

CDISC Implementation Committee

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Agenda

- NCI Requirement
- Project Updates
- FDA Submission Guidance
- NCI CDISC Harmonization WG Update
- LPO Questions

NCI Requirement

- **January 2020** **Date will be assessed based on LPO Impact Analysis*
 - All CTEP IND studies activated on/after 1/1/2020 shall be CDISC compliant.

Project Updates

- **CDISC Mailbox**

- ncicdiscsupport@nih.gov

- **CDISC Wiki**

- CDISC Webinars, Recording and Slides Posted
- LPO FAQs
- CDISC LPO Impact Analysis Feedback Posted

Project Updates

■ LPO Support Webinars/Sessions

- September 3rd, 2019 **CDISC SME Session**
 - Session: 2:00-4:00pm ET
 - Pre-planned agendas based on requests the week before
- October 6th, 2019 **CDISC SME Session**
 - Session: 2:00-4:00pm ET
 - Pre-planned agendas based on requests the week before
- October 15th, 2019 **CDISC SME Session**
 - Session: 2:00-4:00pm ET
 - Pre-planned agendas based on requests the week before

Ensuring Conformant SDTM is Possible from Collected Data

- Are you collecting information that will allow you to produce (at a minimum) valid SDTM domains for:
 - Demographics - to describe your study population
 - Exposure - to describe the specifics of the protocol-specified treatment each study participant was exposed to
 - Disposition - to describe how and when each person exited the study

This requires you to be familiar with the contents and rules for these SDTM domains. Much of the information in Exposure, for example, is derived from what we collect in the EDC + randomization information (which may come from a paper source or may come from an IWRS).

Ensuring Conformant SDTM is Possible from Collected Data

- Then,
 - Use the ALS (which is based on CDASH and SDTM) and standard controlled terminology for everything possible in your study
 - Controlled flexibility built in to CDASH Question Text/Prompt is also available for CTSU GLIB ALS
 - Use the CDASH Model for any forms you add to the study
 - Custom forms should be based on CDASH metadata, too
 - Use published SDTM Controlled Terminology where it is either required or useful (rather than making up your own codelists)
 - Create an SDTM mapping *before* you build the study
 - Map Rave output metadata through to SDTM metadata before study setup (reference CDASHIG and CDASH Model for SDTM mappings)
 - Communicate data origin (e.g., collected vs. derived) and other data handling rules (e.g., coding conventions) to the SDTM programmers

NCI CDISC Harmonization WG Update

- Meetings to date: Aug 12th KO meeting & Aug 26th follow-up meeting
- Reviewed Roadmap and discussed prioritization
 - Priority 1: Addressing LPO specific content
 - Priority 2: RECIST
 - Priority 3: iRECIST
 - Additional priorities to be confirmed as moving forward. The WG will manage LPO-designated high priority content as it is submitted to the NCI Mailbox.
- Reviewed 11 LPO CDISC Use Cases
- Created a mapping tool to use for CDISC Harmonization

NCI CDISC Harmonization WG Update

- High Level WG Discussion Updates
 - Identified instances where additional pre-text options needed to be added to provide flexibility during study build
 - Example: Adding initial diagnosis date as an option for the MHSTDAT
 - Currently it is medical condition or event start date
 - Reviewed items that could be a deficiency in CDASH
 - Discussed the potential benefits of standardized treatment codes (CTEP Agent Codes) across the LPOs
 - CDISC SME recommends taking his approach
 - LPOs are taking it back to their organization for discussion
 - **High Priority item:** discussed the importance of meaningful data dictionary names in front of the Value Domain PID and reuse naming/subsetting considerations
 - NCI is working on a plan to support this request
 - CDSIC SME recommended to use the existing names in the published CDISC submission value as part of the plan development

LPO Support Questions (1)

LPO Question	Response	LPO Feedback
<p>SAS Labels: While we appreciate the intent of the SAS Label to be the SDTM label, we find certain instances of this implementation to be cumbersome for the EDC implementation and raw outputs. One example includes the following from the Standard Forms ALS 7.0 release</p>	<p>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”.</p> <p>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.</p>	<p>Can change SAS labels for both Standard and Non Standard Forms.</p> <p>Field Name can be changed for the non standard forms.</p>

8	CTSU_SUBJECT _ENROLLMENT DS_DSSTDAT	Enrollment Date	The date the Participant is accepted into the study. The study site may also be notified of the treatment arm and Study Participant Identifier on this date.	Start Date of Disposition Event
9	CTSU_SUBJECT _ENROLLMENT DS_DSSTIM	Enrollment Time	The time (hh:mm:ss:rr) an individual agrees to take part in an activity.	Start Time of Disposition Event

