Kidney Transplant	LB PF
Eye Assessment	RNFL(Retinal Nerve Fiber Layer) thickness	TAUG for Multiple Sclerosis	MO DI

Another example: Method for CM domain

Captured Info.	Example	TAUG
Prior Medications Used/Not Used	CMTRT: Medication CMCAT: Category "ASTHMA MEDICATIONS" CMSCAT: Med. Group "SYSTEMIC CORTICOSTEROIDS" CMPRESP: Y CMOCCUR: Y/N CMEVINTX: "PRIOR"	Asthma
Rescue Medications Used/Not Used, Timing, Number of taken	CMTRT: Medication CMCAT: Category "RESCUE MEDICATION" CMPRESP: Y CMOCCUR: Y/N CMEVINTX: "DAYTIME"/"NIGHTTIME" SUPPCM.CMTDSEVI: Total Dose in Evaluation Interval	Asthma
Treatment History, Stop Reason	CMRSDISC: Discontinue Reason "Lack of Efficacy "	Dyslipidemia
Treatment History, Stop Reason, Outcome	SUPPCM.RSDISC: Discontinue Reason SUPPCM.OUTTRT: Outcome of Treatment	Hepa C

Why we give attention to TAUG?

- TAUG (Therapeutic Area Data Standard User Guide) contains various useful contents (Disease/Therapy, CDASH, SDTM, ADaM).
- Data Managers tend to spend time worrying about SDTM mapping.
- TAUG has good Hints for SDTM Mapping.
 - • • But, TOO MUCH information makes hard to grasp.



TAUG SDTM Mapping Index

Useful tool to help Understanding and Usage of
TAUGs for SDTM mapping!!

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TAUG SDTM Mapping Index

- Following **26 TAUGs** issued by December 2017, have been included
- Developed the "TAUG SDTM Mapping Index" to help Data Manager easily search for information that he/she want to know from Key word such as disease name, domain and topics.
- This Index consists of two spreadsheets of **TAUG list** and **Summary**.

TA User Guides	Version	Publication Date	TA User Guides	Version	Publication Date
Alzheimer's Disease	2	16-Dec-13	Major Depressive Disorder	1	5-Dec-16
Asthma	1	26-Nov-13	Malaria	1	9-Jan-17
Breast Cancer	1	16-May-16	Multiple Sclerosis	1	2-May-14
Cardiovascular Endpoints	1	17-Oct-14	Pain	1.1	13-Dec-16
Chronic Hepatitis C Virus	1	8-May-15	Parkinson's Disease	1	18-Dec-12
COPD	1	26-Jan-16	Polycystic Kidney Disease	1	26-Feb-13
Diabetes	1	11-Sep-14	Prostate Cancer	1	10-Jul-17
Diabetic Kidney Disease	1	13-Dec-16	QT Studies	1	12-Dec-14
Duchenne Muscular	1	25-Sep-17	Rheumatoid Arthritis	1	14-Nov-16
Dystrophy	1	19-Jun-15	Schizophrenia	1.1	3-May-17
Dyslipidemia	1	19-Dec-16	Traumatic Brain Injury	1	14-Dec-15
Ebola	1	3-Aug-17	Tuberculosis	2	26-Feb-16
Influenza	1.1	31-Oct-16	Virology	2.1	3-Aug-17
Kidney Transplant	1				

TAUG SDTM Mapping Index

Summary spreadsheet

TAUG	Topics	Section	Related domain		NSV (Non-Standard)	Summary	Editor's note
Schizophrenia Version 1.0 (Provisional) (2015-05-26)	Diagnosing Schizophrenia- DSM-IV-TR versus DSM-5	4.1.1.3	MH	Medical History	MHAGE=Age at Event	統合失調症の診断を受けた年数、診断年齢、最初の精神病エピソードの年齢、および他の臨床的に関連する診断の事例が記載されている。 ・ 診断時の年齢と最初の精神病エピソードの年齢は、非標準変数のMHAGEPに格納。	初回治療時の年齢の年齢はFAになるので、混同しないこと
	Relapse and Remission in Randomized Withdrawal Studies	5.3.1.1	DS	Disposition	RLSIND=Relapse Indicator RPTTRM=Reporter of Term	再発した場合に治験を完了する事例が記載されている。 ・ DSTERMは、再発を特定する逐語的用語格納し、 治験を完了しているため、DSDECODはCompleted格納する。 ・ 再発の有無は非標準変数のRLSIND格納 (RLSIND=Y) 。 ・ 再発の報告者はRPTTRM=SELF を格納	

(Snapshot of TAUG SDTM Mapping Index)

Item	Description
TAUG	TAUG Name and document version
Topic	Topics (Treatment / Assessment / Examination) described in TAUG
Section	Section number for topics in TAUG
Related Domain	Abbreviated name and name of the relevant domain
NSV	Non-standard variables used in the topics
Summary	Summarized the description of Topics (see with Editor's Note)
Editor's Note	Supplementary explanation by Editor

Use case: Which domain should Meal data be mapped to?

