

Clinical Study Data Reviewer's Guide Completion Guidelines

Version 1.4

Revision History

Version	Date	Summary
0.9	2013-02-22	Draft for public comment
1.0	2013-03-18	Updated based on public comments
1.1	2013-05-13	Changed blue headers in template and sample documents to black to conform to FDA's PDF specifications. No changes were made to this Completion Guidelines document.
1.2	2015-01-26	Changed header formats and dropped the TDM dataset navigation table in the template, updated instructions in this Completion Guidelines document, and updated the sample SDRG documents to reflect the changes to the template.
1.3	2018-11-01	<p>Updated to be in compliance with the TCG (March 2018) and to add completion guidelines for the Legacy Data Conversion Plan and Report Appendix.</p> <ul style="list-style-type: none">• Added 'Clinical' to the front page/header/section names and a 'c' before any occurrence of 'SDRG' in order to distinguish from the Nonclinical reviewer's guide.• Added completion guidelines for the Legacy Data Conversion Plan and Report Appendix.• Section 2 (cSDRG Overview) updated to include a sentence regarding the Legacy Data Conversion Plan and Report. Added verbiage that all sections are required. Removed verbiage that discusses section numbering in regards to optional sections.• Template Completion Instructions:

Version	Date	Summary
		<ul style="list-style-type: none"> ○ Section 1.1 – Added guidance for the Legacy Data Conversion Plan & Report Appendix. ○ Section 1.2 – Added standard acronyms. ○ Section 1.3 – Added guidance to be in alignment with the TCG (Sections 6.1.3 and 6.2) regarding deviations from controlled terminology. ○ Section 2.2 - Added guidance when the protocol design is not documented. This is done to ensure the sections are not renumbered and are aligned with the template. ○ Section 3.1 – Added guidance for including the Legacy Data Conversion Plan and Report Appendix. Also added a question regarding adjudication data to be in alignment with the TCG (Section 4.1.1.2). ○ Section 3.2 – This is a new section that shows the traceability of the SDTM data in a diagram. Section 8.3.1 of the TCG discusses Study Data Traceability. Included an example. ○ Section 3.3 – Added verbiage and table for data that were not submitted (Section 4.1.4.6 of the TCG). ○ Section 3.4 – Added guidance to include custom datasets and derivations from controlled terminology to be in alignment with the TCG (Sections 4.1.1.3, 6.1.3, 6.2). Also, added a column in the table for custom datasets and included one in the example. Deleted the Observation Class column in the table and any references to this information (information was shared that this is not meaningful to a reviewer). ○ Section 3.4.x – Added guidance to document the implementation approach for creating a custom domain to be in alignment with the TCG (Section 4.1.1.3). Added guidance to be in alignment with the TCG (Sections 6.1.3 and 6.2) regarding deviations from controlled terminology. Additional information to be included are a description of primary safety and efficacy variables. ○ Section 4.1 – Replaced “OpenCDISC” to be more generic. Also replaced “OpenCDISC” with Pinnacle 21 verbiage in the example. ○ Section 4.2 – Replaced “OpenCDISC” to be more generic. Also replaced “OpenCDISC” with Pinnacle 21 when instructing to document any software other than Pinnacle 21. ○ Section 4.3 - Added guidance when there are no additional conformance details. This is done to ensure the sections are not renumbered and are aligned with the template. ○ Appendix II – Replaced “OpenCDISC” with “Pinnacle 21 Community or Enterprise”.
1.4	2019-07-10	<ul style="list-style-type: none"> ● Replaced “clinical-study-data-reviewers-guide.pdf” with “csdrg.pdf” and “blankcrf.pdf” with “acrf.pdf” to be in alignment with the Technical Conformance Guide.

Version	Date	Summary
		<ul style="list-style-type: none">Updated text for Section 4.2 of the template to be consistent with the ADRG Completion Guidelines.

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Clinical Study Data Reviewer's Guide Completion Guidelines

Overview

1. Clinical Study Data Reviewer's Guide Purpose

The Clinical Study Data Reviewer's Guide (cSDRG) provides FDA Reviewers with additional context for SDTM datasets received as part of a regulatory submission. The cSDRG is intended to describe SDTM data submitted for an individual study in the Module 5 clinical section of the eCTD. The cSDRG purposefully duplicates information found in other submission documentation (e.g. the protocol, clinical study report, define.xml, etc.) in order to provide FDA Reviewers with a single point of orientation to the SDTM datasets.

