PINNACLE 21

BEST PRACTICES FOR ANNOTATED CRFs

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LEAD PRODUCT MANAGER

- Enterprise Expert
- User Advocate
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AGENDA

- Introduction
- Regulatory Requirements
- Industry Guidance
- Creation Methods
- Validation & Verification
- Wrap it up!
- Q & A

INTRODUCTION

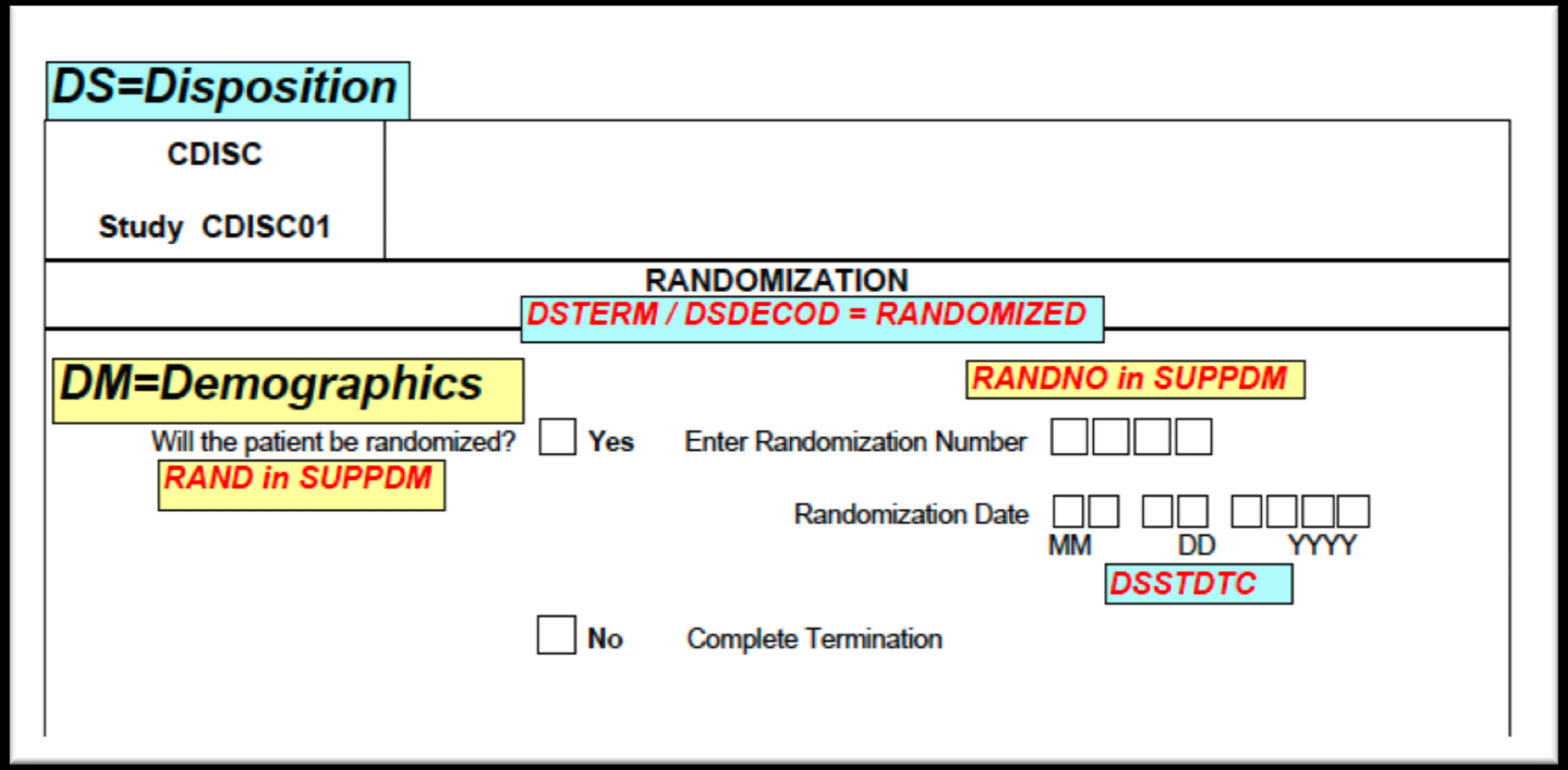
What is the aCRF and why is it important?

DEFINITION

The annotated case report form (aCRF) is a “PDF document that maps the clinical data collection fields used to capture subject data (electronic or paper) to the corresponding variables or discrete variable values contained within the SDTM datasets”

A SHORTER DEFINITION

The aCRF maps clinical data collection fields to variables or discrete variable values within the SDTM datasets.



A SAMPLE ANNOTATED CRF

IMPORTANCE OF THE ANNOTATED CRF

FOR REGULATORY AGENCIES

- Used by regulatory agencies

IMPORTANCE OF THE ANNOTATED CRF

FOR STUDY TEAMS

REGULATORY REQUIREMENTS

Technical Conformance Guide & PDF Specifications

TECHNICAL REQUIREMENTS

TECHNICAL CONFORMANCE GUIDE, SECTION 4.1.4.6

1. The aCRF should be submitted early, preferably at the time a protocol is submitted.
2. It should include treatment assignment forms, when applicable, and should map each variable on the CRF to the corresponding variables in the datasets.
3. It should include the variable names and coding for each CRF item.
4. Items that are not submitted should be annotated with the text ‘NOT SUBMITTED’. There should be an explanation in the Reviewers Guide stating why these data have not been submitted.
5. It should be provided as a PDF with the file name “acrf.pdf”.

