CDISC Implementation Committee

Neesha Desai

January 22nd, 2020

Agenda

- NCI Requirement
- Project Updates
- NCI CDISC Harmonization WG Update
- LPO Status Updates
- Appendix

NCI Requirement

- All CTEP IND studies activated on/after 3/1/2020 shall be CDISC compliant (submit to FDA in SDTM format)
- Studies activated prior to 2/28/20 do NOT need to be CDASH compliant but-LPOs are encouraged to launch CDASH compliant studies prior to the March 1st deadline, if possible.
  - Waivers will only be considered by the NCI for truly extenuating circumstances that meet both of the following criteria
  - The justification is for something beyond LPO control
  - AND the activation date was anticipated to be prior to 1/1/20.

NCI Requirement

- Examples:
  - Acceptable waiver request: Study with an OEWG date of 12/1/19 whose activation is delayed due to drug supply until 3/15/20.
  - Unacceptable waiver request: Study with an OEWG date of 2/1/20 whose activation is delayed due to drug supply until 3/15/20. This study should have been built with the intention of meeting the original CDISC implementation date.

CDISC Harmonization WG Activities

- Next Steps
  - Send out updated list of Off Treatment Code List for review
  - Send out updated list of Primary Cause of Death Code List for review
  - Fragments List Review/Updates
  - Completed NCI Standard Forms
    - RECIST
    - iRECIST
    - Screening
  - Finalizing the following forms
    - Off Treatment
    - Off Study
  - DEWG rules/naming conventions

CTSU Standard Forms ALS

- v2.3 Non-CDISC CTSU Standard Forms ALS
  - Updates pending per feedback/technical updates
  - The new version will be v2.4
  - Timeframe TBD

- v7.0 CDISC CTSU Standard Forms ALS
  - Updates pending per LPO feedback/technical updates
  - The new version will be v7.1
  - Timeframe TBD

LPO Status Updates (1)

LPO	Prior Update	Seed Study identified	Target date to complete Seed Study	# of CDASH/ SDTM harmonized CRFs *(templates/ seed study CRFs)*	Rave Study Build initiated	Target date to initiate Rave Study Build	# of CTEP IND Studies planned for Q1 2020 activation
Theradex	PRIOR UPDATE: Reviewing each of the forms and making updates as needed. Target for completion for 3/1/2020 Deadline • Forms have been built, once completed will work on edit checks • Trying to bring 8-12 studies in activation before 12/31/19. • Target is 8 studies that Jeff Moscow thinks we will be able to get active by 12/31. • Some of those have OEWG deadlines further out. • CURRENT UPDATE: • In final UAT, project to have everything validated by the end of the month. Working through integration with ALS7.0. Have a backlog of studies that will need parallel processing once the validation is complete. 5 studies activated before 12/31, will have a few more.	Yes	~ 11/25/2019	All forms have been built and imported in Rave. Working on edit checks.	Yes	Complete custom functions and validations by end of December	~5 studies w/ Dec 2019 OEWG deadlines *(some study builds already initiated, may need to be rebuilt)* ~7 studies w/ Jan 2020 OEWG deadlines ~1 study w/ March 2020 OEWG deadline 5 studies activated by 12/31 One study has a 2/7 deadline with old standards since seed study is still being validated March activation for CDASH studies.

LPO Status Updates (1)

NCI/Group	Prior Update	Seed Study identified	Target date to complete Seed Study	# of CDASH/ SDTM harmonized CRFs *(templates/ seed study CRFs)*	Rave Study Build initiated	Target date to initiate Rave Study Build	# of CTEP IND Studies planned for Q1 2020 activation
SWOG	PRIOR UPDATE: Rave study build not started close to finalizing mock ups Target for completion for 3/1/2020 Deadline SWOG has prioritized their studies to meet the 3/1/2020 deadline. CURRENT UPDATE: 1 study in Rave, mock ups finalized for the other studies on the list for March	Yes	~ 01/xx/2020	*28 forms fully mapped to SDTM and built in Rave and have been 28 left*	*Yes*	*Should have the first study built in Rave in a few weeks and then working on edit checks*	*2 studies may activate Feb* *Few in March* *6 to activate March 1918,1929,1933, 1925, 1929, 1914 (March or April)* *1918 – Mostly built*