2. cSDRG Overview

The cSDRG has four main sections and two optional appendices - Introduction, Protocol Description, Subject Data Descriptions, Data Conformance Summary, Appendix I: Inclusion/Exclusion Criteria, and Appendix II: Conformance Issues Details. There is a separate appendix to document the conversion of legacy tabulation data to SDTM (Legacy Data Conversion Plan and Report Appendix. The Introduction provides an overview and inventory of standards used on the study. The Protocol Description provides a brief orientation to the study and, if necessary, provides additional context about the Trial Design Datasets. The Subject Data Descriptions section provides additional context for subject-level SDTM domains that are not adequately documented in define.xml or the SDTM Implementation Guide and its supplements. Additionally, the Subject Data Descriptions section describes sponsor-specific annotated CRF conventions as needed. The Data Conformance Summary documents the validation inputs used to evaluate SDTM conformance and summarizes conformance findings.

If the inclusion/exclusion criteria cannot be fully documented in the Trial Inclusion/Exclusion Criteria (TI) dataset due to SAS v5 limitations, the criteria can either be provided in Appendix I, or as a hyperlink to the full criteria in an annotated CRF. All significant conformance findings should be documented in the Data Conformance Summary; however, a detailed record-level description of conformance issues may be included in Appendix II. Sponsors are strongly discouraged from including Appendix II due to its limited usefulness for FDA Reviewers.

All sections are required in order to maintain the cSDRG is following the template sections. When necessary, it is acceptable to document no data is present for the section. ***Do not delete any sections.***

3. cSDRG Completion Guidelines Purpose

The purpose of this document is to provide sponsors with a clear, concise set of instructions that facilitates the consistent development of the cSDRG from the Clinical Study Data Reviewer's Guide Template. In addition to the cSDRG Completion Guideline, cSDRG examples are available as an additional reference.

4. Organization of This Document

This document has three sections: a Guidelines overview, cSDRG Template Completion Instructions, and cSDRG Finalization Instructions. The section number in the cSDRG

Template Completion Instructions corresponds directly to the cSDRG Template. Section headings in *italics* do not contain any content and serve to organize the cSDRG. These have been included in the instructions for completeness. The cSDRG Finalization Instructions describe how to create the document for submission after completing the cSDRG Template.

Clinical Study Data Reviewer's Guide Template Completion Instructions

This section provides companion instructions for the cSDRG Template. The section numbering corresponds directly to the cSDRG Template. Section headings in *italics* (e.g., *1. Introduction*) do not contain any content and are included for completeness. **Note: Certain cSDRG Sections include a series of questions intended to aid FDA Reviewers. Provide complete answers to all questions. Do not delete the primary questions from the final document. Sub-questions may be removed at the discretion of the sponsor.**

1. Introduction

1.1. Purpose

This section states the purpose of the cSDRG. The cSDRG Template includes standard text. Include the additional text if a Legacy Data Conversion Plan and Report Appendix is included.

1.2. Acronyms

This section documents any sponsor-specific or non-industry standard acronyms used in the cSDRG. Standard industry acronyms (e.g. MedDRA, LOINC, CDISC, SDTM, ADaM, etc.) do not need to be documented.

1.3. Study Data Standards and Dictionary Inventory

This section documents the SDTM version(s), controlled terminology version(s), and dictionary version(s) used in the study. Conformance inputs and version(s) are documented in Section 4. Document any custom Controlled Terminology terms that could apply to more than one domain (e.g. EPOCH). If custom terminology is specific to a domain, document that in Section 3.4.

Example:

	Version
SDTM	SDTM v1.2/SDTM IG v3.1.2 including Amendment 1. Oncology Domains, TU, TR, and RS, have been submitted according to the version released for public comment dated 30-Jan-2011
Controlled Terminology	CDISC Controlled Terminology dated 22-Jul-2011 has been used for all domains except for LB. LBTESTCD and LBTEST use terminology from the 29-Jun-2012 CDISC Controlled Terminology package. Added 'WASHOUT PERIOD 1' 'WASHOUT PERIOD 2' to EPOCH extensible codelist as the study design includes two washout periods.
Data Definitions	define.xml v1.0
Medications Dictionary	WHODrug December 2012

	Version
Medical Events Dictionary	MedDRA v14.1

End of Example

2. Protocol Description

2.1. Protocol Number and Title

This section provides the protocol number or identifier, title, and versions included in the submission. For protocol amendments, note changes that affected data collection or interpretation, if any.