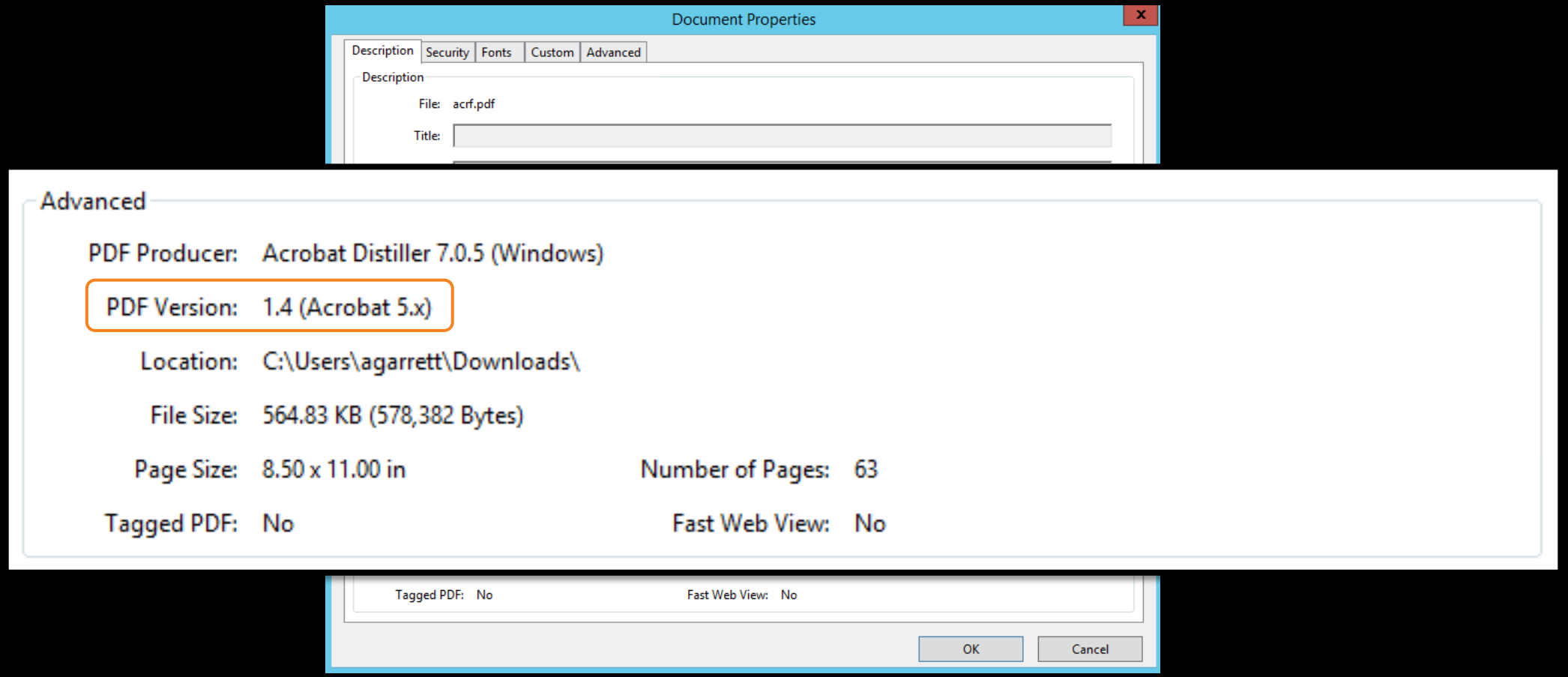
P21

TECHNICAL REQUIREMENTS

FDA'S PORTABLE DOCUMENT (PDF) SPECIFICATIONS

1. Acceptable versions of PDF are 1.4 - 1.7, PDF/A-1, PDF/A-2.
2. Font Size should be size 9 –12.
3. Text should be searchable.
4. Include a Table of Contents with hyperlinks to bookmarked pages.
5. Font color should be black for most text. Hyperlinks can be blue.
6. Readable via Adobe Acrobat.
7. No password protections.
8. Zoom settings should persist when navigating the document.
9. Use a standard font: Times New Roman, Arial, Courier
10. Hyperlinks should be active.
11. The left (top) margin should be at least 3/4 inch. All other margins should be at least 3/8 inch.

