

DIA 11234: CDER Data Standards Common Issues Document webinar questions

	Topic	Questions	CDER	CBER
1	ADaM Define File	<p>Q: What is the preferred data definition format for ADaM analysis data, define.xml or define.pdf?</p> <p>Q: The CRTDDS does not describe how to submit a define.xml for ADaM. Does CDER expect define.xml for ADaM?</p> <p>Q: Can you please clarify if define.xml is expected in addition to define.pdf for analysis. It was not clear from Dr. Cooper's response because he referenced define.pdf.</p> <p>Q: We are still not clear. What is the preferred data definition format for ADaM analysis data, define.xml or define.pdf?</p> <p>Q: Is define.xml required for ADs?</p> <p>Q: We are still not clear. Is it acceptable to submit define.pdf only for ADaM analysis data submissions? Define.xml for ADaM is incomplete.</p> <p>Q: At this point, if a sponsor plans to submit CDISC ADaM ARFs, does CBER expect the metadata in define.xml format or is a define.pdf acceptable for now?</p> <p>Q: Getting back to the question re define.xml and ADaM: Is there guidance available regarding define.xml that is geared specifically to its creation in the context of ADaM as opposed to SDTM?</p> <p>Q: The CRT-DDS defines preparation of define.xml for</p>	<p>The preferred format for the ADaM datasets is define.pdf until such time that CDISC publishes an update to the CRTDDS for ADaM</p> <p>At this time there is no guidance regarding the define.xml and ADaM.</p> <p>Until such time that the definitions are published submit a define.pdf</p> <p>CDER would like sponsors to submit both define.pdf and define.xml for SDTM datasets. The purpose of define.pdf is to provide reviewers an easily printable version of the define.xml.</p> <p>During the transition to define.xml, CDER would prefer both define.pdf and define.xml submitted. The define.pdf does not need to have bookmarks. The primary purpose of this pdf file is to support easy printing of define.xml. When the CRTDDS is updated to allow for easy printing of</p>	<p>The preferred format for the ADaM datasets is define.pdf until such time that CDISC publishes an update to the CRTDDS for ADaM</p> <p>At this time there is no guidance regarding the define.xml and ADaM.</p> <p>Until such time that the definitions are published submit a define.pdf</p> <p>The define.pdf should not be submitted for SDTM datasets, a define.xml is required for SDTM submissions to CBER.</p> <p>CBER prefers only the define.xml be submitted for SDTM and ADaM datasets. The define.pdf is not required unless requested by the Review Office. The define.pdf does not need to have bookmarks. The primary purpose of this pdf file is to support printing of the define.xml.</p>

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		<p>SDTM data only. Some of the “columns” such as Role, are not applicable to ADaM data. Until guidance for define.xml preparation for ADaM data is published, should sponsors just use the define.xml specifications for SDTM and leave non-applicable sections missing? Q:Should the specifications for define.pdf in the “Study Data Specifications”, which are specified for analysis data only, be followed for SDTM data as well (e.g. use “num” and “char” for type instead of “text”, “float”, “integer”, etc. as used for define.xml)?</p> <p>Q:“CDER prefers that sponsors submit both the Define.pdf and define.xml formats”. Does this statement pertain to analysis datasets as well – should define.xml be submitted for analysis datasets too?</p>	define.xml, the define.pdf will no longer be required.	
2	ADaM Data	Q: Are there any recommendations for how much data (e.g. raw data) to include into ADaM datasets in order to facilitate an efficient/comprehensive review? My sense is that FDA reviewers may not have all that is needed in ADaM datasets and may have to "merge in" SDTM data	This is a decision that must be made based on collaboration with the review divisions. Contact the review office prior to preparing your submission to ensure all expected data is included in the analysis datasets.	This is a decision that must be made based on collaboration with the review office. Contact the review office prior to preparing your submission to ensure all expected data is included in the analysis datasets.
3	ADaM ADSL	Q: For sponsors who are not yet following the ADaM standard, is the expectation that ADSL is required now along with the SDTM and other analysis data sets.	For submissions that include SDTM datasets an ADSL file is expected.	For submissions that include SDTM datasets an ADSL file is expected.