2.2. Protocol Design

This section provides a visual representation or brief textual description of the protocol design. This can be taken directly from the protocol or developed specifically for the cSDRG.

If there is no information for this section, **do not delete it**. Add verbiage such as "There is no information to be documented."

2.3. Trial Design Datasets

This section provides additional context for the Trial Design datasets. Additional context may not be required for simple protocol designs that are adequately documented in define.xml or self-evident in the Trial Design Dataset content.

The following question must be answered:

- Are Trial Design datasets included in the submission?

If Trial Design datasets are not included, or if no additional explanations are called for, the rest of section 2.3 should be deleted.

Additional content may include, but is not limited to the following:

- If Trial Design Datasets were submitted, list the dataset name and dataset label only for datasets that benefit from additional explanation.
- Description of the modeling of Trial Arms, Trial Elements, and Trial Visits.
- If inclusion/exclusion criteria are not fully described in TI, complete Appendix I: Inclusion/Exclusion Criteria, or create a hyperlink to the pages in acrf.pdf that contain the full criteria text. (See Finalization Instructions at the end of this document for detailed instructions. Also note that an example hyperlink has been provided in the template from heading 2.3.4 TI – Trial Inclusion/Exclusion Criteria to Appendix I for inclusion/exclusion criteria not fully described in the TI dataset.)
- Method for identifying cross-over or open-label extension periods.
- Explanation of sponsor-defined Trial Summary parameters.

Note that the **dataset section headers are not automatically numbered** in the Trial Design Datasets section, so **check and correct the numbering** when you use this section.

Example:**2.3.1 TA – Trial Arms**

The primary analysis compares Drug A to Drug B; however, as depicted in Section 2.2, subjects may receive one of three different therapies after a response evaluation at Week 24. ARMCD uses the convention randomized treatment underscore post-Week 24 treatment (e.g. A_A, A_D, A_X, B_A, B_D, or B_X).

End of Example

3. Subject Data Description**3.1. Overview**

This section provides a summary orientation to the datasets containing subject data.

Answers to the following questions must be provided:

- Are the submitted data taken from an ongoing study?
- Were the SDTM datasets used as sources for the analysis datasets?
 - If there was a legacy tabulation data conversion, include the template text
- Do the submission datasets include screen failures?
- Were any domains planned, but not submitted because no data were collected?
- Are the submitted data a subset of collected data?
- Is adjudication data present?

Additional content may include, but is not limited to the following:

- Description of any study history or timing relevant to the submitted data (e.g. interim data cutoff, data differences due to protocol amendments, etc.).
- Location of key safety, efficacy, or other data of special interest.
- Explanation of the mapping of death information in the subject level datasets. Explain any differences in the occurrences (frequencies) of death across the datasets.
- Document the method used to differentiate adjudication data from data collected at the investigational site.
- Document any notable subjects of interest within the context of the study.

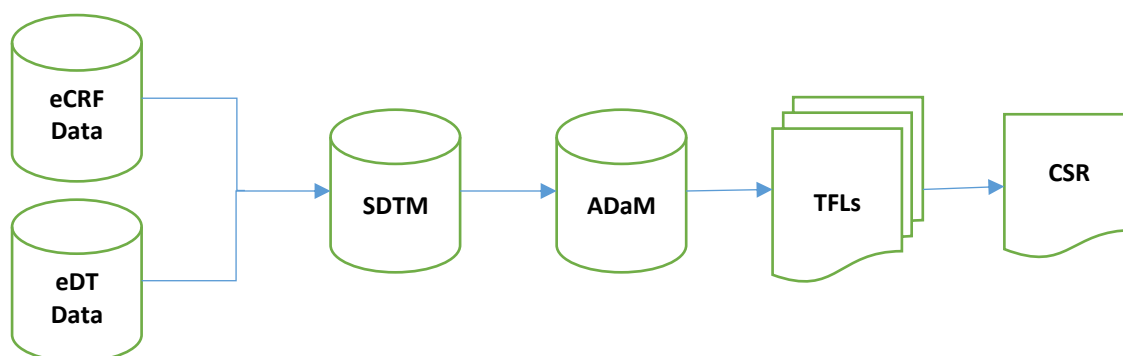
- Description of the reference start date including any differences in the definition across subjects and description of the calculation of study days. These should align with the definitions in define.xml.
- If you are documenting an extension study, include description(s) of any data that have been copied from or are located in another study in the submission.