LPO Status Updates (2)

NCI/Group	Prior Update	Seed Study identified	Target date to complete Seed Study	# of CDASH/ SDTM harmonized CRFs *(templates/ seed study CRFs)*	Rave Study Build initiated	Target date to initiate Rave Study Build	# of CTEP IND Studies planned for Q1 2020 activation
ECOG-ACRIN	PRIOR UPDATE: 10 standard forms into seed study. Target for completion for 3/1/2020 Deadline • EAA171 – Pushed to Feb • EA5191 – Rebuild of 5152, doing a database architect copy, needs to be ready by 5/23. Were going to submit a request to keep the data tables the same • EA2187 – OEWG date of 1/31 – Not sure if that will activate before then. Not CDISC compliant, built this before the ALS. CURRENT UPDATE: EA5191 – Build in CDISC format EA2187 – 1/31/20 – working to getting this activated prior to March 1	Yes	To be verified	All forms have been identified for harmonization, # to be confirmed.	Yes *(in sandbox)*	~ 09/01/2019	EA8185 (Seed study) Late March/Early April EA5191 – Late May EA5182 – July 10th

LPO Status Updates (2)

NCI/Group	Prior Update	Seed Study identified	Target date to complete Seed Study	# of CDASH/ SDTM harmonized CRFs *(templates/ seed study CRFs)*	Rave Study Build initiated	Target date to initiate Rave Study Build	# of CTEP IND Studies planned for Q1 2020 activation
Alliance	PRIOR UPDATE: Taking existing standard forms and seed study and comparing them with both ALS files. Some building has been started, moving forward and making progress. Target for completion for 3/1/2020 Deadline • 2 studies are ready for activations but OEWG keeps extending deadline – activated • 1 study had an OEWG study of 1/20, preparing it to activate on time. – rebuilding protocol CURRENT UPDATE:	Alliance Global Library First actual study identified	1/1/2020 for Global Library	39 forms fully harmonized with CDASH with unit test completed 15 have been built in Rave, but only touched on edit checks, just started on custom functions. All forms have been harmonized with CDASH and built. Working on custom functions with the first three studies for CDASH study specific fields.	TBD	TBD	March and one in April, Confident to reach deadlines Looking to see if there will be a third study, potential activations January…internal discussions A081801 - March A021804 - TBD A071702 - April

LPO Status Updates (3)

NCI/Group	Prior Update	Seed Study identified	Target date to complete Seed Study	# of CDASH/ SDTM harmonized CRFs *(templates/ seed study CRFs)*	Rave Study Build initiated	Target date to initiate Rave Study Build	# of CTEP IND Studies planned for Q1 2020 activation
CCTG	PRIOR UPDATE: Finalizing internal review on CRFs. Submitting a few calls in next couple weeks and training to go over questions. Target for completion for 3/1/2020 Deadline CURRENT UPDATE Almost complete with internal review of GLIB. Two studies that will be using CDISC	Building Global Library first	TBD	Working through Global Library and mock templates	Not yet		*No studies identified at this point. Main concern is not the Rave build, more the SDTM and items touched by our SAS programs.* *Identified 3 studies* *1. MA40* *2. OB27* 3. First IND Trial in late 2020 :AL6

LPO Status Updates (3)

NCI/Group	Prior Update	Seed Study identified	Target date to complete Seed Study	# of CDASH/ SDTM harmonized CRFs *(templates/ seed study CRFs)*	Rave Study Build initiated	Target date to initiate Rave Study Build	# of CTEP IND Studies planned for Q1 2020 activation
NRG	PRIOR UPDATE: Seed study has been built in Rave, planning to send ALS for review to verify. Working on 2nd Rave study build. Target for completion for 3/1/2020 Deadline CURRENT UPDATE: 2nd study is nearing completion.	Yes		Every external form (~50) has been harmonized; internal forms are pending	Yes	~ March 2019	TBD *(update will be provided offline)* *NRGY020 – Feb activation – will implement the CTSU AE forms* *BN006 – Activate mid January *Pushed back but before end of Feb.*

LPO Status Updates (4)

