Current and Forthcoming ADaM Publications

Deb Bauer, Associate Director Biostatistics, Sanofi
Nancy Brucken, Standards Engineer, Clinical Solutions Group, an IQVIA business
Liana Forman, Associate Director Data Standards, Clinical Solutions Group, an IQVIA business
Brian Harris, Standards Developer, Senior Director, AstraZeneca
Karin LaPann, Associate Director Clinical Standards, Takeda Pharmaceutical Company
Luke Reinbolt, Lead Consultant, Clinical SAS Programmer Analyst, Navitas Data Sciences
Jack Shostak, Associate Director, Clinical Trial Statistics, Duke University
Paul Slagle, Sr Director, Data Standards & Process, Biometrics, Clinical Solutions Group, an IQVIA business
Tatiana Sotingco, Assoc Director, Clinical Data Standards Architect – Data Analysis & Reporting, J&J
Julia Yang, Senior Principal Clinical Statistical Developer, Medtronic
Wayne Zhong, Consultant, Accretion Softworks LLC

cdisc 20 YEARS ANNIVERSARY

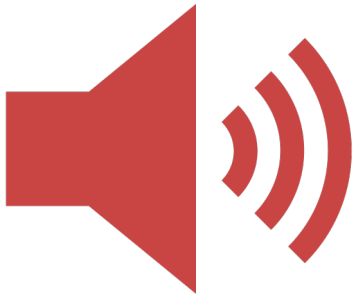
TUE 2 MAR
11:00AM-12:30PM ET

Today’s Agenda

1. Housekeeping
2. Presenter Introductions
3. Feature Presentation(s)
4. Question & Answer Session
5. Upcoming Learning Opportunities & Resources

Housekeeping

Housekeeping



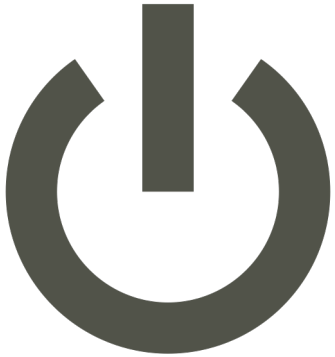
You will remain on **mute**

Housekeeping

There will be a **Q&A**

Submit questions at any time

Housekeeping



Audio issues?

Shut down & restart Zoom

Housekeeping

Webinar slides & recording available
for **CDISC Members**

Our Presenters

- Deb Bauer, Associate Director Biostatistics, Sanofi
- Nancy Brucken, Standards Engineer, Clinical Solutions Group, an IQVIA business
- Liana Forman, Associate Director Data Standards, Clinical Solutions Group, an IQVIA business
- Brian Harris, Standards Developer, Senior Director, AstraZeneca
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Current & Forthcoming ADaM Publications

Presented by ADaM team membership

02 March 2021

Disclaimer and Disclosures

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

- *The authors have no real or apparent conflicts of interest to report.*

Agenda

1. ADaM ADNCA v1.0
2. ADaM Implementation Guide v1.3
3. ADaM Implementation Guide Medical Devices v1.0
4. ADaM guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic
5. ADaM OCCDS v1.1
6. ADaM Oncology Examples
7. ADaM Questionnaire Supplements (ADQRS)
8. ADaM Traceability Examples
9. Q&A

ADaM ADNCA v1.0

Presented by

Luke Reinbolt
Lead Consultant, Clinical SAS Programmer Analyst
Navitas Data Science

ADNCA: Dataset Submitted to Create PK Parameters

- ADNCA → ADaM Non-compartmental Analysis Dataset
- ADNCA is a sub-class of BDS
- The document describes the differences and additions to BDS

ADaM Impentation Guide v1.3

Presented by

Brian Harris
Standards Developer, Senior Director
AstraZeneca

Minor Update to Address Specific Issues

Location	Description
Section 2.2	Text was added (in 2nd sentence of 1st paragraph) clarifying the inclusion of SDTM variables in ADaM datasets to assist traceability.
Section 3.3.3	The following sentence was added to the first paragraph: *If a dataset contains more than one record within a parameter and within a subject then a SDTM or ADaM relative day timing variable must be included.*
Table 3.3.3.1	Added to CDISC notes for ADY, ASTDY, & AENDY: *If a dataset contains more than one record per parameter per subject then a SDTM or ADaM relative day timing variable must be included (ADY would meet this requirement).*
Table 3.3.4.1.1	Added the text noting that BASETYPE does not need to be populated if BASE or BASEC is not populated.

