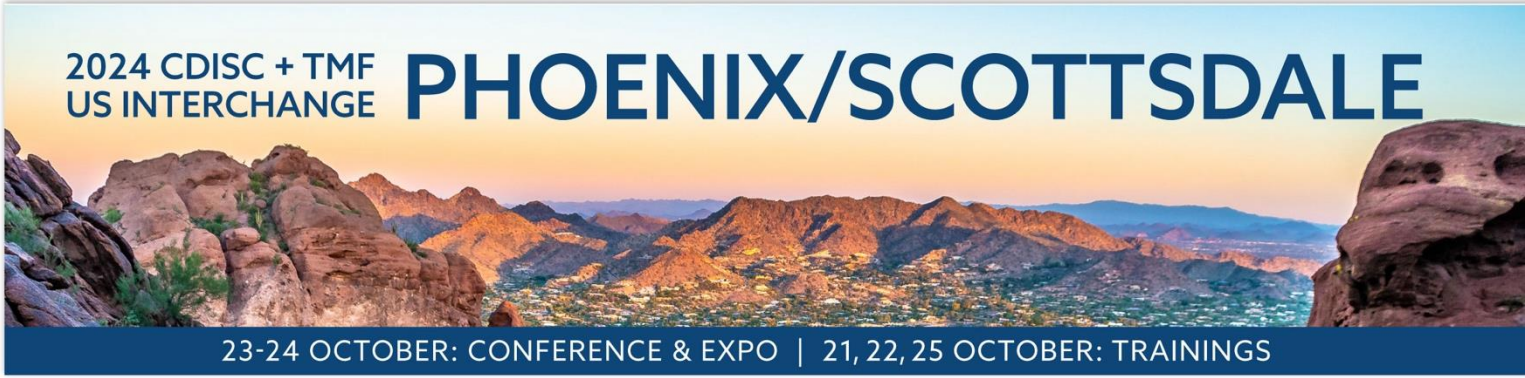


Adjudication of Events and Findings

Presented by Jennifer Mastri, Associate Director, GCDS, GDMS, Merck & Co., Inc., Rahway, NJ, USA
Diana Litvan, Associate Director, GCDS, GDMS, Merck & Co., Inc., Rahway, NJ, USA

Meet the Speakers

Jennifer Mastri

Title: Associate Director

Organization: Global Clinical Data Standards, GDMS, Merck

Jennifer Mastri is an Associate Director in Global Clinical Data Standards at Merck with over 20 years of data management experience across multiple functional areas. She is responsible for oversight and maintenance of the global library vaccine and core data standards.

Diana Litvan

Title: Associate Director

Organization: Global Clinical Data Standards, GDMS, Merck

Diana Litvan is an Associate Director in Global Clinical Data Standards at Merck for Cardiovascular TA. Prior to Merck, Diana had multiple roles including setting up large and complex studies in DMW as well as writing clinical protocols, setting up trials in Inform Central Designer and overseeing data management and data cleaning.

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

Agenda

1. Background
2. Industry Guidance
3. Our Custom Solution
4. Next Steps

Adjudication

What is it?

A process where independent experts evaluate suspected clinical events (e.g., endpoints) reported by the Investigator

An Adjudication Charter defines the events for adjudication, a list of required documents, and criteria for each event

Who's involved?

- **Sponsor** sends required data
- **External adjudication vendor** coordinates adjudication process
- **Adjudicator** conducts assessment

Adjudicators are qualified, independent reviewers

Why do it?

Have a consistent, independent, unbiased, blinded assessment

Reduces the variability of differences in medical assessment across study sites

How can we do this at our company?

First, we looked to see what guidance is available from industry…

- **Health Authority Guidance?**
- **Standards Development Organization Guidance?**
- **Working Group Best Practices?**
- **White Papers or Publications?**

…and we learned that
(next slide)

…There is a lack of formal industry guidance for adjudication procedures.

Therapeutic Area User Guide (TAUG) for Cardiovascular Studies

Released 17-Oct-2014

- **Guidance is out of date**:
  - Instructs to collect cardiovascular (CV) endpoints events as clinical events (CE)
  - Company received agency comments that CV events should be reported as Adverse Events (AE)
  - Therefore, adjudication to FACE would no longer comply with agency requests

Global Study Data Tabulation Model Implementation Guide (SDTMIG)

- **Not able to be adopted because it's still evolving and requires new ways of working for each version:**
  - **Version 3.1.1**: initially had adjudicated data mapped to the clinical findings (CF) domain
  - **Version 3.2**: removed the clinical findings domain, replaced it with the findings about (FA) domain
  - **Version 3.3**: has findings about clinical events (FACE) domain, which is not accommodating to all TAs
  - **Version 3.4**: to be determined

…Best practices have been attempted, but the resulting guidance is still incomplete.