If **Standard Meal** data was collected



Information of
the subject's
meal
consumption

ML

OR

Information of it
given to the
subject as part of
the testing
procedure

AG

Use case: Which domain should Meal data be mapped to?

By using key words of Meal, the difference of SDTM mapping for Standard Meal and Meal can be found from 'TAUG SDTM Mapping Index'.

TAUG	Topic	Domain		Summary	Editor's Note
Diabetes v1	Tolerance Tests (3.2.2)	AG	Procedural Agent	- Oral Glucose Tolerance Testing (OGTT)において、エージェントとしてのGLUCOSEの摂取状況を格納（摂取量、開始/終了日時） - Meal Tolerance Testing (MTT)において、エージェントとしてのSTANDARD MEALの摂取状況を格納（摂取量、開始日時、投与までの時間等） - STANDARD MEALを摂取しなかった場合の理由をSUPPAGに格納	AGドメインはIG3.3で追加される可能性のある新ドメインで、IG3.2ではカスタムドメインの扱いとなることに注意。
	Hypoglycemic Events as Disease Milestones (3.3.2)	ML	Meal Data	イベント（プロトコル定義のDisease Milestones）直前の食事の情報をMLに格納	STANDARD MEALをAGに格納している例と比べると興味深い。

(Snapshot of TAUG SDTM Mapping Index)

The meals that are part of the MTT are treated as procedural agents and mapped to the AG domain

⇒ Well, your case is also mapped to AG

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CASE1: Storage of EG data measured 3 times per point

CASE2: Mapping for Creatinine Clearance(CG Formula)

CASE1:

Storage of ECG data measured 3 times per point



- **Challenge**

- We received following ECG data of Phase IIa study(non-TQT) from central Lab. How to map the data to SDTM?

- **EG data**

TPT	REPEAT#	EGTEST	EGORRES	EGTIM
Pre-dose	1	...	52	09:57:00
Pre-dose	2	...	57	09:58:00
Pre-dose	3	...	51	09:59:00
1hr	1	...	55	11:00:00
1hr	2	...	56	11:01:00
1hr	3	...	57	11:02:00

- **Initial Consideration**

- In SDTMIG 3.2 there is no suitable variable to store “REPEAT #”. I wonder how to store them. These data are measured at different times for each “REPEAT #”. Should I increment “TPTNUM” by 0.1?
Ex.: 0.1 , 0.2 , 0.3 , 1.1 , 1.2 , 1.3

CASE1:

Storage of ECG data measured 3 times per point



- **Consulting with TAUGs**

- --TPTNUM needs one-to-one correspondence with --TPT. Once you add a different TPTNUM, you can not handle them as data at the same time point.
- There may be more examples on TAUGs. Filter "LB" on " **TAUG SDTM Mapping Index** ", and we can find Example of ECG in TAUG of QT studies.

TAUG	Topic	Domain	Summary
QT Studies Version 1.0 (Provisional)	Examples for ECG Assessments(7.1.1)	EG	• 同一時点で複数回測定する情報を識別するためにEGREPNUMを使用。 • 個々の拍動データを記述する際の識別用。 • Time Point Planning(5.2)を参照する。 (Snapshot of TAUG SDTM Mapping Index)

CASE1:

Storage of ECG data measured 3 times per point

- In the TAUG of QT studies, you can find non standard variable EGREPNUM to identify repeat number.

Row	EGSTRESU	EGLEAD	EGMETHOD	VISITNUM	VISIT	EGDTC	EGTPT	...	EGREPNUM
1 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:00:21	1 HR	...	1
2 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:00:21	1 HR	...	1
3 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:00:21	1 HR	...	1
4 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:00:21	1 HR	...	1
5 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:01:35	1 HR	...	2
6 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:01:35	1 HR	...	2
7 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:01:35	1 HR	...	2
8 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:01:35	1 HR	...	2
9 (cont)	msec	LEAD II	12 LEAD STANDARD	2	VISIT 2	2014-03-22T10:02:14	1 HR	...	3

- Searching for EGREPNUM within the same TAUG will also find the following information.