ADaM Implementation Guide Medical Devices v1.0

Presented by

Julia Yang
Senior Principal Clinical Statistical Developer
Medtronic

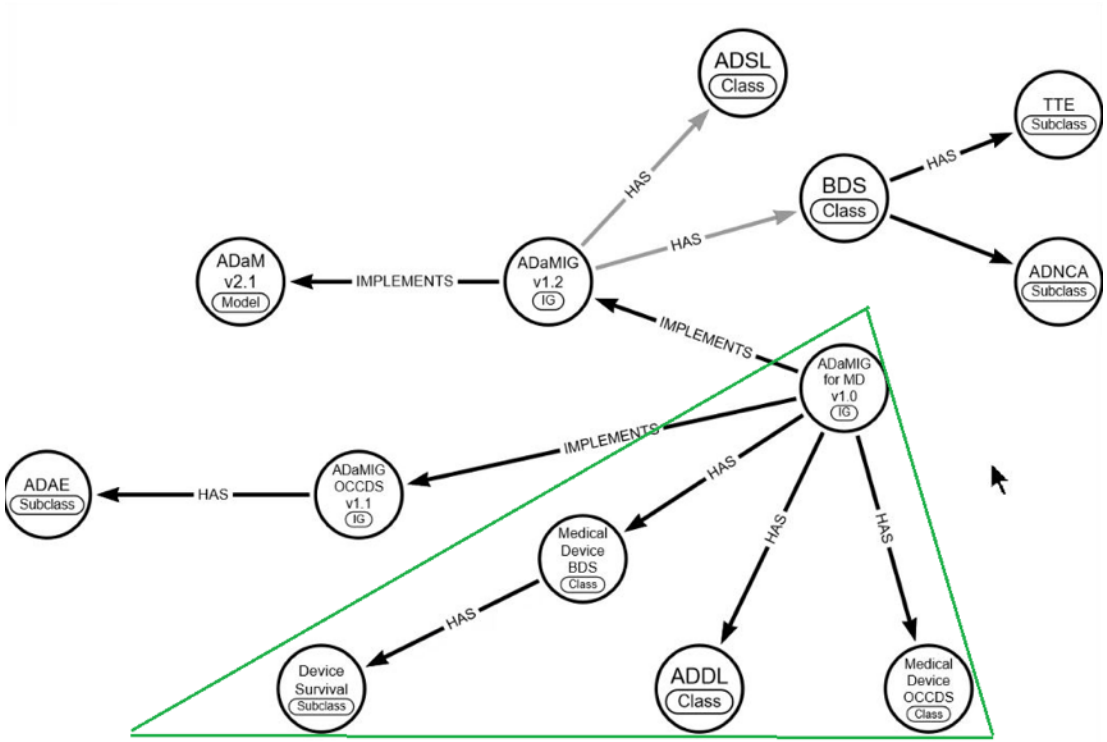
ADaM Implementation Guide for Medical Devices v1.0

- Addresses typical needs for clinical trials using and analyzing medical device data.

- The guide introduces three new classes of data structures
  - ADDL → ADaM Device Level Analysis dataset
  - MDOCCDS → Medical Devices Occurrence Data Structure
  - MDBDS → Medical Devices Basic Data Structure

- One new subclass data structure under MDBDS for device survival analysis
  - Medical Device time-to-event MDTTE

ADaM Implementation Guide for Medical Devices v1.0



ADaM Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic

Presented by

Liana Foreman

Associate Director Data Standards

Clinical Solutions Group, an IQVIA business

ADaM Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic

- Last summer we started COVID ADaM team to address pandemic impact on ADaM, we considered various approaches to data collection and data presentation and very pleased to announce that “ADaM Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic” is very close to being published.
- The guidance provides recommendations for addressing the analysis needs for data capturing epidemic/pandemic impacts on ongoing clinical trials. It includes ADSL and OCCDS metadata with examples.
- We realize that regulatory reviewers need a “handle” in order to differentiate between the levels of pandemic impact on subject and on the clinical trial.

ADaM Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic

We also realize that not all Sponsors may not be able to fully follow SDTM guidance on COVID -19 and create SDTM COVID variables due to some inflexibility with data collection and database design. In ADaM we do have flexibility of combining data for analysis from multiple sources and performing complex derivations on collected data to support analysis.