NCI/Group	Update	Seed Study identified	Target date to complete Seed Study	# of CDASH/ SDTM harmonized CRFs *(templates/ seed study CRFs)*	Rave Study Build initiated	Target date to initiate Rave Study Build	# of CTEP IND Studies planned for Q1 2020 activation
COG	PRIOR UPDATE: Started bi-weekly meetings with Westat. Working on CRFs Target for completion for 3/1/2020 Deadline CURRENT UPDATE:	Not yet	TBD	TBD	Not yet	TBD	No studies planned for Q1

Next Steps

- Next Meeting is February 26th 2020, from 2-3pm

Appendix

CDISC Harmonization Workflow
NCI CBIIT: CDEs for EC Forms Overview
CDISC Implementation Workflow
CTSU Change Matrix
eCRF Build Scenarios
LPO I.A.: Beta Release GLIB

CDISC Harmonization Workflow *v06/25/2019*

1) LPO submits new supplemental question details to CDISC Project team via ALS file within 15 business days of question implementation.
2) CDISC Project team adds the new supplemental question to the **CDISC LPO Supplemental Question Listing**[1].
3) CDISC Project team prepares and submits the supplemental questions (partial or no match) to the CDISC Harmonization Working Group (WG).
4) CDISC Harmonization WG reviews, standardizes and harmonizes the supplemental question/s.
5) CDISC Project team prepares a supplemental questions review request for submission to CDSIC.
6) CDISC Project team submits and tracks review requests to CDISC.

Footnotes

1. *The **CDISC LPO Supplemental Question Listing** is a document created and maintained by the NCI CDISC Project team. This document will specify:*
   a. *Supplemental questions that have been recently created and implemented by an LPO for a specific protocol;*
   b. *Supplemental questions that have been harmonized/ standardized by the **CDISC Harmonization WG** and submitted by the CDISC Project team to CDISC for review.*

Project Updates (1)

- **CDISC Mailbox**
  - ncicdiscsupport@nih.gov
- **CDISC Wiki**
  - CDISC Webinars, Recording and Slides Posted
  - LPO FAQs
  - CDISC LPO Impact Analysis Feedback Posted
  - CDISC Harmonization WG Meeting Materials

NCI CBIIT: CDEs for EC Forms Overview

1. EC CDEs – *Inclusion/Exclusion Criteria*

- CDASH does not provide a variable for individual inclusion/exclusion questions
- Continue to curate these CDEs using your current process