The --REPNUM (Repetition Number) variable is a variable which has been approved by SDTM Governance but has not yet been included in a formally published version of the SDTM.

- Then, you can learn that SDTMIG 3.2 does not contain variables to store them appropriately.
- In this case, EGREPNUM was created as SUPP, because this study is based on SDTM IG 3.2.

CASE1:

Storage of ECG data measured 3 times per point



- **Summary**

- It's not a QT study, so Data Manager did not expect that TAUG to be helpful.
- By using "**TAUG SDTM Mapping Index**", Data Manager could find one useful TAUG from all TAUGs.
- Since this variable is not described in the version of SDTMIG acceptable to PMDA, Data Manger decided to store it in SUPPEG.

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CASE2:

How to map Creatinine Clearance (CG Formula)



- **Challenge**

- We received following data from central Lab. How to map the data to SDTM?

- **Lab data**

Test Name	Unit	Spec
Creatinine	mg/dL	SERUM
Creatinine Clearance (CG Formula)	mL/min	SERUM

*CG Formula: $CLCr = ((140 - \text{age}) * \text{weight}) / (72 * \text{SerumCr})$
(Multiply by 0.85 if female)

- **Initial Consideration**

- OK, it is Creatinine Clearance. It should be

LBTESTCD	LBTEST	LBSPEC
CREAT	Creatinine	SERUM
CREATCLR	Creatinine Clearance	SERUM

CASE2:

How to map Creatinine Clearance (CG Formula)

- **Consulting with TAUGs**

- Filtering "LB" on " **TAUG SDTM Mapping Index** ", and we could find followings. So we could consult with following 2 TAUGs.

TAUG	Topic	Domain		Summary	Editor's Note
Diabetes v1	Laboratory Tests (3.1)	LB	Laboratory Test Results	• Glucose Homeostasis and Diabetes Related Markers • Lipid Panel • Kidney Function	例えば、Kidney Functionの章に、Creatinine ClearanceとeGFRの説明がある。...
Diabetic Kidney Disease v1	Measured GFR (3.1.1)	LB	Laboratory Test Results	• GFR, GFRBSAの値を格納、GFRではLBMETHODにCALCULATIONを使用、LBSPECは未使用	METHODの使い方には様々な議論がある。
	Estimated GFR (3.1.2)	LB	Laboratory Test Results	• eGFRで、LBMETHODに"CALCULATION"、LBANMETHにeGFR equationの名称を格納する方法を例示	METHODの使い方には様々な議論がある。

(Snapshot of TAUG SDTM Mapping Index)

CASE2:

How to map Creatinine Clearance (CG Formula)

- On section 3.1.3 of Diabetes v 1 TAUG, CG Formula is categorized as "Estimated GFR", not "Creatinine Clearance"

CCr CrCL	Creatinine Clearance	Creatinine clearance rate is defined as the volume of blood that is cleared of creatinine per unit time and is a useful measure for approximating the glomerular filtration rate. Creatinine clearance is important in assessing the excretory function of the kidneys. A creatinine clearance test is done by measuring both a serum creatinine concentration along with a urine creatinine in a urine sample collected over a specific time period.
eGFR	Estimated Glomerular Filtration Rate	Instead of requiring the laborious creatinine clearance test, which involves collecting urine over time, a variety of formulas have been developed that rely on a single measurement of serum creatinine, taking into account variables such as the subject's age, gender, race, and weight An estimated glomerular filtration rate (eGFR) can be derived from the following formulae 1) Modification of Diet in Renal Disease (MDRD) formula 2) CKD-EPI formula 3) Mayo Quadratic formula 4) Schwartz formula, used for children 5) <u>Cockcroft-Gault formula</u>

CASE2:

How to map Creatinine Clearance (CG Formula)



- Definition of both tests are as follow (SDTM CT 2016-09)
- In this case, "Creatinine Clearance (CG Formula)" is "Estimation", not "Measurement"... So it is better to adopt "GFRE" as TESTCD.