We introduce variables and algorithms around these variables that can be derived regardless of the availability of SDTM COVID related variables.

In “ADaM Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic” we are introducing ”strongly recommended” composite in nature Broad and Specific Subject Epi/Pandemic Related indicators, and optional Trial Epi/Pandemic Related indicator. In addition we are introducing supportive epidemic/pandemic related disease/pathogen classification variables that can assist with analysis.

ADaM Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic

- All Epidemic/Pandemic related variables with start with “EP” prefix. We realize that same study/compound may potentially be affected by more than one epidemic and or pandemic during its course, therefore variables we are introducing can hold multiple pandemics in lower-case letter “w” within the variable name, which will be replaced with a single digit [1-9].
- We strongly feel that reviewers will benefit from the “indicator” variables more then from the “flag” variables. Most of our epidemic/pandemic related variables in ADSL are indicators with allowable values as Y (Yes), N (No), U (Unknown) and NA (Not Applicable).
- In OCCDS we introduce EPSEwFL (Epi/Pandemic Specific Event Flag w) to flag Events with Epidemic/Pandemic pathogen positivity at a record level. In OCCDS examples we demonstrate how to use SMQ, CQ, ANLzzFL to present Epidemic/Pandemic adverse events.

- Stay tuned for the publication!

ADaM OCCDS v1.1

Presented by

Deb Bauer
Associate Director Biostatistics
Sanofi

ADaM OCCDS v1.1

- First public review was Feb/March 2020
- Recently completed a second public review to address the addition of four new variables to allow multiple treatment-emergent and on-treatment flags to handle multiple periods or other analysis needs.

Version 1.1 Key Updates

- Added a subclass of ADVERSE EVENT, based on the new metadata element defined in the release of Define-XML v2.1 document
  - For OCCDS Variables 2 Core columns are added, 1 for ADVERSE EVENT subclass
- Introduction of “U” prefix for Unmodified SDTM variables when combining multiple SDTM domains (e.g. MHTERM, AETERM becomes UTERM)
- Added SRCSEQ, SRCDOM, and ASEQ for traceability
- Added ADECODy for Analysis Dictionary-Derived Term y
- Text Updated to be consistent with ADaM IG v1.2
- Added 3 new examples
  - AE that change over time collecting this information in FA
  - Analysis of AEs from multiple input domains (AE, CE)
  - Analysis of Protocol deviations
- Added additional treatment-emergent and on-treatment variables

Additional treatment emergent variables added

Variable Name	Variable Label	Core	SubClass ADVERSE EVENT Core	CDISC Notes
TRTEMFL	Treatment Emergent Analysis Flag	Cond	Req	Treatment-emergent flag as defined for analysis Example derivation: If ADSL.TRTSDT<=ASTDT<=ADSL.TRTEDT + x days then TRTEMFL="Y" The number x in this derivation is defined by the producer and often incorporates the known half-life of the drug. For datasets other than SubClass ADVERSE EVENT, this variable is conditional on whether the concept of treatment emergent is a key feature of the analysis.
TREMxxFL	Treatment Emergent Period xx Flag	Cond	Cond	This variable is required if there are multiple periods where treatment emergence is a key feature of the analysis for each period. If TREMxxFL is included, TRTEMFL is defined as the overall treatment-emergent flag.
TRTEMwFL	Treatment Emergent Analysis w Flag	Perm	Perm	This variable is used if there are other analysis needs (e.g., different cut-offs) where treatment emergence is a key feature of the analysis. If TREMwFL is included, TRTEMFL is defined as the overall treatment-emergent flag.

Same was applied to ONTRTFL

Variable Name	Variable Label	Core	CDISC Notes
ONTRTFL	On Treatment Record Flag	Cond	Character indicator of whether the observation occurred while the subject was on treatment. A codelist of Y, N, null may be used as described in ADaMIG Section 3.3.8, Indicator Variables for BDS Datasets. Example derivation: If ADSL.TRTSDT <= ASTDT <= ADSL.TRTEDT then ONTRTFL = "Y" This variable is conditional on whether the concept of on treatment is a feature of the study and used in analysis.
ONTRxxFL	On Treatment Period xx Flag	Perm	This variable is used if there are multiple periods where on treatment is a key feature of the analysis for each period. If ONTRxxFL is included, ONTRTFL is defined as the overall on-treatment flag.
ONTRTwFL	On Treatment Record w Flag	Perm	This variable is used if there are other analysis needs (e.g., different cut-offs) where on treatment is a key feature of the analysis. If ONTRTwFL is included, ONTRTFL is defined as the overall on-treatment flag.