TI – Examples for Trial Inclusion/Exclusion Criteria Dataset

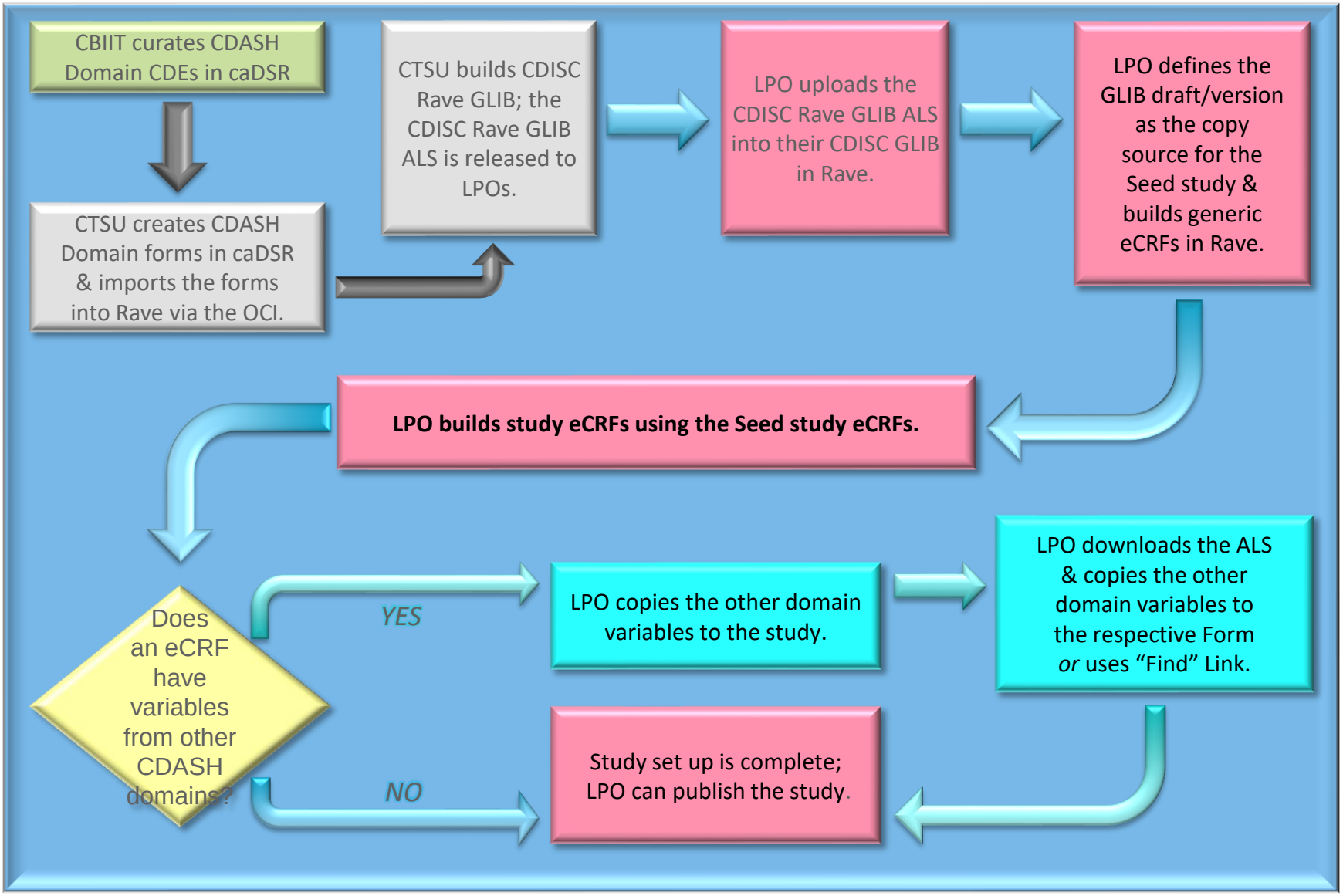
This example shows records for a trial that had two versions of inclusion/exclusion criteria.
Rows 1-3 show the two inclusion criteria and one exclusion criterion for version 1 of the protocol.
Rows 4-6 show the inclusion/exclusion criteria for version 2.2 of the protocol, which changed the minimum age entry from 21 to 18.

Row	STUDYID	DOMAIN	IETESTCD	IETEST	IECAT	TIVERS
1	XYZ	TI	INCL01	Has disease under study	INCLUSION	1
2	XYZ	TI	INCL02	Age 21 or greater	INCLUSION	1
3	XYZ	TI	EXCL01	Pregnant or lactating	EXCLUSION	1
4	XYZ	TI	INCL01	Has disease under study	INCLUSION	2.2
5	XYZ	TI	INCL02A	Age 18 or greater	INCLUSION	2.2
6	XYZ	TI	EXCL01	Pregnant or lactating	EXCLUSION	2.2

2. EC CDEs – Supplemental Qualifiers Domain Questions

- NCI CBIIT team will curate CDEs for the LPOs requesting assistance please submit request(s) to the NCI CDISC Mailbox
- Will curate only EC Forms where questions are not already curated CDASH or Inclusion/Exclusion
- For curation we will need CDISC details – LPOs provide map to SDTM:
  - Variable label
  - Variable name
  - Data format
  - List of values (if enumerated)