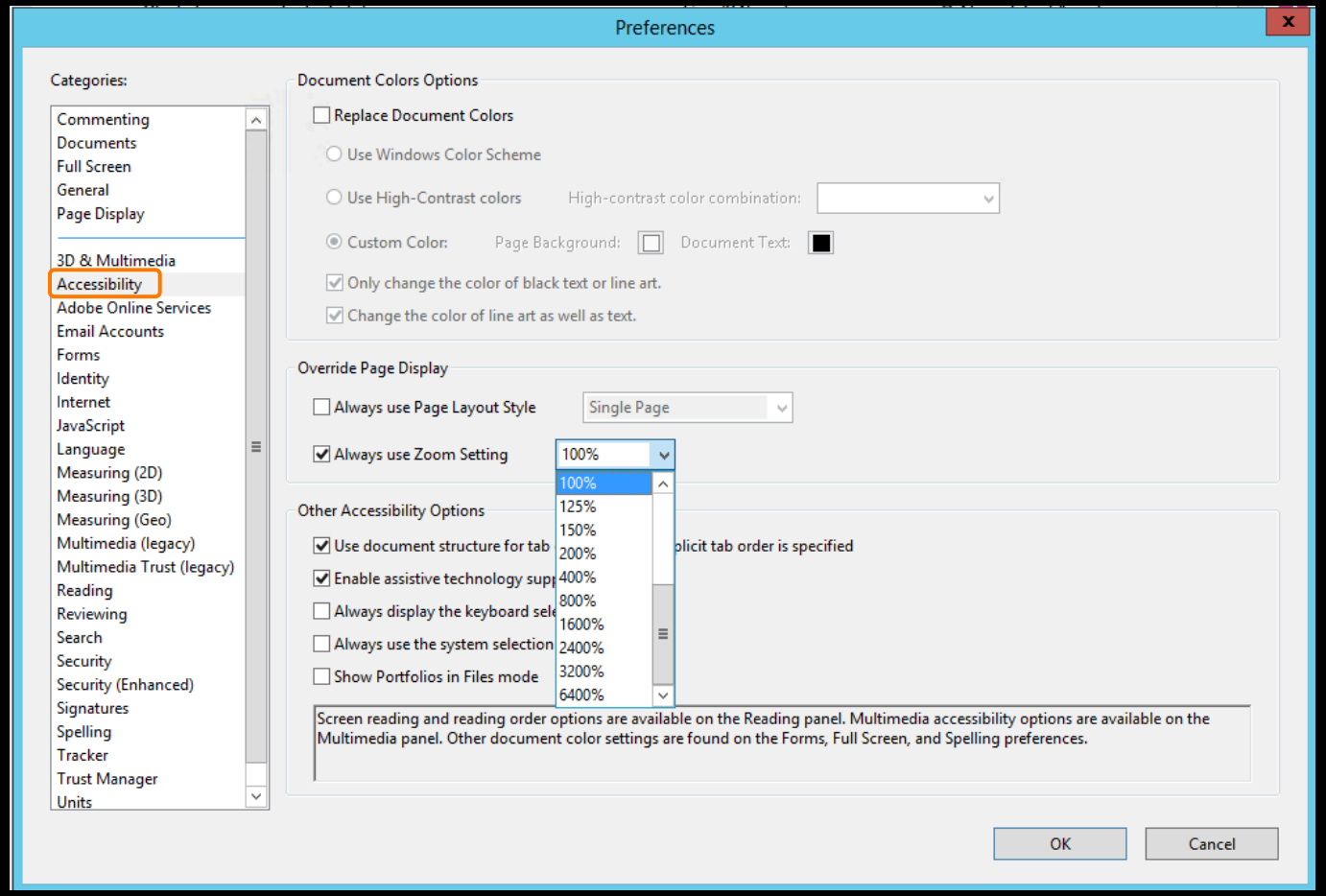
P21



HOW TO CHECK PDF VERSION

Navigate to File > Properties on Adobe Reader (latest version)

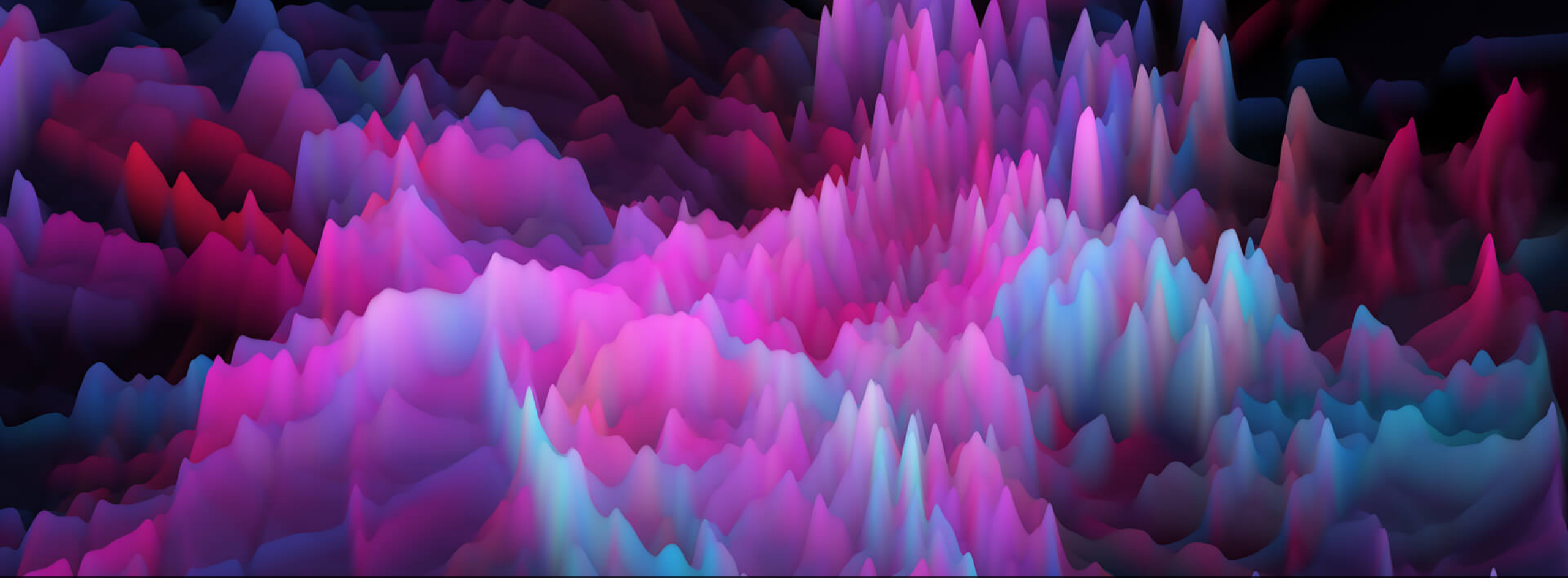
Acceptable versions of PDF are 1.4 – 1.7, PDF/A-1, PDF/A-2



HOW TO PERSIST ZOOM

Navigate to View > Preferences on Adobe Reader (latest version)