ADaM Oncology Examples

Presented by

Paul Slagle
Senior Director, Data Standards & Process, Biometrics
Clinical Solutions Group, an IQVIA business

ADaM Oncology Examples

- Provide examples for supporting ADaM development of oncology data

- Providing specific examples of
  - Subject level – including coverage for:
    - Common Analysis Populations
    - Histology / Pathology
    - Prior Treatments
    - Interim Analysis identification
  - Laboratory – Coverage of bidirectional lab toxicity grades
  - Exposure – Creation of both ADEX for analyzing subject / time period data and ADEXSUM for summarizing by subject level.
  - Cycle / Visit – Creation of an interim dataset for tracking treatment cycles

ADaM Oncology Examples

- Close to being sent out for review / In development
  - Adverse Events
  - Biomarkers
  - Blood Transfusions
  - Survival Analysis
    - Including PARQUAL

ADaM Questionnaire Supplements (ADQRS)

Presented by

Nancy Brucken
Standards Engineer
Clinical Solutions Group, an IQVIA business

ADaM Questionnaire Supplements (ADQRS)

- Published first ADaM QRS supplement which describes the structure of a typical dataset that could be used for summarization and analysis of the Geriatric Depression Scale Short Form (GDS-SF)
- Sent out for internal CDISC review, Generalized Anxiety Disorder – 7-Item (GAD-7) questionnaire supplement.
- Published 4 ‘readme’ files, which provide rationale for not developing ADaM supplements for corresponding single-item instruments
- Finalized templates for creating ADaM QRS supplements and ‘readme’ files

Sub-team is accepting new volunteers- please contact us if there is a questionnaire supplement you would like to help develop!

ADaM Traceability Examples

Presented by

Wayne Zhong
Consultant
Accretion Softworks LLC

ADaM Traceability Examples

- Provide various simple and complex traceability examples using current ADaM dataset structures
- Document contains no new guidance, recommendations, or standards
- Currently in CDISC team internal review, no public
- Publication targeted for Q3 2021

Traceability Definition

- Current ADaM documents describe need for traceability, provide elements to support traceability

- ADaM Model v2.1
  - Foundational principle: “provide traceability between the analysis data and its source data”

- ADaMIG
  - “ADaM datasets and metadata must clearly communicate how the ADaM datasets were created”

- OCCDS
  - “In general, include all variables from the SDTM dataset and corresponding supplemental qualifiers that are needed for analysis or traceability “

Purpose of Traceability

- Submissions provide evidence new drugs and therapies are safe and effective
- Suppose a new vaccine shows promise, seen in table below

Table 1.2-1: Sample Efficacy Table

Table xx.x Primary Efficacy Endpoint (ITT Population)

	Drug n (%) (N=8000)	Control n (%) (N=8000)	Odds Ratio	P-Value
Occurrence of Primary Study Disease at 2 Years	8 (0.1%)	64 (0.8%)	0.1241	< 0.0001

Purpose of Traceability

- Define.xml metadata supporting efficacy table

Table 1.2-2: Sample Analysis Results Metadata

Display	Table xx.x Primary Efficacy Endpoint
Analysis Result	Occurrence of Primary Study Disease at 2 Years
Analysis Parameter(s)	PARAMCD = "PRI" (Primary Efficacy Endpoint)
Analysis Variable(s)	AVAL (Analysis Value)
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADEF [PARAMCD = "PRI" and ITTFL = "Y"]
Documentation	SAP Section 4.1
Programming Statements	[SAS Version 9.4] proc freq data=adef(where=(ittfl='Y' and paramcd='PRI')); table trt01pn*aval; exact or; run;

Purpose of Traceability

- ADEF source data, can reproduce numbers and p-value in table
- How is ADEF created? What is the source data?