CDISC Implementation Workflow



CDISC Rave Global Library: CTSU Change Matrix

Rave Attribute	caDSR/ OCI Attribute	CTSU CDISC Global library	Change Management
Form Name	caDSR Form Long Name *(e.g., DEMOGRAPHICS)*	CDASH Domain Name *(e.g., DEMOGRAPHICS)*	*<no change: same as caDSR>*
Form OID	caDSR Form Long Name *(e.g., DEMOGRAPHICS)*	2 letter CDASH Domain Name *(e.g., DM)*	**Update by CTSU**
Variable OID	Short Name of the CDE *(e.g., RACE)*	CDASH/SDTM Variable Name *(e.g., RACE)*	*<no change: same as caDSR>*
Field Name	caDSR CDE Long Name + PID + MajorV + MinorV *(e.g., Race PID6343384_V1_0)*	Variable Label + PID + MajorV + MinorV *(e.g., Race PID6343384_V1_0)*	*<no change: same as caDSR>*
Field OID	2 letter domain prefix + CDASH/ SDTM variable *(e.g., RACE)*	2 letter domain prefix + CDASH/SDTM Variable Name (e.g., RACE)	*<no change: same as caDSR>*
Field Label	Question Text *(e.g., Which of the following five racial designations best describes you? (More than one choice is acceptable.))*	Question Text or Variable label *(e.g., Which of the following five racial designations best describes you? (More than one choice is acceptable.))*	**Update by CTSU** ***Specify the Variable label for Field Labels without question text ***
Data Dictionary Name	caDSR Value Domain Long Name + PID + MajorV *(e.g., CDISC_SDTM_RACE_PID6343345_V1_0F)*	caDSR Value Domain Long Name + PID + MajorV	*<no change: same as caDSR>*
Data Dictionary Values- User Data String	Permissible Value Meaning (PVM) *(e.g., Native Hawaiian or Other Pacific Islander)*	NCI preferred term *(e.g., Native Hawaiian or Other Pacific Islander)*	*<no change: same as caDSR>*
Data Dictionary Values- Coded Data String	Permissible Value (PV) *(e.g., NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER)*	Submission Value *(e.g., NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER)*	*<no change: same as caDSR>*
Format- Date	char - $11	dd MMM yyyy	**Update by CTSU**
Format- Time	char - $10	24 hr HH:nn:ss	**Update by CTSU**
Format- Char (W/ Dictionary)	char *(may be either the max length of dictionary value or extendable value;; e.g., $100)*	char *(may be either the max length of dictionary value or extendable value; e.g., $100)*	*<no change: same as caDSR>*
Format- Char (W/O Dictionary)	char -$200	char -$200	*<no change: same as caDSR>*
Format- Numeric	num	num	*<no change: same as caDSR>*
Control Type	*(e.g., DropDownList)*	DATE/TIME update	**Update by CTSU**
SAS Label	*n/a*	Variable Label from SDTM; if no SDTM variable, use CDASH variable label	**Update by CTSU**
Auto-Query for Required data entry	*n/a*	SDTM -Required & Expected Variables CDASH - HR and R/C	**Update by CTSU**
Auto-Query for future Date	*n/a*	Set flag in the CDISC Rave GLIB ALS	**Update by CTSU** ***Applicable to all dates***

eCRFs Build Scenarios *(1)*

Rave eCRFs may have different build scenarios:

1) Variables from a **single domain**
2) Variables from **multiple domains**
3) Custom variables that do not map to CDASH/SDTM

1) Single Domain: All variables in an eCRF are from a single domain.

Example: Concomitant Medication (CM) domain

- Set the CDISC Global library as the copy source for the study.
- Identify the Domain variables needed for the CRF.
- Use copy wizard to select and copy the variables from the domain identified for eCRF build.
- Multiple eCRFs can be built using the same domain by changing the FORM OID during the copy process.

eCRFs Build Scenarios *(2)*

2) Multiple Domains: Variables in an eCRF are from more than one domain.

Example: an Exposure form with variables from the EX and AE domains

- Follow the steps specified in the *"eCRFs Build Scenarios: Single Domain"* slide to build an Exposure form with variables from the EX domain.
- Using the copy wizard, copy the required variables from the AE domain to the study draft.
- Add AE domain variables to an Exposure form:

Option 1

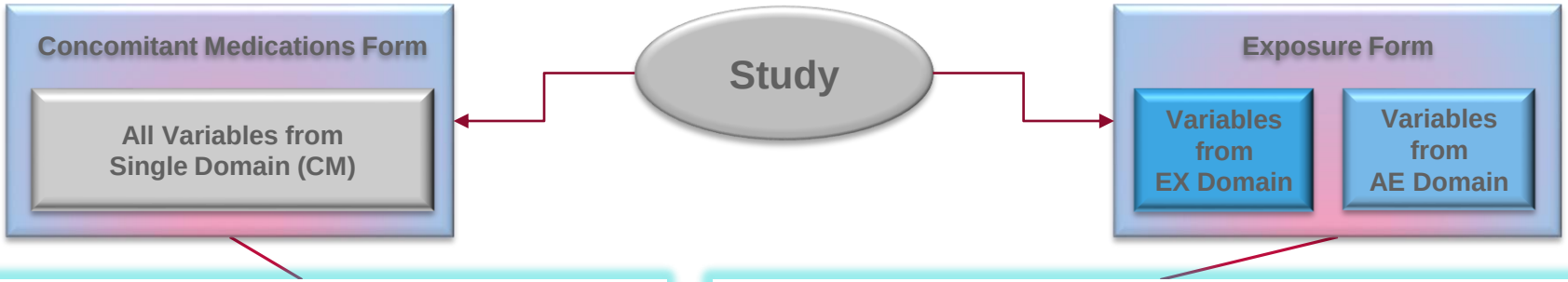
- Open the Exposure form; click add a new variable.
- Use the "Find" link on the variable definition screen to select the AE variable; click Apply to copy.

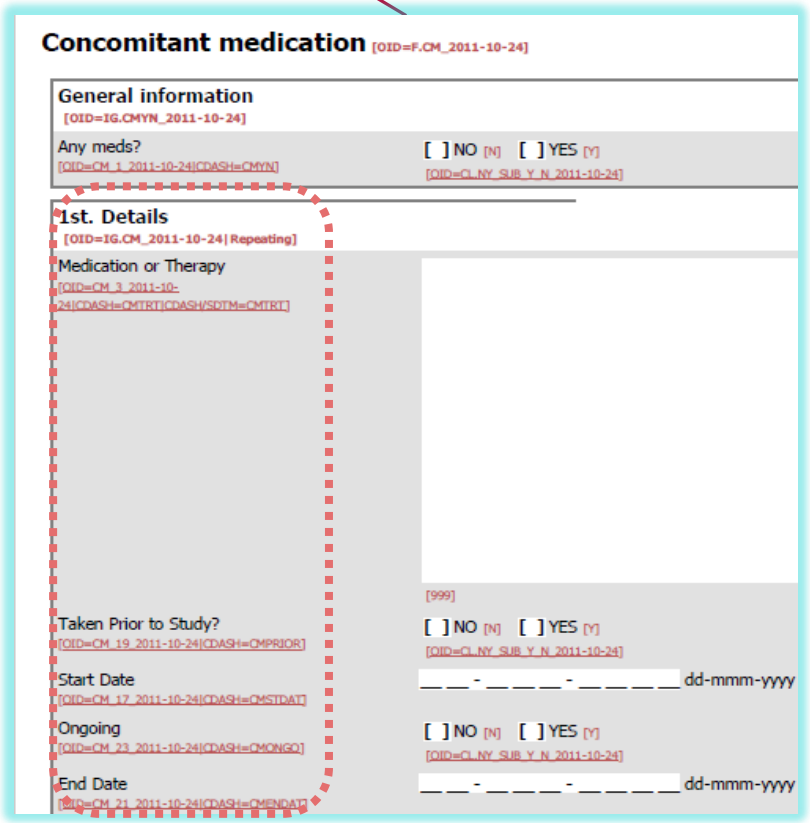
Note: the "Find" link brings only the Variable OID, Format and Data/Unit dictionary, not the associated Field attributes.