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4	ADaM vs. SDTM Treatment Emergent Flag	<p>Q: Currently treatment-emergent is determined in SDTM. However, sometimes there is information in data that could be important to determine whether or not an AE is treatment-emergent (for example, partial dates are derived in ADaM). Could treatment-emergent flag be determined in ADaM?</p> <p>Q: Document talks about a treatment-emergent flag in SDTM AE dataset -- but this is really a derived value more appropriate for ADaM/analysis datasets. Shouldn't use of this flag be done on analysis datasets rather than SDTM?</p>	<p>Please refer to amendment 1 for SDTM to learn more about the inclusion in AE of a treatment or exposure related variable.</p>	
5	SDTM and Legacy Data	<p>Q: I would like to hear more about the FDA's view of legacy conversions</p> <p>Q: If we have some studies which are completed and CSR written, do you still expecting them to be CDISC converted as part of the submission?</p> <p>Q: On page 4 FDA warn that converting legacy data to SDTM is problematic. Are FDA advising against this approach?</p> <p>Q: can we submit legacy data used for CSR under Data Listings and then SDTM under tabulations (SDTM being used for integrated analyses)?</p> <p>Q: Can you clarify if legacy data should not be converted if the analysis was done from the raw data?</p>	<p>CDER is not expecting studies to be converted after they are completed; this is the discretion of the sponsor. CDER does prefer SDTM and ADaM and expects that new studies will be collected using CDISC standards. It is critical that there is traceability from source documents (CRF) to tabulation datasets (SDTM) to analysis datasets (ADaM) to actual analysis result presented in the CSR's. If performing a data conversion results in disruption of traceability then this is potentially problematic.</p> <p>CDER does not advise against</p>	<p>CBER is not expecting studies to be converted after they are completed; this is the discretion of the sponsor. CBER does prefer SDTM and ADaM and expects that new studies will be collected using CDISC standards. It is critical that there is traceability from source documents (CRF) to tabulation datasets (SDTM) to analysis datasets (ADaM) to actual analysis result presented in the CSR's. If performing a data conversion results in disruption of traceability then this is potentially problematic.</p>

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			<p>converting legacy datasets. However, the traceability described above must be maintained. The converted SDTM data must be able to support the analysis datasets and analyses contained in CSR's.</p> <p>In general CDER does not recommend this; however, in some circumstances this may be reasonable. For example in a situation where legacy datasets are in different formats such that integration requires conversion to a single common format.</p> <p>CDER reviewers must be able to recreate the analysis datasets and analyses in the CSR.</p>	<p>CBER does not advise against converting legacy datasets. However, the traceability described above must be maintained. The converted SDTM data must be able to support the analysis datasets and analyses contained in CSR's.</p> <p>It is not acceptable to submit both legacy data and SDTM data unless this approach is agreed upon with the Review Office as a mechanism to deal with a specific integration issue. There is no way for the Center to ensure that both versions of the datasets contain the same information, this is a quality issue.</p> <p>CBER reviewers must be able to recreate the analysis in the CSR and the analysis datasets.</p>

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6	SDTM - SUPPQUAL	Q: I also would like to hear more about what this statement means in the common issues doc: "SUPPQUAL datasets are often used as a "waste basket"	Submissions to CDER often include very large SUPPQUAL datasets that contain information that is not relevant to the review process. In other instances these datasets include data that belong to another domain or possibly in a custom domain.	SUPPQUAL is used to house data that belongs in other domains/variables or to house data such as initials which have no value in the regulatory review. For any domain that is published there is a list of appropriate variables that can go in a Findings, Event or Intervention domain. Any variable from the appropriate list can be added to the parent domain. Rather than doing this Sponsors create SUPPQUAL domains. Before creating SUPPQUAL's sponsors should have a discussion with the review office to ensure that the dataset is being created according to the rules of the standard and the needs of the review.