Zoom settings should persist when navigating the document

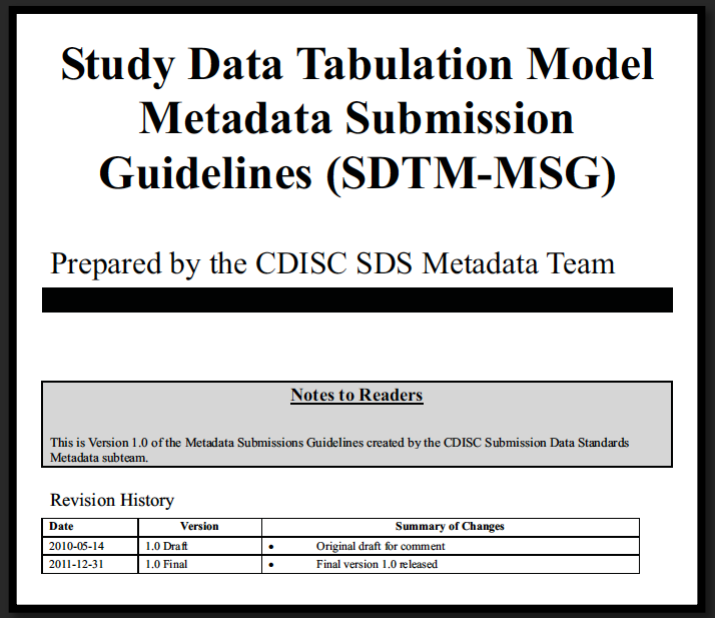


INDUSTRY GUIDANCE

Suggestions from CDISC and the Literature

INDUSTRY GUIDANCE

SUGGESTIONS FROM CISC



Study Data Tabulation Model Metadata Submission Guidelines (SDTM-MSG)

Prepared by the CDISC SDS Metadata Team

Notes to Readers

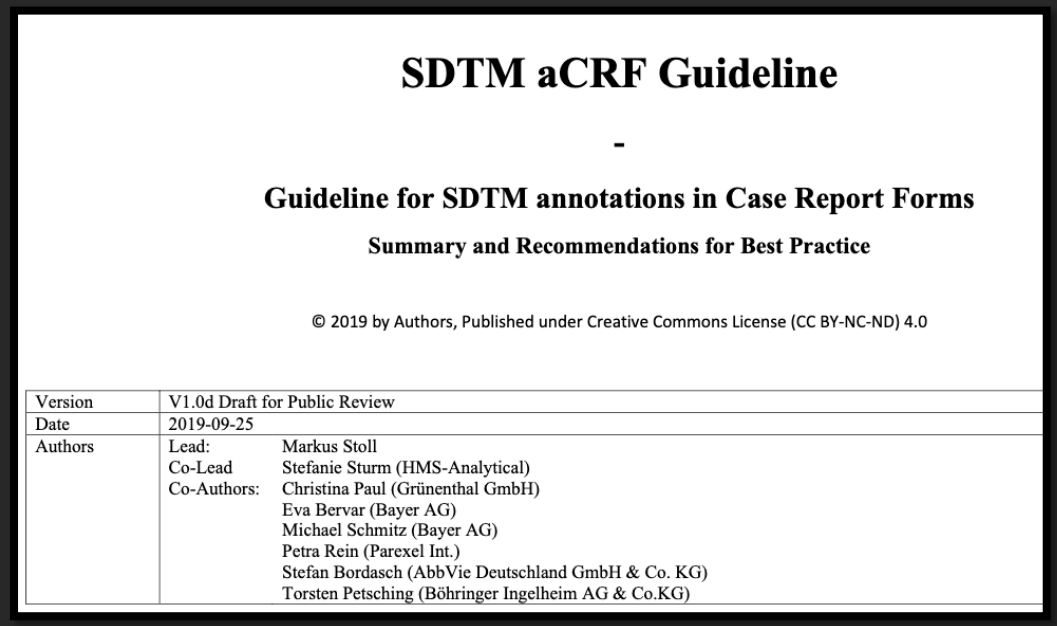
This is Version 1.0 of the Metadata Submissions Guidelines created by the CDISC Submission Data Standards Metadata subteam.

Revision History

Date	Version	Summary of Changes
2010-05-14	1.0 Draft	• Original draft for comment
2011-12-31	1.0 Final	• Final version 1.0 released

Metadata Submission Guidelines (MSG)

Published by CDISC SDS Metadata Team, Dec 2011



SDTM aCRF Guideline

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Guideline for SDTM annotations in Case Report Forms

Summary and Recommendations for Best Practice

Version	V1.0d Draft for Public Review	
Date	2019-09-25	
Authors	Lead:	Markus Stoll
	Co-Lead	Stefanie Sturm (HMS-Analytical)
	Co-Authors:	Christina Paul (Grünenthal GmbH)
		Eva Bervar (Bayer AG)
		Michael Schmitz (Bayer AG)
		Petra Rein (Parexel Int.)
		Stefan Bordasch (AbbVie Deutschland GmbH & Co. KG)
		Torsten Petsching (Böhringer Ingelheim AG & Co.KG)

SDTM aCRF Guidelines (Draft)

Published by German Speaking CDISC User Group, Sept 2019

INDUSTRY GUIDANCE

SUGGESTIONS FROM CDISC

1. The aCRF should be bookmarked in two ways – by visit and by form.
2. The aCRF must be complete – it contains all final unique CRF pages/modules. It should not contain any blank pages.
3. If more than one domain exists on a page, each domain annotation, and all of its variables, should be color-coded.
4. The aCRF should not have database annotations on it.

INDUSTRY GUIDANCE

SUGGESTIONS FROM CDISC (CONT'D)

5 Each domain that is represented on a page should have its own annotation on the upper left side of the CRF page with the 2-letter domain code and domain name.

6 All text in the annotations that represent variable and domain names should be capitalized. If possible, the annotations should not obstruct any text on the CRF page.

7 If additional data sources are used (i.e. patient diaries), they should be appended to the aCRF instead of submitted separately or as part of the SDRG*. In this case, the origin should still be eDT.

*Note, this requirement is only needed if the additional data source is not transcribed into the eCRF.