Table 1.2-3: Sample ADEF Records

USUBJID	SRCDOM	SRCSEQ	PARAMCD	PARAM	AVAL	AVALC
XYZ-01-001	PF	2	PRI	Primary Efficacy Endpoint	0	DISEASE
XYZ-01-002	LB	52	PRI	Primary Efficacy Endpoint	0	DISEASE
XYZ-01-003			PRI	Primary Efficacy Endpoint	1	NO DISEASE
XYZ-01-004			PRI	Primary Efficacy Endpoint	1	NO DISEASE

Purpose of Traceability

- Define.xml metadata supporting ADEF

Table 1.2-4: Sample ADEF Variable Level Metadata

ADEF Variable Metadata

Name	Variable Label	Variable Metadata
USUBJID	Unique Subject Identifier	ADSL.USUBJID
SRCDOM	Source Data	If AVAL=0, identify whether the corresponding record is from PF or LB SDTM domain
SRCSEQ	Source Sequence	If AVAL=0, copy over the corresponding PFSEQ or LBSEQ value from the corresponding record
PARAMCD	Parameter Code	Set to "PRI"
PARAM	Parameter	Set to " Primary Efficacy Endpoint"
AVAL	Analysis Value	If subject has a biopsy record in PF where PFTEST="BIOMARKER 1" and PFSTRESC="PRESENT" then set AVAL=0. Else if subject does not have any biopsy records in PF and has an enzyme record in LB where LBTEST="ENZYME A" and LBSTRESC="POSITIVE" then set AVAL=0. (note: if a biopsy absent record is present, do not check enzyme test records) Otherwise set AVAL=1 Refer to SAP section 4.1 for more details
AVALC	Analysis Value (C)	If AVAL=0 then set AVALC="DISEASE" If AVAL=1 then set AVALC="NO DISEASE"

Purpose of Traceability

Table Values

⇩

Metadata Traceability

⇩

Table 1.2-3: Sample ADEF Records

USUBJID	SRCDOM	SRCSEQ	PARAMCD	PARAM	AVAL	AVALC
XYZ-01-001	PF	2	PRI	Primary Efficacy Endpoint	0	DISEASE
XYZ-01-002	LB	52	PRI	Primary Efficacy Endpoint	0	DISEASE
XYZ-01-003			PRI	Primary Efficacy Endpoint	1	NO DISEASE
XYZ-01-004			PRI	Primary Efficacy Endpoint	1	NO DISEASE

⇩

Data-point Traceability

⇩

SDTM PF & LB Records

⇩

Data collection instrument

Traceability in Practice

- Good traceability in a submission unambiguously shows the data lineage, allows reviewers to reproduce results and identify supporting source data

- ADaM Examples document has 12 examples from actual projects
  - ADSL, BDS, OCCDS
  - Creating parameters from, stacking, merging with multiple SDTM domains
  - Using intermediate datasets when creating ADSL, BDS
  - Look-up-tables
  - More...

- Publication targeted for Q3 2021

Questions & Answers

Led by

Bernard Klinke
Virtual Experience Manager
CDISC

Q&A Panelists

- Deb Bauer
  Sanofi
- Nancy Brucken
  CSG, an IQVIA business
- Liana Forman
  CSG, an IQVIA business.
- Nate Freimark
  The Griesser Group
- Brian Harris,
  AstraZeneca
- Karin LaPann
  Takeda
- Luke Reinbolt
  Navitas Data Science
- Julia Yang
  Medtronic
- Paul Slagle
  CSG, an IQVIA business.
- Jack Shostak
  Duke
- Tatiana Sotingco
  Janssen R&D
- Wayne Zhong
  Accretion Softworks LLC

Thank You!

Questions & Answers

Audience Questions

When will all of these publications be finished, released, and published?