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7	SDTM Version (Amendment) – when to start using	<p>Q: when will the amendment to SDTM 3.1.2 be finalized? As we are using SDTM to create ADaM we cannot modify SDTM once we have created ADaM. What is the expectation once a sponsor has started using a version of SDTM in analysis?</p> <p>Q: Your recommendation to add a TESS variable to the AE domain is inconsistent with the SDTM IG 3.1.2. Wouldn't it be better to add new content in the next release of the IG?</p> <p>Q: How quickly will FDA start to accept the data generated according to the new version of the SDTM IG, like the 3.1.2 amendment? We would like know when we should start to program after a new version has been released.</p> <p>Q: when will the amendment to SDTM 3.1.2 be finalized? As we are using SDTM to create ADaM we cannot modify SDTM once we have created ADaM. What is the expectation once a sponsor has started using a version of SDTM in analysis?</p> <p>Q: It would be interesting to hear at what point we need to address 3.1.2 amendment especially if another version has already been started for a study</p>	<p>CDER does not expect sponsors to update the SDTM versions this late in the process.</p> <p>The inclusion of the EPOCH variable is fine for now. CDER is interested in exploring ways of including Trial element information in different domains.</p> <p>The acceptance data for any new releases of SDTM, ADaM and SEND will be published on the data standards webpage</p> <p>When an amendment is finalized it is published as final by CDISC. To implement Domains and changes that are in draft contact edata@fda.hhs.gov for guidance.</p> <p>Once a version is started for a study that is the version that should be followed. CDER does not expect Sponsors to up version their data when new there are new updates to the CDISC standards.</p>	<p>The acceptance data for any new releases of SDTM, ADaM and SEND will be published on the data standards webpage.</p> <p>When an amendment is finalized it is published as final by CDISC. To implement Domains and changes that are in draft contact CBER.CDISC@fda.hhs.gov for guidance.</p> <p>Once a version is started for a study that is the version that should be followed. CBER does not expect Sponsors to up version their data when new there are new updates to the CDISC standards.</p>

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8	SDTM and Integrated Summaries	<p>Q: Page 6, DM domain. "Integrated summaries may contain more than one record per unique subject in the case that an individual enrolled in more than one study."</p> <p>Q: Is the agency expecting consolidated SDTMs for Integrated summaries?</p> <p>Q: The common issues document assumes that sponsor and reviewers have an open channel of communication. By EOP2 meetings many phase II's are completed and a reviewer may not be assigned. If sponsors get detailed requests at EOP2 or just prior to filing, are we expected to redo the previous study datasets and CSRs? Or can phase III's and ISS be different?</p>	<p>If the data is collected or submitted in SDTM then the integrated summaries should utilize SDTM. Again, traceability of the tabulations, integrated studies, analysis datasets and the Clinical Study Reports it absolutely required.</p> <p>For CDER a phase in is acceptable and we do not expect Sponsors to redo previous studies.</p>	<p>If the data is collected or submitted in SDTM then the integrated summaries should utilize SDTM. Again, traceability of the tabulations, integrated studies, analysis datasets and the Clinical Study Reports it absolutely required.</p> <p>For CBER a phase in is acceptable and we do not expect Sponsors to redo previous studies.</p>
9	SDTM RFSTDTC and Study Day Variables	<p>Q: Page 8: Required vs. Expected vs. Permissible, 3rd bullet, "--DY and --SDTY variables..." Q: bullet says "...--STDY should be calculated based on first treatment date." Is the agency saying that DM.RFSTDTC should always be first treatment date?</p> <p>Q: In Amendment 1 of the SDTMIG, it is confirmed that RFSTDTC is used to calculate study day variables and it acknowledges that this date is not necessarily the date of first treatment. However, page 9 of this document specifies that " --STDY should be calculated based on the first treatment date". Will Amendment 1 of the SDTMIG be revised to require that RFSTDTC must be the first treatment date?</p>	<p>This is a general recommendation. CDER recognizes that there may be instances where a different derivation DM.RFSTDTC may be reasonable based on study design.</p>	<p>No comment</p>