P21

INDUSTRY GUIDANCE

SUGGESTIONS FROM THE LITERATURE

1. Use conventions for annotations.
2. When applicable, annotate the --CAT.
3. Use a separate annotation for each variable. Only combine variables that map to the same value.
4. When the variables prefix doesn't match the domain's prefix, include the domain name in the annotation

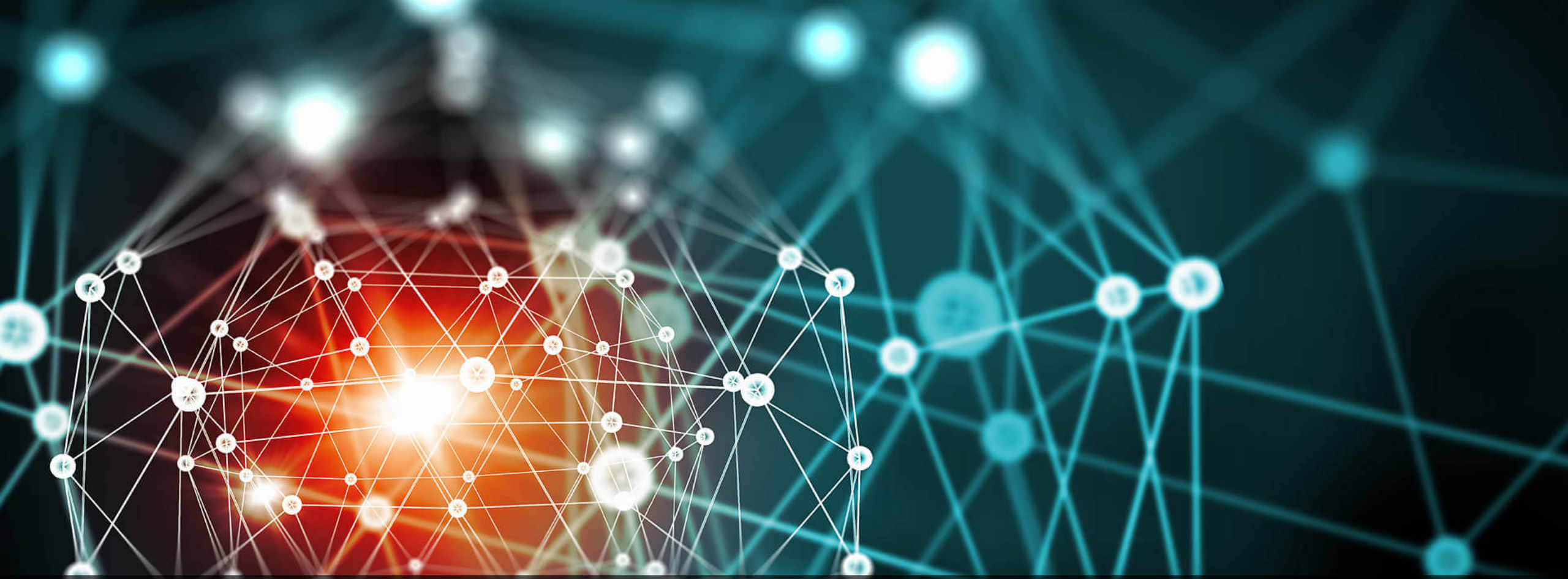
P21

Type	Annotation Pattern	Examples
Domain	[Domain Short Name] = [Domain Long Name]	(1) AE = Adverse Events
Variable	VARNAME	(1) AETERM (2) DS.DSSTDTC
Variable & Value	VARNAME = VALUE	(1) DSTERM = “RANDOMIZED” (2) DSTERM/DSDECOD = “RANDOMIZED”
Supplemental QVAL	QVAL where QNAM = VALUE	(1) QVAL where QNAM = “RACE1” (2) SUPPDM.QVAL where QNAM = “RACE1”
Value Level (non-SUPP)	VARNAME1 where VARNAME2 = VALUE1 VARNAME1 where VARNAME2 = VALUE1 AND VARNAME3 = VALUE2	(1) VSORRES where VSTESTCD = “SYSBP” (2) VS.VSORRES where VSTESTCD = SYSBP (3) FAORRES where FATESTCD = “ONSETDTC” and FAOBJ = “TRIAL DISEASE”
Unsubmitted data	[NOT SUBMITTED]	[NOT SUBMITTED]