Working Groups

- There is no best practice available from current working groups
- Historically, no one has wanted to take on adjudication data mapping
- Adjudication data is now under evaluation & review

Best Practices for Submission of Event Adjudication

Released 18-Oct-2019

- White paper from the PHUSE team that involved multiple stakeholders and regulatory authorities to map out the common practices and challenges for submission of event adjudication data
- Leveraged to map the adjudication event assessment to the EA findings domain
- Included some, but not all company-required SDTM variables (missing variables in red below):

XCNAM	XCSPID	XCCAT	XCSTAT	XCSTRESN	XCMETHOD
STUDYID	XCLNKID	XCSCAT	XCREASND	XCSTRESU	XCEVAL
USUBJID	XCLNKGRP	XCOBJ	XCORRES	XCLOC	XCEVALID
SUBJID	XCTPT	XCTESTCD	XCORRESU	XCLAT	XCACPTFL
XCREFID	XCTPTNUM	XCTEST	XCSTRESC	XCDIR	

So, what did we do?

1 Identified Key Stakeholders and Subject Matter Experts

Consulted with industry experts
Review of FDA NASH Guidance

2 Reviewed the EA Domain Proposal for Adjudication

Followed a similar approach to the PHUSE white paper

3 Created a Custom Domain (XC)

Allowed flexibility across all studies to collect AEs, Procedures, etc.

- Why XC?
  - Our Company maps all custom domains to begin with "X" and incrementally names them alphabetically, which allows for easier re-evaluation and mapping as new domains become available through CDISC

Our XC custom domain was able to accommodate the inclusion of SUPPXC, which is needed for company data collection

The EA domain did not include variables needed by the company to adjudicate the data

SUPPQUAL QNAM	SUPPQUAL QLABEL	Description
XCCHNGBL	Change from Baseline	Used when result is compared to a baseline value. Values are per adjudication charter. Field can be Null.
XCCHNGPD	Change from Predose	Used when result is compared to a predose value. Values are per adjudication charter. Field can be Null.
XCAESID1	Associated AE Sponsor ID Number 1	Item to be used to capture Adverse Event Sponsor ID number(s) from the AE form for adjudication. If multiple Adverse Events, enter with a comma between numbering (i.e., 1,4,6).
XCPRSID1	Associated PR Sponsor Number 1	Item to be used to capture Procedure Sequence Number(s) from the PROC form for adjudication. If multiple Procedures, enter with a comma between numbering (i.e., 1,4,6).

Sample data mapping

		Arterial Revascularization Peripheral Adjudication Form	XCOBJ
1.	Event ID		
2.	Date of Event	DD/MMM/YYYY	SUPPXC.XCADJDTC
3.	Duplicate event	Is this event a duplicate of an existing event? ❍ Yes (specify event #_____) ❍ No	SUPPXC. XCDUPIND SUPPXC.XCADRFID
4.	Region of Revascularization	❍ Aorta ❍ Lower Extremity ❍ Upper Extremity ❍ Mesenteric ❍ Renal ❍ Other (specify_____) ❍ No procedure performed that meets criteria of a peripheral arterial revascularization per Charter	TESTCD
6.	Procedure(s)	☐ Endarterectomy	

Adjudication Mapping

XC

STUDYID	SUBJID	XCSEQ	XCREFID	XCOBJ	XCDTC	XCNAM	XCTESTCD	XCTEST	XCORRES	XCSTRESC	XCCAT	XCLOC	XCDIR	XCEVAL
12345	100001	10011	101	PERIPHERAL REVASCULARIZATION	20-Feb-2024	ADJUDCATION VENDOR	RVASCR	REVASCULARIZATION REGION	LOWER EXTERMITY	LOWER EXTERMITY	ADJUDICATION EVENT			ADJUDICATOR
12345	10009	10091	109	PERIPHERAL ISCHEMIC AMPUTATION	25-Mar-2023	ADJUDCATION VENDOR	AMPTLVL	AMPUTATION LEVEL	UPPER EXTREMITY	UPPER EXTREMITY	ADJUDICATION EVENT	WRIST JOINT	DISTAL	ADJUDICATOR
12345	10002	10022	102	MYOCARDIAL INFARCTION	20-Feb-2024	ADJUDCATION VENDOR	MI Type	TYPE 1: SPONTANEOUS MYOCARDIAL INFARCTION	STEMI	STEMI	ADJUDICATION EVENT			ADJUDICATOR

SUPPXC

STUDYID	RDOMAIN	USUBJID	IDAR	IDVAREVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
12345	XC	100001	XCSEQ	10011	XCPRSPID	Associated PR Sponsor ID Number 1	3	EDT	
12345	XC	100001	XCSEQ	10011	XCADJDTC	Assigned Adjud Event Date	10-Jan-2024	EDT	
12345	XC	100001	XCSEQ	10011	XCDUPIND	Adjudicated Event Duplicate Indicator	N	EDT	
12345	XC	100009	XCSEQ	10091	XCADJDTC	Assigned Adjud Event Date	12-Jan-2024	EDT	
12345	XC	100009	XCSEQ	10091	XCDUPIND	Adjudicated Event Duplicate Indicator	N	EDT	
12345	XC	10002	XCSEQ	10022	XCAESID1	Associated AE Sponsor ID Number 1	2	EDT	