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10	SDTM EX Implementation for Oncology	<p>Q: In oncology drugs many are dosed by cycle, how have sponsors separated the dose per visit from dose per cycle? The SDTM only has one domain- EX for dose administration?</p> <p>Note from CDISC: Please review the Oncology domains when they are published for Public Review for examples and more information. Also reference SDTMIG Section 7.2.3.4 for Trial Design examples of dosing by cycle.</p>	No comment	CBER has not received any submissions for oncology treatments.
11	Harmonized Guidance / Requirements	<p>Q: CDER and CBER continue to publish separate guidance with regard to SDTM and ADaM submissions. For companies, such as ours, that submit to both, these separate rules add to the confusion as to what is recommended by which entity.</p> <p>Q: Would it be possible for CDER to coordinate with Amy Malla of CBER to harmonize what is requested of sponsors?</p>	CBER and CDER continue to try to harmonize their processes and guidance's as much as possible. Due to differences in Organizational Structure, internal business processes and products this is not always feasible.	CBER and CDER continue to try to harmonize their processes and guidance's as much as possible. Due to differences in Organizational Structure, internal business processes and products this is not always feasible.
12	CDISC Project Management	Q: where can we find the list of therapeutic area standards FDA/CDISC are or plan to work on?	Link to Therapeutic Area List	Does not apply to CBER
13	ADaM (?) Executable Programs	Q: Some reviewers are requesting executable programs. The Common Issues document does not suggest that programs should or need to be executable. Where does the FDA stand on executable programs?	This should be determined in discussion with the review divisions.	CBER does not expect executable programs, text files are acceptable. In the event there is such a request the Sponsor should ask for a meeting with the Statistical Team lead to discuss the issue.

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14	SDTM – CDER’s request for additional Timing Variables	<p>Q: “Please include the variables EPOCH, ELEMENT, and ETCD (element code) for every subject-level observation (e.g., adverse events, laboratory, concomitant medications, exposure, vital signs)”</p> <ul style="list-style-type: none"> • What information is FDA hoping to gain from this request? • It will be very time consuming to do this on every dataset, is it possible to limit this request to a few key SDTM datasets? • Clear guidance would be needed on handling imputation of partial dates <p>Q: EPOCH in the SDTM datasets could be different from the analysis EPOCH does the FDA expect these to be in alignment?</p> <p>Q: For Dr. Cooper: But, epoch variables are not ADaM variables. Does CDISC intend to include them as AD variable to enhance analysis of events with element, etc?</p> <p>Q: The document instructs to “Please include the variables EPOCH, ELEMENT and ETCD”. ELEMENT and ETCD are not allowable in general observation class domains as per SDTM. Until this is added to Amendment 1 of the SDTMIG, should sponsors add these variables in the supplemental qualifier datasets for each domain?</p>	<p>The inclusion of the EPOCH variable is fine for now. CDER is interested in exploring ways of including Trial element information in different domains.</p> <p>CDER does not expect this to be in alignment. The EPOCH variables in the SDTM variables are determined by trial design.</p> <p>The inclusion of the EPOCH variable is fine for now. CDER is interested in exploring ways of including Trial element information in different domains.</p>	No comment