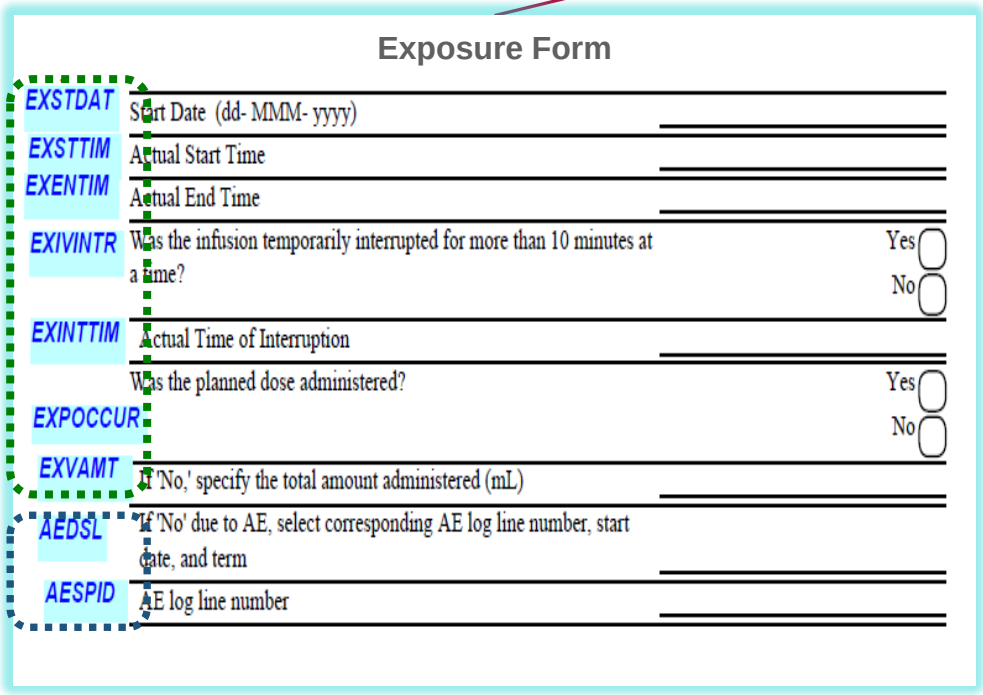
Option 2

- Download the ALS for the selected domains.
- Copy and paste the AE domain variables to the Exposure Form.
- Upload the ALS into Rave.

eCRFs Build Scenarios *(3-Examples)*







LPO Impact Analysis: Beta Release GLIB *(1)*

#	Document	LPO Findings/ Recommendations/ Questions	Decision
1	GLIB ALS	04/18/2019: I'm assuming a new release of the Controlled Terminology (CT) will be released prior to July. I wanted to confirm the final ALS release will contain the most up-to-date information. KL With the final release in July, will the GLIB and other ALS files be updated using the newest CDASH and SDTM controlled terminology packages?	CTSU will do an impact analysis (for CT Packages released by CDISC before July 2019) to understand the potential impact to our timeline. The intent it to provide documents as current as possible to CDISC releases/ updates; this must be done in consideration of the implementation timelines.
2	GLIB Release Notes: Section 3.2 Standard Conventions – Table 6	This table states that we cannot modify the Field OID. However, on the Variable Naming NVS webinar (3/28), Shannon presented several instances where it is expected and best practice to rename field OIDs in Rave for data collection purposes. In addition, the guide provides examples in 6.3 where it is OK/expected to change the field OIDs thus conflicting with the table. Please confirm Table 6 will be updated to reflect this.	05/02/2019 CDISC Integration FG: • LPOs can not change the field OIDs on Standard Forms • LPOs can change the field OIDS on Non-Standard forms if they have a strong reason to do so. "Standard Forms" applies to the CTSU Standard Forms ALS, "Non-Standard Forms applies to variables not specified in the CTSU Standard Forms ALS.
3	GLIB Release Notes: Section 3.2 Standard Conventions – Table 7	Given the needed updates to the Field OID to be specific (see situations/comment from 2), the SAS label should be modified for Rave data collection to ensure our programmers using CDASH Rave outputs can correctly identify the fields using the OIDs and Labels. Therefore, the SAS Label should be allowed to be modified when the Form OID is changed. (When data is transformed into SDTM format, the SAS Label can also be updated)	Maintain the same SAS label as in the CDISC GLIB for consistency across LPOs.
4	GLIB ALS	In the ALS, the Field name is the Variable Label + PID. Why the Variable Label? At the Alliance, we find having the Field Name match the Field OID + PID is much easier for specification writing, debugging and general viewing. (Medidata help guides state that in most cases, the Field name is the same as the Field OID.) As far as we understand, the Field Name isn't used for anything site facing or outputs. If the global ALS will not be changed, can the Alliance modify this?	No changes to the Rave Field Names in the CDISC GLIB ALS and CDISC CTSU Standard Forms ALS; the default naming convention will remain as-is, "the caDSR Long Name of the CDE + PID details". LPOs can use "the caDSR Long Name of the CDE + PID details" or choose to use "the caDSR Short Name of the CDE + PID details" as the Rave field name as needed. If the LPO chooses to use "the caDSR Short Name of the CDE + PID details" for the Rave field name, they are responsible for this update in Rave.