Adjudication Mapping

XC

STUDYID	SUBJID	XCSEQ	XCREFID	XCOBJ	XCDTC	XCNAM	XCTESTCD	XCTEST	XCORRES	XCSTRESC	XCCAT	XCEVAL
12445	20009	20091	201	CONTINUOUS ECG (HOLTER) FINDING	15-Jul-2023	ADJUDCATION VENDOR	NVTABNS	Non-VT ECG Abnormalities	QRS PROLONGATION	QRS PROLONGATION	ADJUDICATION EVENT	ADJUDICATOR
12445	20009	20092	202	CONTINUOUS ECG (HOLTER) FINDING	17-Jul-2023	ADJUDCATION VENDOR	BRPTNTYP	Brugada Pattern Type	NON-SPECIFIC BRUGADA PATTERN	NON-SPECIFIC BRUGADA PATTERN	ADJUDICATION EVENT	ADJUDICATOR
12445	20009	20093	203	VT EVENT FINDING	25-Jul-2023	ADJUDCATION VENDOR	RHYTHM	Rhythm	NSVT 4-10 BEATS	NSVT 4-10 BEATS	ADJUDICATION EVENT	ADJUDICATOR

SUPPXC

STUDYID	RDOMAIN	USUBJID	IDAR	IDVAREVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
12445	XC	20009	XCSEQ	20091	XCAMFDTC	Assigned Med Facility Event Date	10-Jan-2024	EDT	
12445	XC	20009	XCSEQ	20091	XCDUPIND	Adjudicated Event Duplicate Indicator	N	EDT	
12445	XC	20009	XCSEQ	20091	XCCHNGBL	Change From Baseline	Y	EDT	
12445	XC	20009	XCSEQ	20092	XCCHNGPD	Change From Predose	N	EDT	
12445	XC	20009	XCSEQ	20093	XCVTDTL	Non VT Event Details	4 beats	EDT	

Future Considerations for Remapping

- Non-Standard Variables replacing the supplemental in the future
  - Replaces the need for the supplemental variables
    - Adds a variable to collect the SPID of the event being adjudicated to relrec data to the source

ae.xpt

Row	STUDYID	DOMAIN	USUBJID	AESEQ	AESPID	AETERM	AEDECOD	AEREL	AESTDTC	AEENDTC
1	DEF	AE	DEF-02-002	7	7	HEART ATTACK	Myocardial infarction	RELATED	2021-01-15	2021-01-15
2	DEF	AE	DEF-04-001	3	3	STABLE ANGINA	Angina pectoris	RELATED	2021-01-22	2021-01-23

ea.xpt

Row	STUDYID	DOMAIN	USUBJID	EASEQ	EASPID
1	DEF	EA	DEF-02-002	1	7
4	DEF	EA	DEF-04-001	1	3

relrec.xpt

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
1	DEF	AE		AESPID		ONE	AE_EA
2	DEF	EA		EASPID		MANY	AE_EA

Adjudication Domain Review

Where do we go from here?

This is a sponsor-defined way of working, we'd like to adopt it via an industry standard

- Define an industry standard for adjudication procedures.
- The Cardiovascular TAUG should be updated
- Expand the adjudication findings framework into additional therapeutic areas

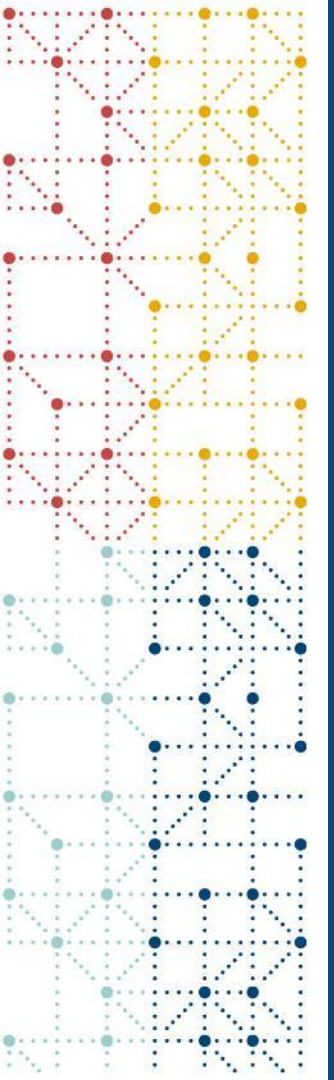
What does everyone else do?

As a company, we want to hear from our fellow colleagues!

Did you implement the EA findings domain from the PHUSE white paper?

What was your experience?

How do you manage updates as guidance evolves?



Thank you!

Feel free to connect with us offline, we'd love to hear from you!

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