3.2. Traceability Flow Diagram

This section provides a flow diagram showing the SDTM dataset creation and traceability. Identify the various sources of data used to create the SDTM datasets. Include any integrations.

If this is in the Legacy Data Conversion Plan and Report Appendix, indicate that this is located there. **Do not delete this section.**

Example:



End of Example

3.3. Annotated CRFs

This section describes the sponsor-specific annotated CRF conventions.

Additional text may include but is not limited to the following:

- Organization of bookmarks if different from what is specified in the SDTM Metadata Submission Guidelines v1.0, section 4.2 (by time points and CRF topics).
- Explanation of content organization when acrf.pdf includes multiple sources (e.g. primary CRF, secondary forms for PRO, format of central laboratory data, etc.).
- Description of the representation for amended or updated CRF (e.g. does acrf.pdf include all versions of amended CRFs or only the last version?).
- Description of notable annotation conventions.

A table is included to describe any data collection fields on the CRF that were not submitted and the reason why. If the table is not necessary, the table (not the section) can be deleted. The information in the table should be limited to clinical study data and should not contain CRF fields for operational purposes or is a trigger for other page(s). The information should be provided in a way that is helpful to a reviewer.

If there is no information for this section, **do not delete it**. Provide proper verbiage to document this situation.

3.4. SDTM Subject Domains

This section provides an overview of the subject-related SDTM domains. Provide hyperlinks to domains that merit additional explanation within the context of the study.

Prior to the table of domains, list any deviations from Controlled Terminology described in Section 1.3, if applicable, and not described in Section 1.3. Also, explain the reason for the deviation. This applies to extensible and non-extensible codelists within CDISC Controlled Terminology. It is understood that Pinnacle 21 will flag this. However, it does not explain the reason for the deviation.

- List all subject-related datasets included in the submission alphabetically by domain code.
 - Include a separate row for each split dataset and describe the method for splitting in the domain-specific section.
 - Include a row for each Findings About (FA or FA--) dataset.
 - Do not include a row for RELREC, as related records are indicated in a column and described in the associated domain-specific section.
 - Do not list SUPP-- datasets. The presence of a SUPP-- dataset is indicated in a column.
 - Include a separate row for each custom dataset.
 - Do not list Trial Design datasets. Do include SE and SV.
 - Provide a hyperlink from the Dataset – Dataset Label cell to the domain description below for any domain that requires additional explanation within the context of the study. Do not provide a hyperlink or domain description section for standard datasets that do not have supplemental qualifiers and do not need additional explanation.
- Specify the functional category or categories for each domain.
 - Include categories of Efficacy, Safety, and Other.
 - Category of Custom indicates the domain is not modeled in the SDTM IG.
 - Additional categories may be defined at the discretion of the sponsor.
- Indicate if a Supplemental Qualifiers dataset is submitted for the domain.
 - Include a Supplemental Qualifiers inventory table in the domain-specific section.

- If relationships between the domain and other domains have been described in RELREC, specify the related domains.
 - Explain a domain's key relationships to other domains in the domain-specific section. Provide the explanation of the relationship within the context of a one of the related domains. Do not create a separate section for RELREC.

- **Example:**

Dataset – Dataset Label	Efficacy	Safety	Other	Custom	SUPP-	Related Using RELREC
AE - Adverse Events		X			X	CM, DS
CE - Clinical Events	X					
CM - Concomitant Medications	X	X			X	AE, FA
CO - Comments			X			
DM - Demographics			X		X	
DS - Disposition			X			AE
EX - Exposure			X		X	
FA - Findings About	X	X				CM, MH
LB - Laboratory Test Results	X	X				
LB1 - Hematology		X				
LB2 - Chemistry		X				
LB3 - Biomarkers	X					
MH - Medical History					X	FA
...						
SE - Subject Elements			X			
SV - Subject Visits			X			
XL - Laboratory Test Results Conventional				X		
...						