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15	CDISC Team Involvement	<p>Q: How can sponsors get involved, participate and contribute to the Therapeutic area data standards development?</p> <p>Note from CDISC: see information about becoming involved with Technical Teams on our contact web page: http://www.cdisc.org/contact/</p>	No comment	No comment
16	SDTM Custom Domains	<p>Q: Sponsors will create different custom domains for the same type of data. Is this a problem for the FDA?</p> <p>Q: If a key domain has no good parent domain, would you prefer we just send that in a non SDTM version (can we send you a mix of SDTM and non SDTM). Or make custom domains for these, which do you prefer?</p>	<p>This is why CDER is interested in the development of additional data standards to cover therapeutic areas and other types of data not addressed in the current standard.</p> <p>CDER expects sponsors to create a custom domain in accordance with the instruction in the SDTM IG.</p>	<p>CBER is continuing to monitor the custom domains to identify those domains that require engagement by CDISC for development and publication to enable standardization. Due to the nature of science we expect that there will always be a need for custom domains.</p> <p>Do not send a mix of SDTM and non-SDTM, the appropriate action is to create a custom domain.</p>
17	Submission Dataset File Size and Splitting Data sets	<p>Q: what is the size limit of SDTM/ADaM datasets</p> <p>Q: In the section on the LB Domain regarding datasets > 400 MB, the document states that “The size issue can be addressed by splitting the large LB dataset into smaller datasets according to LBCAT and LBSCAT. It would seem logical that the splitting pertains to other</p>	<p>Refer to the Study Data Standards Specification. There are a number of issues weighing into dataset size at this time and changes to the requirements are under discussion. An update to the</p>	<p>Refer to the Study Data Standards Specification. There are a number of issues weighing into dataset size at this time and changes to the requirements are under</p>

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		<p>domains besides LB as well. How should a findings dataset that exceeds 600 MB that has one –TEST be split since there will be no –CAT or –SCAT variables?</p> <p>Q: Having both the split and non-split data in the same submission will cause a load failure for WebSDM and presumably for OpenCDISC. Will the FDA remove the non-split datasets from the submission if they plan on loading into WebSDM?</p> <p>Q: Presently the CDISC metadata subteam plans to recommend that the define.xml supply metadata for each split dataset as a separate entity and to no include any metadata for the large non-split domain. Is this FDA’s preference?</p> <p>Q: Common issues document recommend splitting up big datasets and submitting both split and un-split, while Study Data Specification document recommends that big SDTM datasets should not be split, please clarify.</p> <p>Q: This same section on the LB Domain regarding datasets > 400 MB further states “Sponsors should submit these smaller {split} files in addition to the larger non-split standard LB domain file.”</p> <ul style="list-style-type: none"> • Having both the split and non-split in the same submission will cause a load failure for WebSDM and presumably for OpenCDISC. Will the FDA remove the non-split datasets from the submission if they plan on loading it into WebSDM? • Presently the CDSISC metadata subteam plans to 	<p>Data Standards Specification will be published when the changes to file size requirements are solidified.</p> <p>Yes, CDER will remove the non-split data when loading in WebSDM.</p> <p>CDER expects metadata to be included for every submitted dataset.</p> <p>CDER would prefer sponsors to follow the Common Issue document recommendation.</p>	<p>discussion. An update to the Data Standards Specification will be published when the changes to file size requirements are solidified.</p> <p>For CBER do NOT send both split and non-split datasets in your submission. CBER prefers that non-split data sets are submitted, when this is not possible split the datasets using __CAT and document in the reviewers guide and/or the define.xml</p> <p>CBER does not want both sets of data so the preference is the metadata for the submitted data is included in the define.xml</p> <p>This is duplicate to above</p>

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		recommend that the define.xml supply metadata for each split dataset as a separate entity and to not include any metadata for the large non-split domain. Is this the FDA's preference?		
18	SDTM --TESTCD/ --TEST Case	Q: Currently we submit test name values in UPPERCASE (e.g. SYSTOLIC) - we have heard this will change to Mixed case in future? Is this rumor true?	For all published controlled terminology, the case of the published terms should be used in a submission. Published CDISC --TEST values are in title case. Refer to SDTMIG V3.1.2 Section 4.1.2.4.	For all published controlled terminology, the case of the published terms should be used in a submission. Published CDISC --TEST values are in title case. Refer to SDTMIG V3.1.2 Section 4.1.2.4.
19	SDTM Data Quality	Q: As a CRO, we often get locked client data with problems (e.g. end date before start date). Is it a problem if our SDTM datasets reflect these inconsistencies in the source data?	This is expected and the inconsistencies should be documented in the SDTM Validation and Data Interpretation Report and/or the Reviewers Guide	This is expected and the inconsistencies should be documented in the SDTM Validation and Data Interpretation Report and/or the Reviewers Guide
20	SDTM Common Problems	Q: What are the most common issues with SDTM submission that you are finding ? Is there any website where we can find that information	CBER and CDER are working on a mechanism to publish these issues.	CBER and CDER are working on a mechanism to publish these issues.
21	SDTM – Facilitating Review Process	Q: To All: Is there any evidence that SDTM submissions are leading to earlier FDA decisions? Q: Can you comment on the time of review of SDTM vs. Legacy data?	No comment.	No comment