LPO Status Updates

NCI/Group	Seed Study Status	Road blocks/Concerns
Alliance	Taking existing standard forms and seed study and comparing them with both ALS files. No building yet, waiting on higher level decisions to move forward	
Theradex	Comparing seed study forms and mapping those, built some of the forms in caDSR in draft and ran through a mock SDTM modeling spec	
NRG	Build first CDISC compliant study in Rave and doing a lessons learned and looking at the ALS files on how to move forward	
SWOG	13 Forms created that are CDASH compliant and have partial SDTM mapping with notes. Don't have enough to build first study but getting close	
ECOG-ACRIN	Identified seed study, put together existing forms and identified CDASH variables on the annotated CRF. Now putting them into Rave, 6 to 7 own standard forms into Rave and working with programmers at the same time	
CCTG	Have a global library of mock forms and working to make that CDISC compliant...working on an annotated CRF and applying that to a study but not started building	
COG	13 forms and looking through forms to identify which are 1 to 1 mapping, forward mapping and backwards mapping to see if any require CDASH domains and variables to questions. Have not started study build at this time.	

Next Steps

- Next Meeting is September 25th 2019, 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.

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.

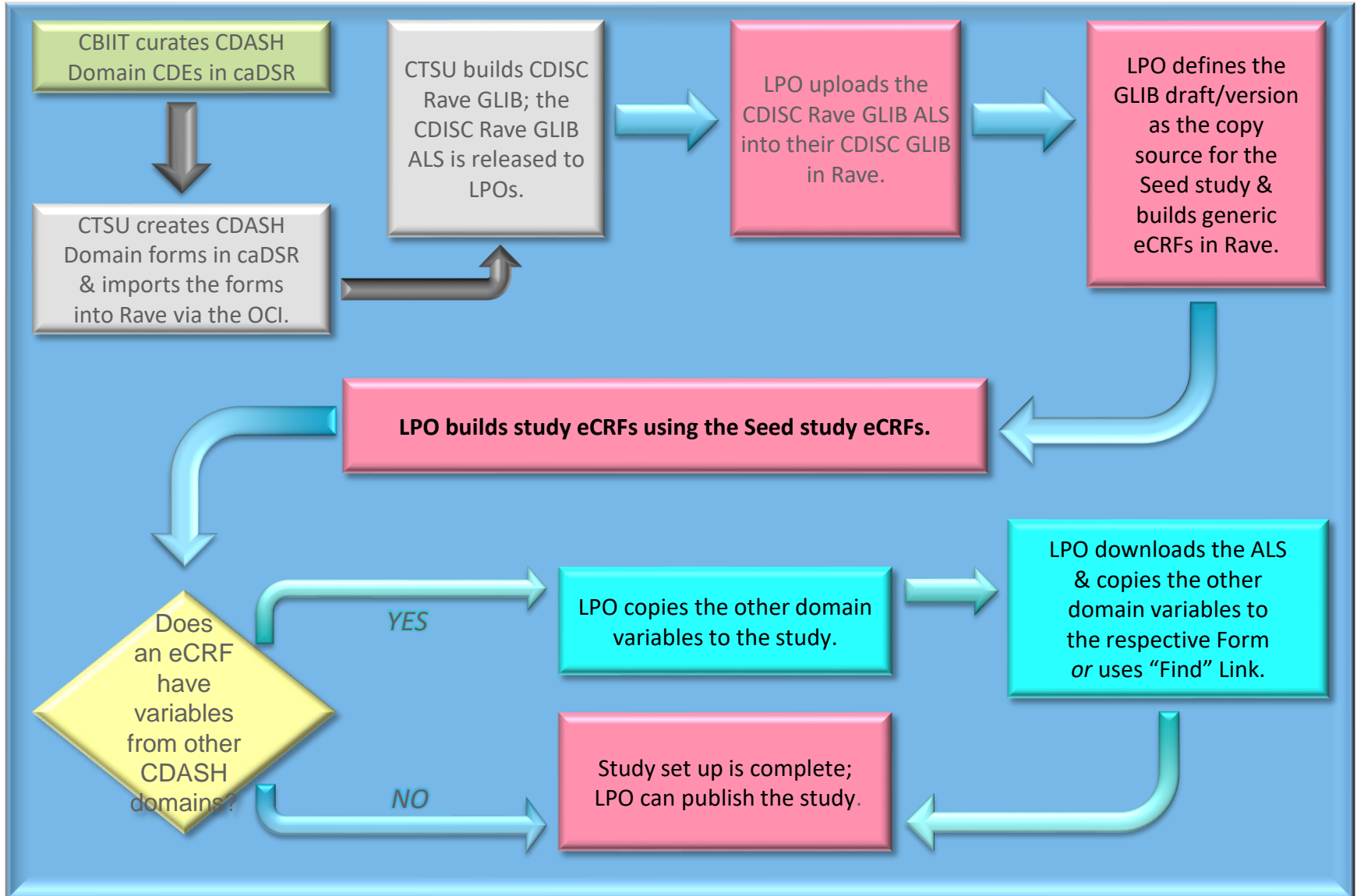
Rows 4-6 show the inclusion/exclusion criteria for version 2.2 of the protocol, which changed the minimum age entry from 21 to 18.