End of Example

3.4.x Dataset – Dataset Label

Provide explanation beyond that which is documented in define.xml or the SDTM Implementation Guide and its supplements. This section is required for datasets for which hyperlinks have been provided in the Section 3.3 table. Provide a section number for each dataset requiring additional explanation (e.g. 3.3.1, 3.3.2, 3.3.3, etc.). This section describes the subject-related SDTM domains that benefit from additional description. **Note: to easily add another dataset, copy and paste an existing dataset heading and text prompt. The**

headings in this section are NOT automatically numbered, so be sure to verify and correct the numbering for the dataset descriptions.

Content should include the following, where applicable:

- Description of custom domains and the implementation approach or organization of content (e.g. Findings About [FA]) for which the content is very specific to the study. **All custom domains must have a description, including the General Observation Class.**
- A table of all Supplemental Qualifiers for a given domain. Include the explanation for inclusion in the Description column if this information is beneficial to a reviewer. Descriptions of relationships to other domains that are documented in RELREC.
- Description of criteria used to split datasets and the content of the split datasets.
- Descriptions of derivations that may benefit from additional detail beyond that included in define.xml.

Content may also include, but is not limited to the following:

- Description of notable, sponsor-defined uses of category and sub-category.
- Description of notable sponsor extensions to CDISC Controlled Terminology.
- Descriptions of notable mapping of legacy sponsor terminology to CDISC Controlled Terminology.
- Description of primary safety and efficacy endpoint variables.
- General validation issues resulting from data collection (e.g., missing start date for prior medications due to start date not being collected).
- Description of the representation of disposition information in the Disposition (DS) domain especially for submissions where the study is ongoing.
- Description of the representation of collected treatment administration data in the Exposure (EX) domain (e.g., describe what data were collected and what data were derived).
- If all protocol-specified medications (e.g. “companion” or “background” medications) are not in then Exposure (EX) domain, document the domain(s) that contain these medications and how to identify them.
- Any deviations from extensible and non-extensible codelists when Controlled Terminology is utilized.

Example:

3.4.1 AE – Adverse Events

A relationship has been defined in RELREC between the disposition event and the primary adverse event leading to discontinuation. The observations are related by AEGRPID and DSGRPID. A relationship has also been defined between the adverse events and

concomitant medications used to treat the AE. The observations are related by AEGRPID and CMGRPID. The MedDRA coding hierarchy is located in SUPPAE.

QNAM	Description
AELLT	MedDRA Lowest Level Term
AELLTCD	MedDRA Lowest Level Term Code
AEPTCD	MedDRA Preferred Term Code
AEHLT	MedDRA High Level Term
AEHLTCD	MedDRA High Level Term Code
AEHLGT	MedDRA High Level Group Term
AEHGLTCD	MedDRA High Level Group Term Code

End of Example

4. Data Conformance Summary

4.1. Conformance Inputs

This section describes the validation checks and inputs used to evaluate conformance.

Answers to the following questions must be provided:

- Was a validator used to evaluate conformance?
 - If yes, specify the version(s) of the validation rules (for example, Pinnacle 21 Enterprise 3.4 (FDA), SDTM 3.1.3).
 - If software other than Pinnacle 21 Community or Enterprise was used to assess compliance, describe under "Provide any additional compliance evaluation information."
- Were sponsor-defined validation rules used to evaluate conformance?
- Were the SDTM datasets evaluated in relation to define.xml?
- Was define.xml evaluated?
- Provide any additional compliance evaluation information.

4.2. Issues Summary

This required section summarizes compliance findings.

- Summarize findings from a SDTM conformance report (e.g., the validation report's Issues Summary tab or similar) in table form.
- Include additional information regarding conformance to FDA business rules and FDA validator rules if not addressed in the SDTM conformance report.
- List only those findings that appear in the submission.
- Do not include skipped validation checks or validation checks for which datasets do not exist.
- If your conformance diagnostics do not include severity, leave that column blank.
- If non-automated issues were detected, these should be explained as well.
- Explanations should be sufficiently detailed and data-specific (not generic or vague).