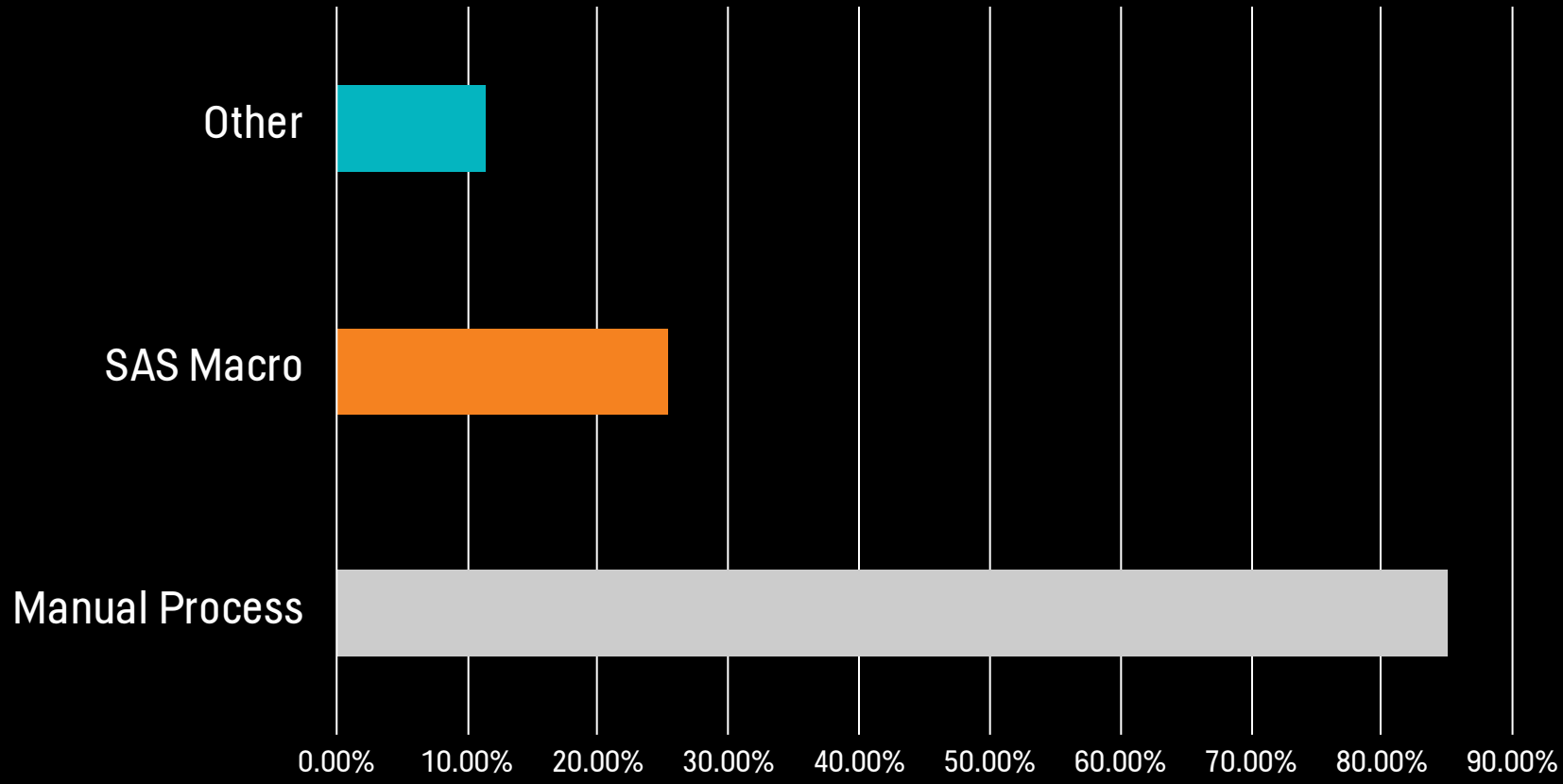
ANNOTATION CONVENTIONS

Adapted from *SDTM Annotations: Automation by Implementation of a Standard Process*, 2015, Geo Joy & Andre Couturier

Use conventions for Annotations



CREATION METHODS



Q: WHAT METHODS(S) DO YOU CURRENTLY USE TO CREATE THE SDTM aCRF? CHECK ALL THAT APPLY.

Responses from 350 Clinical Programmers

Results from P21 Survey, conducted Jan 8th - Jan 15th 2020

VALIDATION AND VERIFICATION

VALIDATION & VERIFICATION

SUGGESTIONS TO ENSURE QUALITY

- **Verification**: Perform programmatic comparisons between the aCRF and the define.xml and/or mapping specifications to verify metadata matches

- **Verification**: Visually inspect the aCRF against a validation checklist

VALIDATION

SAMPLE VALIDATION CHECKLIST

- The document meets FDA technical requirements
- The document meets MSG requirements
- Each domain that is represented on the page should be listed at the top of the page
- All annotations follow the pre-defined convention syntax
- When all annotations on the page belong to the same domain, the background color should be light blue
- When annotations on the page come from multiple domains, the annotations should be color-coded by domain

VALIDATION

SAMPLE VALIDATION CHECKLIST (CONT'D)

- EVAL is only annotated on the CRF when collected
- Annotations do not obstruct any text on the page
- It's clear for each annotation which domain it belongs to
- All data points are annotated, [NOT SUBMITTED] is used when data are not mapped to SDTM
- When applicable, --CAT is annotated
- All annotations do not contain typos and are searchable
- Annotation text does not contain pseudo-code