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22	SDTM Submission Process	Q: we've made 2 submissions to the FDA in SDTM format and got absolutely no response in how our data were received. Is it possible to get more response from the reviewers if the data we submitted were useful or not?	CDER is currently developing a process and format for communicating a CDER data assessment to sponsors shortly after a submission is received. This is not in production at this time, but is projected to be available mid to late 2012.	All CBER submissions are reviewed by Amy Malla and a copy of the validation report as well as issues that could impact the review are sent to the Sponsor
23	SDTM – USUBJID	Q: USUBJID requirement: Does FDA expect sponsors to identify subjects who participated in an early phase trial and then subsequently enrolled in a later phase trial? This is difficult due to privacy concerns.	"if the Sponsor knows" that the same person has been involved in more than one study for their compound, they must identify that person with a unique USUBJID across all of those studies.	"if the Sponsor knows" that the same person has been involved in more than one study for their compound, they must identify that person with a unique USUBJID across all of those studies.
24	FDA Mailbox - FAQ	Q: Can CDER and CBER share the Q&A resulting from questions posed to edata@fda.hhs.gov? Q: Can CDER and CBER share the Q&A from edata@fda.hhs.gov?? Q: Will the FAQ database be available to sponsors?	CDER receives questions at to edata@fda.hhs.gov CBER and CDER are working on identifying mechanisms to share lessons learned, Q&A to support the submission of CDISC Formatted submission.	CBER receives questions at CBER.CDISC@fda.hhs.gov. CBER and CDER are working on identifying mechanisms to share lessons learned, Q&A to support the submission of CDISC Formatted submission.

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25	SEND	<p>Q: If a CDISC SDTM complaint submission is planned by a sponsor, is it expected that any pre-clinical data be compliant with the CDISC SEND model?</p> <p>Q: Is there an expectation that in future FDA will "expect" non-clinical data to be submitted using the SEND standard routinely? That is currently in pilot by FDA</p>	The CDER pilot for submission of SEND data is completed. CDER now strongly encourages sponsors to submit electronic pre-clinical data following the SEND format.	CBER is not accepting SEND at this time but are looking for voluntary pilot participants to test the standard for biologic products. A Federal Register request for pilot participants will be published in Q2/2012
26	Access to Reviewer Training	Q: Is there an opportunity for sponsors to review the FDA Reviewer - Data Standards Training to help the sponsors understand the possible review methods of the submission data to help streamline the review?	CDER is exploring this as an option.	CBER Reviewers were trained by CDISC using the standard CDISC SDTM and ADaM training.
27	SDTM – MedDRA versions	Q: are there any requirements for what version of MedDRA a submission should be in other than all integratable data use the same version?	<p>CDER and CBER currently accept MedDRA versions 8.0 through the current version.</p> <p>For integrated AE datasets, the version be harmonized.</p>	<p>CDER and CBER currently accept MedDRA versions 8.0 through the current version.</p> <p>For integrated AE datasets, the version be harmonized.</p>
28	SDTM Amendment and Validation	Q: treatment emergence is indicated as needing to be included in AE domain but this variable is not in SDTM - how do you think this is to be implemented? If we add it to AE it will error out in OpenCDISC	Amendment 1 has been finalized and includes a "treatment-associated" variable. Data standards development is a never-ending iterative activity. Conformance checking tools like OpenCDISC will have to evolve to include newly developed standards as they become finalized.	Amendment 1 has been finalized and includes a "treatment-associated" variable. Data standards development is a never-ending iterative activity. Conformance checking tools like OpenCDISC will have to evolve to include newly developed standards as they become finalized.