In addition, address any specific data quality issues that were not fixed (i.e. data issue discovered post-lock and sponsor decided not to unlock the database). Note what the data should be, why it was not fixed, and any impact assessment that was done.

Example:

Dataset	Diagnostic Message	Severity	Count	Explanation
LB	Missing Units on Value	Error	22	Not an error: Lab results for pH and Specific Gravity have no units

End of Example

4.3. Additional Conformance Details

This section documents summary findings from validation rules other than the ones previously reported, which in the sponsor's opinion merit explanation. Fill in the table in this section as you would the one in section 4.2. Leave columns blank where not applicable.

This section is not intended to contain the full validator details report. Sponsors are discouraged from submitting the full report, but if the sponsor considers it necessary, the full report may be submitted as cSDRG Appendix II.

If there are no additional conformance details to be documented, **do not delete the section**. Add verbiage such as "There are no additional details to be documented."

Appendix I: Inclusion/Exclusion Criteria

This optional Appendix provides the complete set of inclusion/exclusion criteria when they cannot be fully documented in the Trial Inclusion/Exclusion Criteria (TI) dataset. For example, if inclusion/exclusion criteria are too long to be fully described in the TI dataset, include the full text in Appendix I. This section is not necessary if a hyperlink is supplied (in section 2.3.x) to the full inclusion/exclusion criteria contained in an annotated CRF. If criteria are provided in this Appendix I, there is no need to include a separate document in the submission as described in the SDTM Metadata Submission Guideline v1.0, Section 5.1.3. We recommend that you provide a link from define.xml to the cSDRG.

Appendix II: Conformance Issues Details

A detailed record-level description of conformance issues (e.g., the Pinnacle 21 Community or Enterprise report Details tab or similar) may be included in this optional Appendix. Sponsors are strongly discouraged from including this appendix due to its limited utility for FDA Reviewers. All significant findings should be described in Sections 4.2 or 4.3.

Legacy Data Conversion Plan & Report Appendix

This optional section provides information about legacy tabulation data that was converted to SDTM. If there was no conversion, delete the appendix pages as they are not required.

Include this appendix when the SDTM data that are included in the submission were not the source data used to derive the tables, figures, and listings of the CSR. Some common variations are when CSR results were derived:

- Directly from data management system extracts and SDTM was produced later for the purpose of submission.
- From non-ADaM analysis data whose source was non-SDTM tabulations data.
- From a version of SDTM that is no longer supported by the FDA's Data Standards Catalog and therefore the data was up-versioned to a more current standard that is supported.

Note that in any of these circumstances, the submission of data should include both the original source data *and* the standardized data. The combination of original and standardized data, with the explanations contained in this appendix, will enable the reviewer to understand how results they derive from the standardized data equate to the results in the CSR.

1. Introduction

This section states the purpose of the Legacy Data Conversion Plan and Report Appendix. The cSDRG Template includes standard text.

2. Conversion Data Flow

This section will contain a diagram showing the flow of all study data from collection through analysis. This is a forward view of the data flow. See the Conversion Traceability Data Flows document for examples that are available for incorporation in this section.

Also, when appropriate explain the rationale for the data conversion.

3. Converted Data Summary

This section provides a summary of the legacy data that was converted to SDTM. Content may include, but is not limited to the following:

- Describe any changes in SDTM Controlled Terminology
- Describe the validator tool that was used on the converted data
- Describe any additional QC done on the data

3.1 Issues Encountered and Resolved

This section describes any issues encountered as a result of the conversion and the resolution of the issues.

Content may include, but is not limited to the following:

- MedDRA – describe any recoding that was required and the result
- WHODrug – describe any recoding that was required and the result
- Lab ranges – describe any discrepancies between the legacy data and the converted data
- Custom domains that are now standard domains as a result of the conversion
- Any changes in a domain or supplemental domain as a result of the conversion

4. Traceability Data Flow

This section will contain a diagram showing the traceability of all study data from collection through analysis. This is a forward and backwards view of the data. See the Conversion Traceability Data Flows document for examples that are available for incorporation in this section.

5. Outstanding Issues

This section will describe any other issues not previously documented and that would be helpful to a reviewer. If there are no outstanding issues, do not delete the section. Add verbiage such as “There are no outstanding issues to be documented.”