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 <i>(e.g., DEMOGRAPHICS)</i>	CDASH Domain Name <i>(e.g., DEMOGRAPHICS)</i>	<no change: same as caDSR>
Form OID	caDSR Form Long Name <i>(e.g., DEMOGRAPHICS)</i>	2 letter CDASH Domain Name <i>(e.g., DM)</i>	Update by CTSU
Variable OID	Short Name of the CDE <i>(e.g., RACE)</i>	CDASH/SDTM Variable Name <i>(e.g., RACE)</i>	<no change: same as caDSR>
Field Name	caDSR CDE Long Name + PID + MajorV + MinorV <i>(e.g., Race PID6343384_V1_0)</i>	Variable Label + PID + MajorV + MinorV <i>(e.g., Race PID6343384_V1_0)</i>	<no change: same as caDSR>
Field OID	2 letter domain prefix + CDASH/ SDTM variable <i>(e.g., RACE)</i>	2 letter domain prefix + CDASH/SDTM Variable Name <i>(e.g., RACE)</i>	<no change: same as caDSR>
Field Label	Question Text <i>(e.g., Which of the following five racial designations best describes you? (More than one choice is acceptable.))</i>	Question Text or Variable label <i>(e.g., Which of the following five racial designations best describes you? (More than one choice is acceptable.))</i>	Update by CTSU **Specify the Variable label for Field Labels without question text **
Data Dictionary Name	caDSR Value Domain Long Name + PID + MajorV <i>(e.g., CDISC_SDTM_RACE_PID6343345_V1_0F)</i>	caDSR Value Domain Long Name + PID + MajorV	<no change: same as caDSR>
Data Dictionary Values-User Data String	Permissible Value Meaning (PVM) <i>(e.g., Native Hawaiian or Other Pacific Islander)</i>	NCI preferred term <i>(e.g., Native Hawaiian or Other Pacific Islander)</i>	<no change: same as caDSR>
Data Dictionary Values-Coded Data String	Permissible Value (PV) <i>(e.g., NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER)</i>	Submission Value <i>(e.g., NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER)</i>	<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 <i>(may be either the max length of dictionary value or extendable value;; e.g., \$100)</i>	char <i>(may be either the max length of dictionary value or extendable value; e.g., \$100)</i>	<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	<i>(e.g., DropDownList)</i>	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

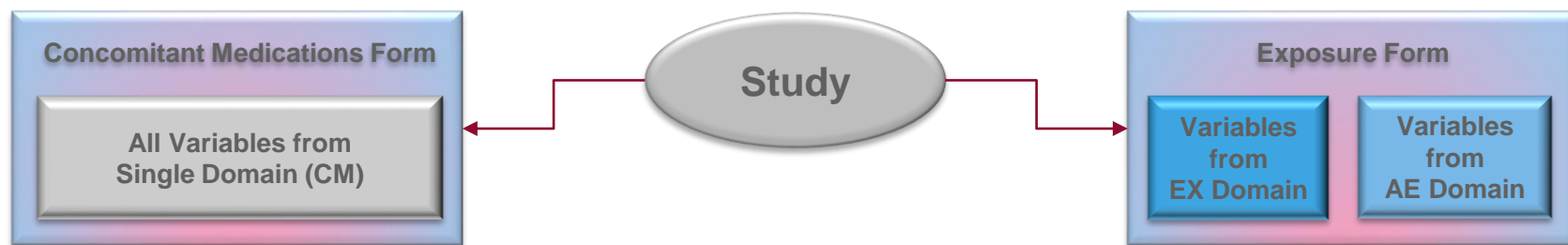
- Open the Exposure form; click add a new variable.
- Use the “**Find**” link on the variable definition screen to select the AE variable; click Apply to copy.