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29	SDTM Controlled Terminology	Q: Is it a mandate to submit the data as per the Control terms listed by SDTM for all set of variables that are non-extensible in nature? Or can sponsor submit their specific choices for all such variables?	The controlled terminology specified by SDTM represents an important part of the standard and should be followed. If a non-extensible codelist does not adequately represent the data needs, then please contact the agency for discussion and include edata@fda.hhs.gov so that future development needs are accounted for.	It is a requirement to use controlled terminology and standard dictionaries such as MedDRA whenever possible. Sponsors cannot extend non-extensible codelists. In the event that the data was not collected utilizing CDISC controlled terminology and was converted to SDTM the non-extensible codes must be documented and explained in the SDTM Validation and Interpretation Document as they will result in validation rule failures.
30	SDTM / ADaM and non-CRF data	Q: If we submit data from DMC/ISMB meetings and decisions do they need to be SDTM/ADaM ?	Data that is contained in SDTM/ADaM that results from a determination by DMC/ISMB, must be properly identified as such and not serve as a replacement for the originally collected data in the CRF. If such data is used for specific key analyses, then it should be available in ADaM and possibly SDTM, if the study protocol specified DMC/ISMB assessments as part of the study design.	No comment

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31	SDTM Define file	Q: if SDTM and ADaM datasets are submitted together should there be only one define.xml for both datasets?	SDTM and ADaM data sets are to be located in different folder directories, each with its own define file.	SDTM and ADaM data sets are to be located in different folder directories, each with its own define file.
32	Company Standards vs. SDTM	Q: For Chuck Cooper: For our submission our intent is to provide company standard datasets with the analysis based on company standard datasets. Should we also send SDTM datasets for the purpose of the reviewers. Is this common practice/useful?	Traceability from analyses in the CSR to the analysis data sets to the SDTM data sets to the CRFs is important for reviewers. It is strongly discouraged to submit SDTM data sets that do not match up with the analysis datasets and CSR analyses.	No comment
33	Controlled Terminology in Legacy Data Conversion	Q: How to handle controlled terminology during legacy data conversion...extensible and non extensible CT?	Converted data sets that do not contain controlled terminology will be considered as "quasi-CDISC" data.	It is a requirement to use controlled terminology and standard dictionaries such as MedDRA whenever possible. Sponsors cannot extend non-extensible codelists. In the event that the data was not collected utilizing CDISC controlled terminology and was converted to SDTM the non-extensible codes must be documented and explained in the SDTM Validation and Interpretation Document as they will result in validation rule failures.

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DIA 11234: CDER Data Standards Common Issues Document webinar questions

	Topic	Questions	CDER	CBER
34	Analysis Variables in SDTM	<p>Q: Does FDA expect that potentially highly derived analysis variables such as baseline flags and population flags be included in SDTM? Must values be consistent with study-specific analysis plans or can general definitions be used?</p> <p>Q: SDTM is the source for analysis datasets. Amendment 1 has requested some highly derived variables such as treatment-emergent AEs. This poses operational challenges. Does the FDA expect these derived variables be in alignment with the analysis datasets?</p>	<p>Amendment 1 specified a pre-defined treatment associated flag, which is not the same as a treatment-emergent flag and represents a simple derivation that has particular usefulness for reviewers.</p>	<p>Baseline flag is an acceptable variable in SDTM. Population flags should be in ADaM. Typically SDTM variables have general definitions and ADaM variables should follow study specific analysis plans.</p>
35	Oncology Data	<p>Q: Can you expand on your experience with Oncology data, specifically tumor assessment and response assessments?</p> <p>Q: Chuck, Where can we find this oncology list that you just mentioned?</p>	<p>The list of oncology-specific data standards is available upon request to the division and by submitting a request to the edata@fda.hhs.gov website. There are plans to post it on the CDER data standards website.</p>	<p>No comment</p>