LPO Impact Analysis: Beta Release GLIB *(2)*

#	Document	LPO Findings/ Recommendations/ Questions	Decision
5	GLIB Release Notes: Table 6	For the User Data String, Table 6 states we must use the NCI Preferred term. However, CDISC training has stated we can use the NCI Preferred Term or CDISC Synonym. Please clarify which is correct.	LPOs can decide to use the NCI Preferred Term or the CDISC Synonym for the User Data String in Rave. If LPOs decide to use the CDISC Synonym instead of the NCI Preferred Term, they will be responsible for related study build activities and mapping activities for SDTM submission. The 'CDISC GLIB Release Notes' document will be updated to provide details for use of the CDSIC Synonym versus the NCI Preferred Term. The CDISC GLIB ALS will remain as is, no changes will be made to the User Data String and NCI Preferred Terms.
6	GLIB ALS	Why is the Data Dictionary Name not modifiable? Some dictionaries will be used across several fields; however, different sub-sets of responses will be needed for the questions. i. Rave does not allow us to subset the dictionary choices at the field level – a separate dictionary must be created ii. Example: NY. Sometimes Unknown or Not Applicable are not valid responses for a question iii. The Alliance would be open to a standard naming convention in this situation.	If authoring a form directly in Rave: LPOs should use the vetted CSC Data Elements Work Group (DEWG) naming convention (caDSR Value Domain Long Name + PID + MajorV + MinorV + _0F) for dictionary names and append an integer when subsetting a dictionary. If building a form in the caDSR/ using the OCI to import the form into Rave: the OCI will append an integer to the dictionary name when a dictionary is reused/ subsetted. Dictionary Names have been reverted to No changes will be made to the CDISC GLIB ALS. The CDISC GLIB Release Notes will be updated to include this naming convention for subsetted dictionary names.
7	GLIB ALS	When the GLIB is updated/versioned, can we get a detailed change log with the future releases?	A change log will be provided in the release notes for each updated GLIB release.

LPO Impact Analysis: Beta Release GLIB *(3)*

#	Document	LPO Findings/ Recommendations/ Questions	Decision
8	NCI/CDISC Best Practices Document	04/18/2019: In this section, it talked about all of these documents needed to be provided. I'm curious if there is any guidance to expected/required format and/or the level that we have to have prepared for CTEP-IND trials. We do not submit data directly to the FDA; I'm curious if we have to have annotated CRFs, and all these other documents that are listed for all trials. And if the trial has intent to submit to FDA, can we negotiate with our pharma partner on these. KL Section 4.3: What does this mean for us as LPO's? We are not translating all of these statements into what actions need to be done on Alliance trials. (Maybe the training is still coming?)	All CTEP IND studies activated on/after 1/1/2020 must be CDISC compliant. CDISC Compliance is highly recommended for studies that activate prior to the 2020 date. The CDISC SME to provide additional feedback at the "Overview of FDA Submission Process" Webinar on May 22nd, 2019.
9	NCI/CDISC Best Practices Document	Could a real life example/demo of the described best practices for the Eligibility Checklist Forms be provided? We're not following the workflows, when to curate/not curate, etc.	The CBIIT caDSR team presented the curation support/ process for eligibility criteria at the December Committee Meeting and an overview of this process at the April Committee Meeting.
10	NCI/CDISC Best Practices Document	Does NCI/CTEP submit data to FDA on NCTN trials? If so, study by study or aggregated across studies?	No decision required, NCI does not submit to the FDA.
11	NCI/CDISC Best Practices Document	Throughout the entire document, please be specific what CDISC compliant means. CDASH, SDTM, ADaM, etc. a. Additionally, our understanding from previous meetings is that the requirement is to be CDASH compliant only. We understood that it is up to the LPOs discretion and negotiations with the Pharma partner on SDTM programming. Please be specific in the document about whether we are referring to CDISC-CDASH or CDISC-SDTM.	The FDA requirement is SDTM. the NCI requirement is CDASH. CDASH compliance makes SDTM compliance easier to achieve. CDISC PM to review and update the NCI CDISC Best Practices document as needed to ensure clear communication of the NCI requirement for CDASH compliance.

NATIONAL CANCER INSTITUTE

www.cancer.gov

www.cancer.gov/espanol