EXAMPLES

WHAT NOT TO DO

DM=Demographics

Enrollment Form

Enroll the subject by entering the 3-digit Site # and the 5-digit Subject ID#

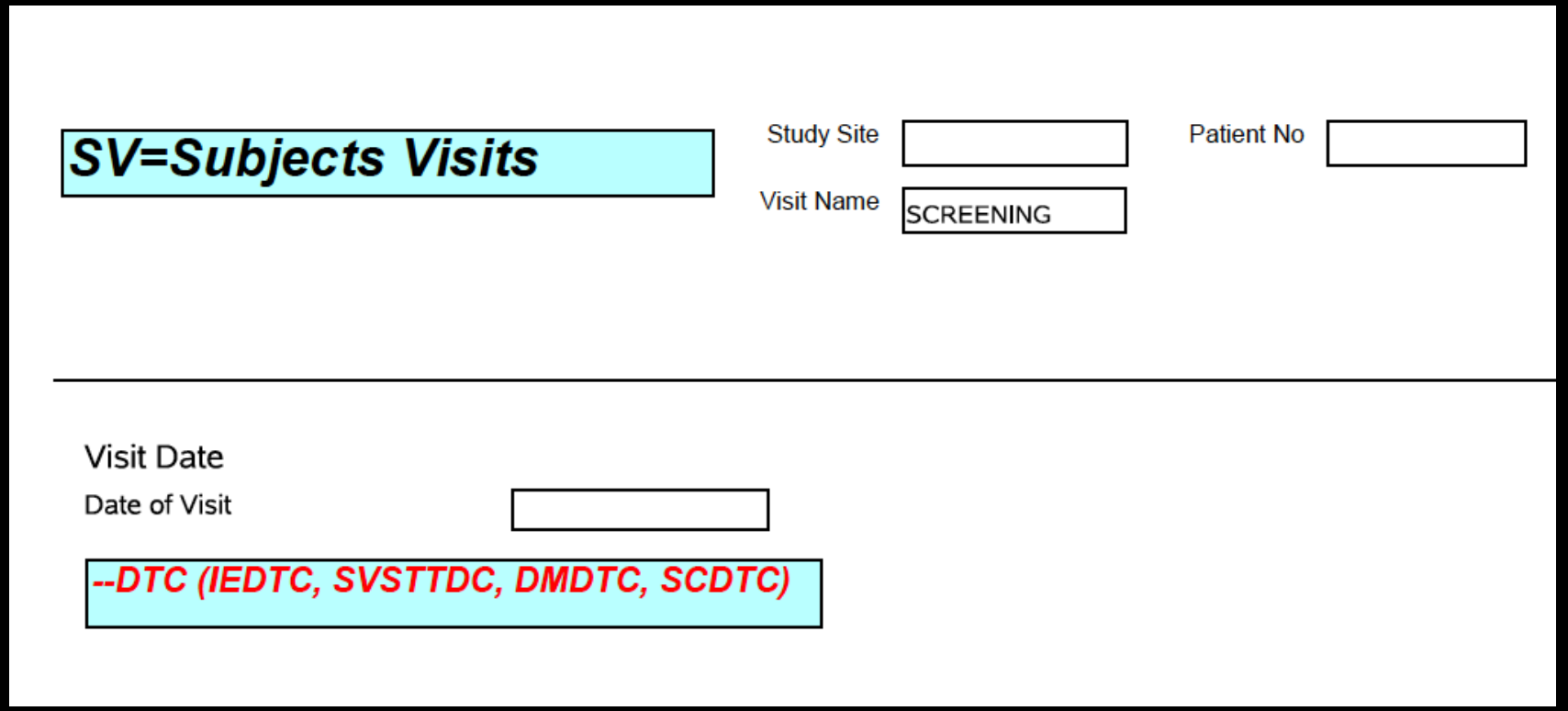
Site #	___	***SITEID***
Subject ID#	_____	***SUBJID***

SC=Subject Characteristics

Subject Initials	___	***SCORRES when SCTESTCD = SUBJINIT***

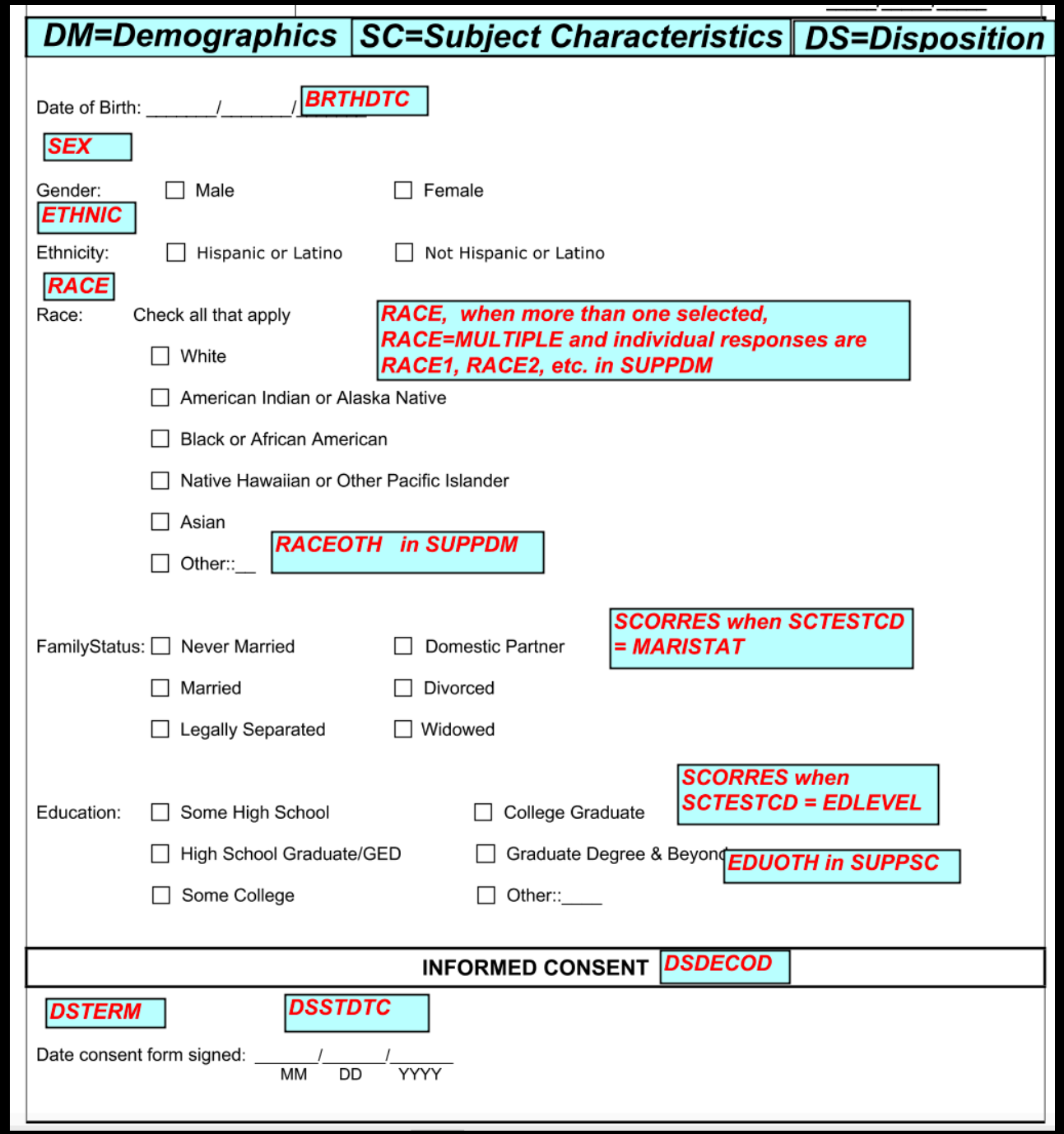
EXAMPLES

WHAT NOT TO DO



EXAMPLES

WHAT NOT TO DO



DM=Demographics | **SC=Subject Characteristics** | **DS=Disposition**

Date of Birth: _____/_____/_____ **BRTHDTC**

SEX

Gender: ☐ Male ☐ Female

ETHNIC

Ethnicity: ☐ Hispanic or Latino ☐ Not Hispanic or Latino

RACE

Race: Check all that apply

RACE, when more than one selected, RACE=MULTIPLE and individual responses are RACE1, RACE2, etc. in SUPPDM