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36	TESTCD/TEST and standard units	<p>Q: The document lists one of the “Common Errors” as “Inconsistent Value for Standard Units”.</p> <ul style="list-style-type: none"> Please note that this error is often not avoidable due to the fact that --TEST and --TESTCD cannot uniquely identify a record because, as per CDISC controlled terminology rules, method and specimen are not allowed to be included in --TEST/-TESTCD (problem = same test, but different method or specimen, so different standard units). 	No comment	The keys that are provided for the dataset in your Define file should include all the variables needed to make the --TESTCD/--TEST unique. If method and specimen type are part of that, they should be included as keys. If you pre-validate your data and see errors like this, you should explain them in your Reviewer’s Guide.
37	SDTM Validation (Web SDM)	<p>Q: are you still using WebSDM to validate data? Is it still a valuable tool to validate SDTM datasets?</p>	CDER is using OpenCDISC. However, WebSDM is used to aid in determining if the data is fit for loading into WebSDM for review purposes.	CBER is no longer using WebSDM for validation. We are utilizing OPENCDISC

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38	Sponsors Discussing Data Submissions with Review Division	<p>Q: CDER requests that sponsors discuss proposed solutions for representing data with them. Is CDER prepared to address questions for each trial at the time of study initiation?</p> <p>Q: “It is expected that significant discussion between the sponsor and CDER reviewers will be necessary to appropriately determine which analysis datasets and associated content are needed to support application review.” Is there a process established for this kind of discussion? Do reviewers across the agency have the capacity to engage in this?</p> <p>Q: The common issues document states that “Close adherence to ADaM Implementation Guide” is expected. This seems to contradict Study Data Specification which say that CDISC/ADaM standards for analysis datasets <i>may</i> be used if acceptable to the review division. Is it possible that FDA reviewer could inform sponsor that ADaM datasets will not be accepted?</p>	<p>CDER is prepared to discuss proposed solutions. Sponsors can contact edata@fda.hhs.gov to initiate those discussions.</p>	<p>CBER is prepared to discuss proposed solutions. Sponsors can contact CBER.CDISC@fda.hhs.gov to initiate those discussions.</p>

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39	CDER Common Standard Data Issues document	<p>Q: Why did you feel the need to create a Data Standards Plan when CDISC standards are already in place and the accepted model for data standards.</p> <p>Q: The common data standards issues document refers to the SDTM Amendment which is not yet released for production. However, the common data standards issues document implies it should be implemented right away. Will there be any clarifications in V1.1?</p> <p>Q: What is the role of the common issue document which is a live document and may have a new version quicker than SDTM IG, which one should we follow when there is a conflict between SDTM IG and the issue document?</p>	<p>The CDER Data Standards Plan is not a plan that aims to position CDER as a SDO (Standards Development Organization) or replace the function/purpose of SDOs. It merely serves to communicate, on a very high level, how CDER intends to adopt, implement, leverage, and aid in development of data standards to improve the review process. It is a first version and revisions are expected as the effort evolves.</p> <p>The issues in the CID represent requests/preferences from actual reviewers so that the data they receive is optimally useful. There is no desire to conflict with the SDTM IG, but instead inform a sponsor’s implementation such that it enables sponsors to deliver data that meets the reviewers needs. If there is a concern or question about a perceived conflict, please email us at edata@fda.hhs.gov</p>	<p>CBER is developing a Data Standards Plan for publication as well. It is an opportunity for each center to communicate their intentions and business practices with Industry.</p>

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40	SDTM data used for pooling	Q: For Dr. Cooper: How many of the SDTM submissions are used for pooling?	They are frequently used for pooling within a submission in order to perform integrated analyses of safety and efficacy – many of which are often exploratory in nature. It is too early to consider broader pooling activities given the lack of a data warehouse, the variability of submissions, absence of a mechanism – at this time.	No comment