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)



Concomitant medication [OID=F.CM_2011-10-24]

General information
[OID=IG.CMYN_2011-10-24]

Any meds? NO [N] YES [Y]
[OID=CM_1_2011-10-24|CDASH=CMYN] [OID=CL.NY.SUB.Y.N_2011-10-24]

1st. Details
[OID=IG.CM_2011-10-24|Repeating]

Medication or Therapy
[OID=CM_3_2011-10-24|CDASH=CMTRT|CDASH/SDTM=CMTRT]

[999]

Taken Prior to Study? NO [N] YES [Y]
[OID=CM_19_2011-10-24|CDASH=CMPRIOR] [OID=CL.NY.SUB.Y.N_2011-10-24]

Start Date _____ dd-mmm-yyyy
[OID=CM_17_2011-10-24|CDASH=CMSTDAT]

Ongoing NO [N] YES [Y]
[OID=CM_23_2011-10-24|CDASH=CMONGO] [OID=CL.NY.SUB.Y.N_2011-10-24]

End Date _____ dd-mmm-yyyy
[OID=CM_21_2011-10-24|CDASH=CMENDAT]

Exposure Form

EXSTDAT Start Date (dd- MMM- yyyy) _____

EXSTTIM Actual Start Time _____

EXENTIM Actual End Time _____

EXIVINTR Was the infusion temporarily interrupted for more than 10 minutes at a time? Yes No

EXINTTIM Actual Time of Interruption _____

Was the planned dose administered? Yes No

EXPOCCUR _____

EXVAMT If 'No,' specify the total amount administered (mL) _____

AEDSL If 'No' due to AE, select corresponding AE log line number, start date, and term _____

AESPID AE log line number _____

LPO Impact Analysis: Beta Release GLIB (1)

#	Document	LPO Findings/ Recommendations/ Questions	Decision
1	GLIB ALS	<p>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</p> <p>With the final release in July, will the GLIB and other ALS files be updated using the newest CDASH and SDTM controlled terminology packages?</p>	<p>CTSU will do an impact analysis (for CT Packages released by CDISC before July 2019) to understand the potential impact to our timeline.</p> <p>The intent is to provide documents as current as possible to CDISC releases/ updates; this must be done in consideration of the implementation timelines.</p>
2	GLIB Release Notes: Section 3.2 Standard Conventions – Table 6	<p>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.</p>	<p>05/02/2019 CDISC Integration FG:</p> <ul style="list-style-type: none"> 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. <p>“Standard Forms” applies to the CTSU Standard Forms ALS, “Non-Standard Forms applies to variables not specified in the CTSU Standard Forms ALS.</p>
3	GLIB Release Notes: Section 3.2 Standard Conventions – Table 7	<p>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)</p>	<p>Maintain the same SAS label as in the CDISC GLIB for consistency across LPOs.</p>
4	GLIB ALS	<p>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?</p>	<p>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”.</p> <p>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.</p>

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.	<p>LPOs can decide to use the NCI Preferred Term or the CDISC Synonym for the User Data String in Rave.</p> <p>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.</p> <p>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.</p>
6	GLIB ALS	<p>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.</p> <p>i. Rave does not allow us to subset the dictionary choices at the field level – a separate dictionary must be created</p> <p>ii. Example: NY. Sometimes Unknown or Not Applicable are not valid responses for a question</p> <p>iii. The Alliance would be open to a standard naming convention in this situation.</p>	<p>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.</p> <p>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.</p> <p>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.</p>
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	<p>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</p> <p>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?)</p>	<p>All CTEP IND studies activated on/after 1/1/2020 must be CDISC compliant.</p> <p>CDISC Compliance is highly recommended for studies that activate prior to the 2020 date.</p> <p>The CDISC SME to provide additional feedback at the "Overview of FDA Submission Process" Webinar on May 22nd, 2019.</p>
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	<p>Throughout the entire document, please be specific what CDISC compliant means. CDASH, SDTM, ADaM, etc.</p> <p>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.</p>	<p>The FDA requirement is SDTM. the NCI requirement is CDASH.</p> <p>CDASH compliance makes SDTM compliance easier to achieve.</p> <p>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.</p>



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