C-Code	TESTCD	TEST	CDISC Definition
C25747	CREATCLR	Creatinine Clearance	A measurement of the volume of serum or plasma that would be cleared of creatinine by excretion of urine for a specified unit of time (e.g. one minute).
C110935	GFRE	Glomerular Filtration Rate, Estimated	A kidney function test that estimates the fluid volume that is filtered from the kidney glomeruli to the Bowman's capsule per unit of time.

CASE2:

How to map Creatinine Clearance (CG Formula)

- There is a following example on section 3.1.2 of Diabetic Kidney Disease v1.
 - LBSPEC** should be null for Calculated Value
 - It is good idea to express "CG formula" using **LBMETHOD** and **LBANMETH**. But any other way to express it easier?

lb.xpt

Row	STUDYID	DOMAIN	USUBJID	LBSEQ	LBREFID	LBTESTCD	LBTEST	LBCAT	LBORRES	LBORRESU	LBORNRL0
1	ArBit 01	LB	AB01-001	1	A12567	CREAT	Creatinine	CHEMISTRY	1.5	mg/dL	0.7
2	ArBit 01	LB	AB01-001	2	A12567	CYSTATC	Cystatin C	CHEMISTRY	1.4	mg/L	0.52
3	ArBit 01	LB	AB01-001	3	A12567	GFRE	Glomerular Filtration Rate, Estimated	CHEMISTRY	51	mL/min/1.73m2	90
4	ArBit 01	LB	AB01-001	4	A12567	CREAT	Creatinine	CHEMISTRY	1.6	mg/dL	0.7
5	ArBit 01	LB	AB01-001	5	A12567	CYSTATC	Cystatin C	CHEMISTRY	1.37	mg/L	0.52
6	ArBit 01	LB	AB01-001	6	A12567	GFRE	Glomerular Filtration Rate, Estimated	CHEMISTRY	47	mL/min/1.73m2	90

Row	LBORNRI	LBSTRESC	LBSTRESN	LBSTRESU	LBSTNRLO	LBSTNRHI	LBNRIND	LBSPEC	LBMETHOD
1 (cont)	1.3	1.5	1.5	mg/dL	0.7	1.3	HIGH	SERUM	ENZYMATIC COLORIMETRY
2 (cont)	0.9	1.4	1.4	mg/L	0.52	0.9	HIGH	SERUM	PARTICLE-ENHANCED TURBIDIMETRIC IMMUNOASSAY
3 (cont)	120	51	51	mL/min/1.73m2	90	120	LOW		CALCULATION
4 (cont)	1.3	1.6	1.6	mg/dL	0.7	1.3	HIGH	SERUM	ENZYMATIC COLORIMETRY
5 (cont)	0.9	1.37	1.37	mg/L	0.52	0.9	HIGH	SERUM	PARTICLE-ENHANCED TURBIDIMETRIC IMMUNOASSAY
6 (cont)	120	47	47	mL/min/1.73m2	90	120	LOW		CALCULATION

Row	LBANMETH	VISIT	VISITNUM	LBDC
1 (cont)		Week 1	1	1999-06-19
2 (cont)		Week 1	1	1999-06-19
3 (cont)	IDMS-4-VARIABLE MDRD EQUATION-US VERSION	Week 1	1	1999-06-19
4 (cont)		Week 2	2	1999-06-26
5 (cont)		Week 2	2	1999-06-26
6 (cont)	IDMS-4-VARIABLE MDRD EQUATION-US VERSION	Week 2	2	1999-06-26

CASE2:

How to map Creatinine Clearance (CG Formula)

- On section 3.2.2 of Diabetes V1

TAUG	Topic	Domain	Summary	Editor's Note
Diabetes v1	Tolerance Tests (3.2.2)	TS Laboratory Test Results	TS(TSPARM=Standardized Meal Description)にSTANDARD MEALの内容を記載	この手法は他にもいろいろと応用が効くと思う。

- "CG Formula" is not Subject Level Information, it is Study Level. So we may use TS for it.
- Conclusion in this study

LB

LBTESTCD	LBTEST	LBSPEC
CREAT	Creatinine	SERUM
GFRE	Glomerular Filtration Rate, Estimated	(null)

TS

TSPARM	TSVAL
GFRE Description	Cockcroft-Gault formula

Conclusion

TAUG SDTM Mapping Index

- ◆ Final version is going to be published in Summer 2018.
- ✓ Examples of various Examinations/Evaluations and SDTM domains.
- ✓ Compare easily the SDTM mapping methods among TAUGs.
- ✓ Useful tool to help Understanding and Using TAUGs for SDTM mapping.

Thank you !!

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