Content may include issues related to the CSR, but is not limited to the following:

- Changes in variable values in SAEs, deaths, and disposition
 - Examples: DM.RACE and DS.DSDECOD. Include the number of the value collected on the CRF and also what is in the SDTM domain
- Changes in treatment-emergent adverse events
- Legacy lab test names and units will match names in CSR listings but will not match the lab test names and units in the SDTM LB dataset

Clinical Study Data Reviewer's Guide Finalization Instructions

This section describes how to create the document for submission after completing the cSDRG Template.

1. Create hyperlinks from dataset names in section 3.3 to descriptions in 3.3.x

Select the text in the first column of Table 3.3 that needs a hyperlink. **Right click the selected text** and choose **"Hyperlink"** from the menu. In the left panel of the Hyperlink window, make sure that **"Place in this document"** is selected. Then, in the list of document places select the dataset name's header under SDTM Subject Domains (e.g. AE – Adverse Events) and click **OK**. Ctrl+click the hyperlink to test it.

2. Remove unused sections from the document.

Before converting the document to PDF format ensure all sections are in the document. If the appendixes (prior to the Legacy Data Conversion Plan and Report Appendix) were not used highlight the section heading, text prompt, and any trailing blank lines. Press the Delete key.

3. Update the Table of Contents, document header and version date

After all edits have been completed, update the table of contents at the top of the document. **Right click on any line in the table** and select **"Update Field."** In the dialog window, select **"update entire table,"** then click **OK**.

Do not edit the document header or footer. The study number in the header references the study number on the title page. When you edit the study number on the title page, the study number in the header is updated automatically. To update the version date on the title page and the PDF creation date in the document footer, **save and close the document**, then **re-open it**. All necessary fields will be updated.

4. Convert the document to PDF format

These instructions are for Microsoft Word 2003 or newer, using either the Adobe Acrobat plug-in or the MS Office PDF creation feature.

1.1 Using the Adobe Acrobat plug-in for Microsoft Office:

Click the **Acrobat tab** in the Word menu at the top of the screen. Select **"Create PDF."** If a dialog window pops up asking you to save and continue, click **Yes**. In the second dialog window, **navigate to the directory** in which you want to save the PDF, **name the file "csdrg.pdf"**, and click **Save**.

1.2 Conversion without Adobe Acrobat plug-in:

Click the **Office button** at the top left of your screen. Select **"Save As,"** then **"PDF or XPS"**. **Navigate to the directory** in which you want to save the PDF, **name the file "csdrg.pdf"**, and click **Save**.

1.3 Formatting and verifying the PDF

Open the PDF. Go to the **File menu** and select **"Properties."** Navigate to the **Initial View tab**. In the drop-down menu for **Navigation tab**, select **"Bookmarks Panel and Page."** In the drop-down menus for both **Page Layout** and **Magnification**, select **"Default."** Click **OK**.

Still in the **"Document Properties"** window, navigate to the **Description tab** and delete the information in the **Title, Author, Subject** and **Keywords** boxes. Click **OK** and then **save the file**. While there, verify at the bottom of the dialog window that the **PDF version is 1.7** or lower.

If the version is too high, go to the **Document menu** and select **"Reduce File Size."** In the drop-down list select **"Acrobat 8.0 and later."** Click **OK**, then **navigate to the directory** in which you want to save the PDF, **name the file "csdrg.pdf"**, and click **Save**.

Go to **File**, and select **"Properties."** Verify at the bottom of the dialog window that the **PDF version is 1.7** or lower.

5. Create a hyperlink to full inclusion/exclusion text in acrf.pdf

If you need to link to the full inclusion/exclusion criteria in acrf.pdf: open both the **csdrg.pdf** and the **acrf.pdf** in separate windows. In the top menu of **csdrg.pdf**, click **Tools**, then **Advanced Editing**, and finally the **Link Tool**. **Draw a box around the text that you want you turn into a hyperlink** in section 2.3.x. Under **Link Action**, make sure **"Go to a page view"** is selected, then click **Next**. While the next dialog box is still open, **navigate to the page in acrf.pdf** that you would like to hyperlink to. **While still in the acrf.pdf window**, click **Set Link**.