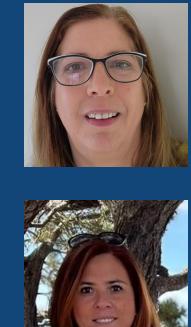




Adjudication of Events and Findings

Presented by Jennifer Mastri, Associate Director, GCDS, GDMS, MSD Diana Litvan, Associate Director, GCDS, GDMS, MSD





Meet the Speakers

Jennifer Mastri

Title: Associate Director

Organization: Global Clinical Data Standards, GDMS, MSD

Jennifer Mastri is an Associate Director in Global Clinical Data Standards at MSD 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, MSD

Diana Litvan is an Associate Director in Global Clinical Data Standards at MSD for Cardiovascular TA. Prior to MSD, 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.

Agenda

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



Adjudication



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

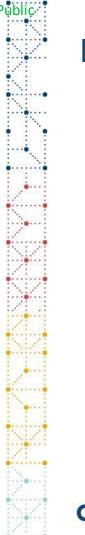
Adjudicators are qualified, independent reviewers

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?

Working Group Best Practices?

Standards Development Organization Guidance?

White Papers or Publications?



...and we learned that



... 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 cardiovascular 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

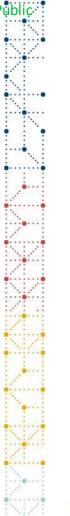
- There is no best practice available from current working groups
- · Historically, no one has wanted to take on adjudication data mapping
- Adjudication data is now under evaluation & review

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?

Identified Key Stakeholders and Subject Matter Experts

Consulted with industry experts

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



1

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 w hen 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 com ma between numbering (i.e., 1,4,6).



Sample data mapping

Public

		Arterial Revascularization Peripheral Adjudication Form
1.	Event ID	
2.	Date of Event	DD/MMM/YYYY SUPPXC.XCADJDTC
3.	Duplicate event	Is this event a duplicate of an existing event? SUPPXC. XCDUPIND
		• Yes (specify event #) • No
4.	Region of Revascularization	 Aorta Lower Extremity Upper Extremity Mesenteric Renal
		 O Other (specify) O No procedure performed that meets criteria of a peripheral arterial revascularization per Charter
	Procedure(s)	Endarterectomy 2024 Europe CDISC+TMFInterchange #ClearDataClearImpact

Adjudication Mapping

TUDYID	SUBJID×	CSEQ	XCREFI D	I XCOBJ	ļ	XCDTC	XCNAM	XCTESTC D	XCTEST	XCORRES	XCSTRESC	XCCAT	XCLOC	ACDIR	XCEVAL
12345	100001 1	0011	101	PERIPHER REVASCUI TION		20-Feb-2024	ADJUDCATI ON VENDOR	RVASCR	Revascularization Region	LOWER EXTERMI TY	LOWER EXTERMITY	ADJUDICATION EVENT			ADJUDICAT
12345	10009 1	0091	109	PERIPHER ISCHEMIC AMPUTATIO		25-Mar-2023	ADJUDCATI ON VENDOR	AMPTLVL	Amputation Level	UPPER EXTREMI TY	UPPER EXTREMITY	ADJUDICATION EVENT	WRIST JOINT	DISTAL	ADJUDICAT
12345	10002 1	0022	102	MYOCARE INFARCTIO		20-Feb-2024	ADJUDCATI ON VENDOR	МІ Туре	TYPE 1: SPONTANEOUS MYOCARDIAL INFARCTION	STEMI	STEMI	ADJUDICATION EVENT			ADJUDICAT
SUPPXC	;														
STUDYID	RDOMAI	N USU	IBJID I	DAR	DVARE	EVAL QNAM			QLABEL			QVAL	QORIG	QEVA	\L
2345	XC	1000	001	XCSEQ	10011	XCPRSPI	D		Associat	ed PR Spo	nsor ID Number	1 3	EDT		
2345	XC	1000	001	XCSEQ	10011	XCADJD	ГC		Assigned	d Adjud Eve	ent Date	10-Jan-202	4 EDT		
2345	XC	1000	001	XCSEQ	10011	XCDUPIN	D		Adjudica	ted Event [Duplicate Indicate	or N	EDT		
0045	XC	1000	009	XCSEQ	10091	XCADJD	ГC		Assigned	d Adjud Eve	ont Data	12-Jan-202	4 EDT		
2345	70	1000		COLC	10001		-		Assigned	i Aujuu Eve					
	XC	1000			10091	XCDUPIN			Ŭ		Duplicate Indicate		EDT		



Public

XC

Adjudication Mapping

XC

Public

STUDYID	SUBJID	XCSEQ	XCREFID	ХСОВЈ	XCDTC		XCTEST CD	XCTEST	XCORRES	XCSTRESC	XCCAT	XCEVAL
12445	20009	20091		CONTINUOUS ECG (HOLTER) FINDING		ADJUDCATION VENDOR	S		QRS PROLONGATION	QRS PROLONGATION	ADJUDICATION EVENT	ADJUDIC ATOR
12445	20009	20092		CONTINUOUS ECG (HOLTER) FINDING	17-Jul-2023	ADJUDCATION VENDOR		Pattern	NON-SPECIFIC BRUGADA PATTERN	NON-SPECIFIC BRUGADA PATTERN	ADJUDICATION EVENT	ADJUDIC ATOR
12445	20009	20093	203	VT EVENT FINDING	25-Jul-2023	ADJUDCATION VENDOR	RHYTHM	Rhythm	NSVT 4-10 BEATS	NSVT 4-10 BEATS	ADJUDICATION EVENT	ADJUDIC ATOR

SUPPXC

STUDYID	RDOMA IN	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	Ν	EDT	
12445	XC	20009	XCSEQ	20091	VOOLINIODI	Change From Baseline	Y	EDT	
12445	XC	20009	XCSEQ	20092	VOOLINIOPP	Change From Predose	Ν	EDT	
12445	XC	20009	XCSEQ	20093	VOVITOTI	Non VT Event Details	4 beats	EDT	



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?

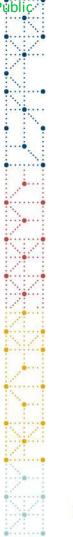
What was your experience?

How do you manage updates as guidance evolves?



Thank you!

Feel free to connect with us offline, we'd love to hear from you! jennifer_cording@merck.com diana.litvan@merck.com



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.





Abstract

Data collection of adjudicated events and findings has been challenging due to the limited guidance from standards organizations and regulatory agencies. Leading to differences in data collection and reporting approaches over the years.

The presentation will cover key points in collecting the finding and events adjudication data and the inputs used to create mapping. Review of the historical data mapping findings adjudication process was examined by the company leading up to the new solution. Using the structure and process included in the PHUSE paper Best Practices for Submission of Event Adjudication Data, Version Date 18-Oct-2019, the team looked at the adjudication findings to improve the data collection and reporting. Findings about collection for the adjudication findings map to the FACE domain and required the creation of a custom domain of XC Adjudication Findings involving cross functional collaboration between internal and external parties ensuring full traceability from end to end.