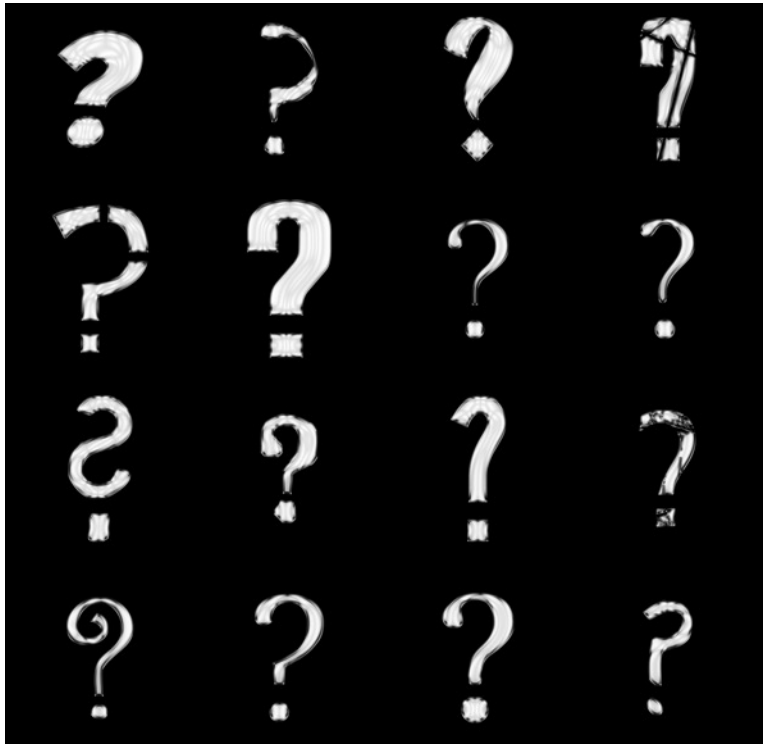
Audience Questions

Will there be guideline for ADaM for integrated analysis, like ISS, ISE?

Audience Questions

What's the status for the ADaM Structures for Integration: IADSL, IOCCDS and IBDS?

Audience Questions



What is MDTTE? what is the difference between TTE and MDTTE?

Audience Questions

What are some reasons for using exclusion flags?

Audience Questions

Is USUBJID still required variable, if my study does not collected subject level information?

Audience Questions

Is ADDL a require ADaM dataset, as a counterpart ADSL?

Audience Questions

Would the new U prefix mentioned in OCCDS be better added to the main ADaM IG? Could then be used if a need was found to combine multiple SDTM findings domains into a single BDS

Audience Questions

Will there be concomitant medication flag in OCCDS guideline?

Audience Questions

How can I participate in the public review of ADaM documents?

Audience Questions

For "ADaM Oncology Examples" what is the document referred during the presentation? And where can we get hold of it within CDISC website?

Audience Questions

What is the publication timeline for the ADaM structures for integration (ISS and/or ISE)? Thank you.

Audience Questions

Question to ADam Oncology Examples speaker: You mentioned PARQUAL which I believe was not included in the ADaM I.G. v. 1.2 ? Could you please elaborate on the inclusion of PARQUAL?

Audience Questions

OCCDS: Did you also consider adding AOCCzzFL variables to highlight the first AE by subject and treatment. Rather than only first by subject? If not, how to add occurrence flag variables in a cross-over design?

Audience Questions

What would be the type/format for a variable similar to SDTM in ADaM. ex: RFSTDTC and TRTSDTC in ADaM.

Audience Questions

Do you have any idea of when the ADaM IG v1.2 will be required by the FDA?

Audience Questions

is ADNCA requested by FDA for this year submission?

Audience Questions

will be the guidlines for ADam data for SCP (summary of clinical pharmacology)?

Audience Questions

Can you reiterate what the big takeaways were for the ADAM IG for medical devices?

Audience Questions

Will there be concomitant medication flag in OCCDS guideline. If concomitant medication is defined as medications with an end date of after TRTSDT, i.e. on treatment and during followup, then there is no flag in the guideline to identify the concomitant medication. The logic we could use is like if ONTRTFL=Y or FUFL=Y then the medication is concomitant.

Upcoming Learning Opportunities

New Virtual Training Methods

- Information available at: www.cdisc.org
- Register at: https://learnstore.cdisc.org/
- Contact us at: training@cdisc.org

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Washington, DC | 18-22 October
Conference | Trade Show

2021 Webinars

Date	Webinar Title
16 MAR	QRS "Office Hours"
25 MAR	Public Review Webinar: Pancreatic Cancer Therapeutic Area User Guide
30 MAR	Meet our New President and CEO: Hear CDISC's 2021 Vision and Direction
1 APR	Controlled Terminology Updates for Q1 2021
8 APR	CDISC Library: Ideas for Using the CDISC Library and a Look at What's Coming Next
1 JUL	Controlled Terminology Updates for Q2 2021
Coming Soon	CDASH "Office Hours"; ADaM "Office Hours"; More Public Reviews – stay tuned!

Visit https://www.cdisc.org/education/webinars for information on additional Public Training events.

Questions

Use CDISC contact form:
https://www.cdisc.org/contact

Contact general EDU inbox:
training@cdisc.org

Contact Bernard directly: bklinke@cdisc.org

Thank You!

Questions, comments, concerns? Email bklinke@cdisc.org

Don’t forget to fill out the feedback survey!