☐ White

☐ American Indian or Alaska Native

☐ Black or African American

☐ Native Hawaiian or Other Pacific Islander

☐ Asian

☐ Other::__ **RACEOTH in SUPPDM**

FamilyStatus: ☐ Never Married ☐ Domestic Partner

SCORRES when SCTESTCD = MARISTAT

☐ Married ☐ Divorced

☐ Legally Separated ☐ Widowed

Education: ☐ Some High School ☐ College Graduate

SCORRES when SCTESTCD = EDLEVEL

☐ High School Graduate/GED ☐ Graduate Degree & Beyond

EDUOTH in SUPPSC

☐ Some College ☐ Other::____

INFORMED CONSENT **DSDECOD**

DSTERM **DSSTDTC**

Date consent form signed: _____/_____/_____
MM DD YYYY

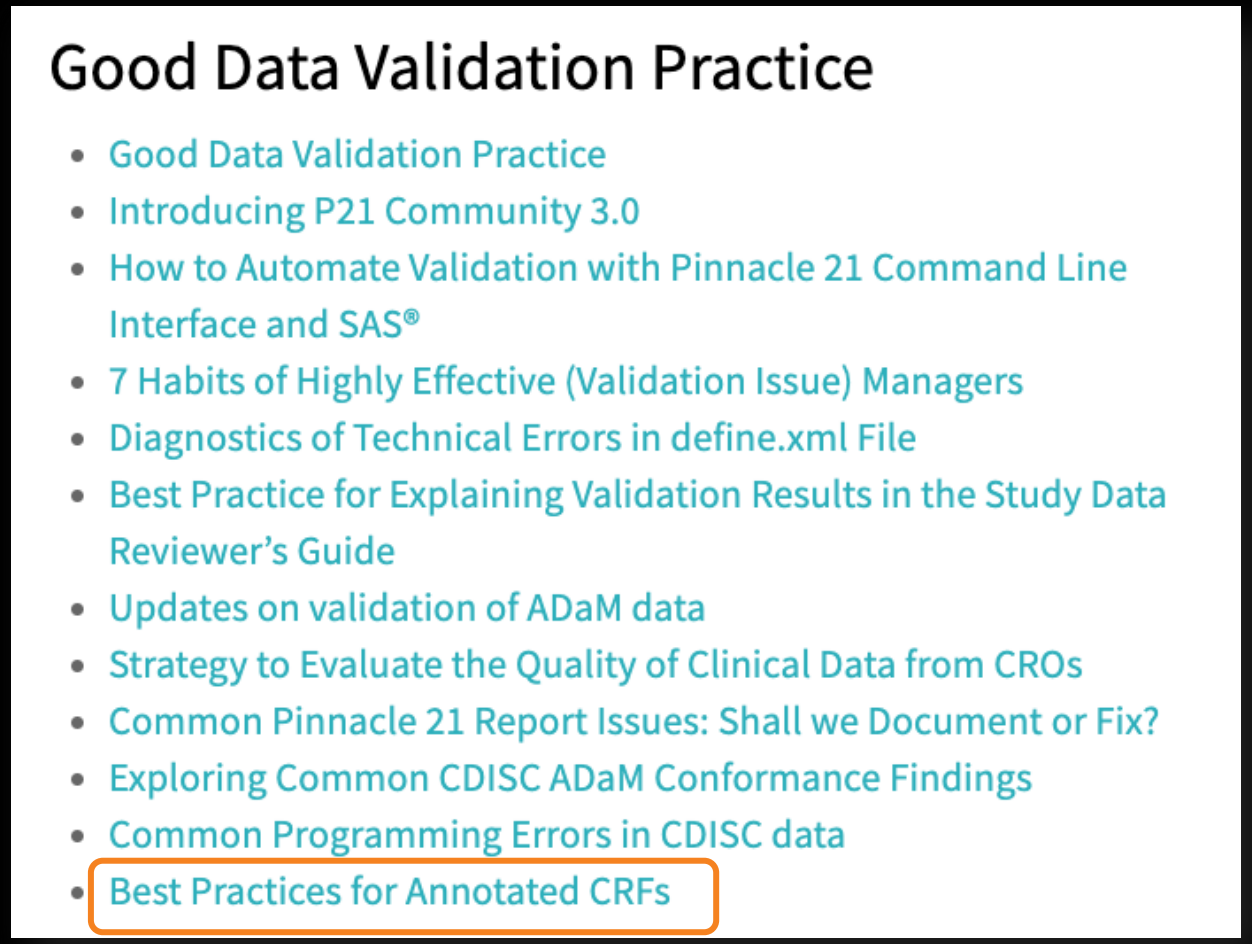
WRAP IT UP

CONCLUSION

- Follow regulatory guidelines
  - Technical Conformance Guide
  - Portable Document (PDF) Specifications
- Consider the industry guidance – if you don't follow it, ask yourself why?
  - Its hard to make a high quality aCRF – don't let this stop you from establishing a good process.
- Establish a process that works for your organization
  - Document your process in a Standard Operating Procedure (SOP) or Working Practice (WP)

MORE RESOURCES

Pinnacle21.com/useful-links



THANK YOU ;)