# PINNÁCLE<sup>21</sup>

### **BEST PRACTICES FOR ANNOTATED CRFs**

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- Enterprise Expert
- User Advocate
- SAS Programmer

### 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

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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**

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

DS=Disposition	1	
CDISC		
Study CDISC01		
		RANDOMIZATION
	DSTERN	I / DSDECOD = RANDOMIZED
DM=Demograp Will the patient be ra		RANDNO in SUPPDM
RAND in SUPP		
		Randomization Date LL LL LL LL MM DD YYYY DSSTDTC
	No	Complete Termination

### A SAMPLE ANNOTATED CRF

### **IMPORTANCE OF THE ANNOTATED CRF** FOR REGULATORY AGENCIES

Used by regulatory agencies



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### **IMPORTANCE OF THE ANNOTATED CRF** FOR STUDY TEAMS





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### **REGULATORY REQUIREMENTS**

Technical Conformance Guide & PDF Specifications

## TECHNICAL CONFORMANCE GUIDE, SECTION 4.1.4.6

The aCRF should be submitted early, preferably at the time a protocol is submitted.

It should include treatment assignment forms, when applicable, and should map each variable on the CRF to the corresponding variables in the datasets.

It should include the variable names and coding for each CRF item.

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.

It should be provided

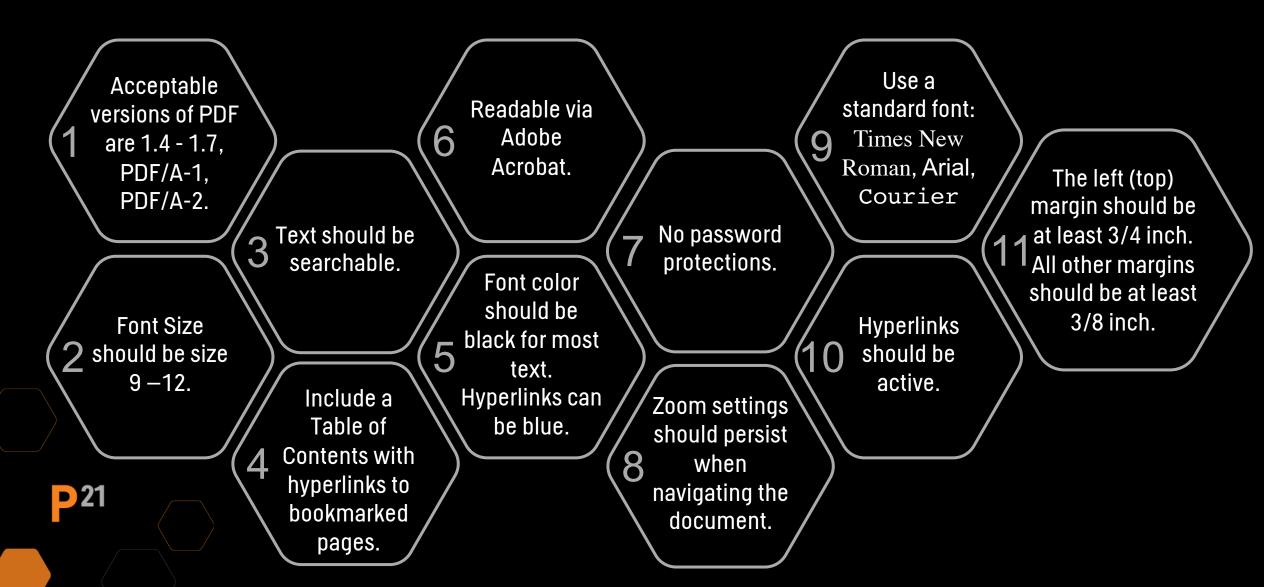
as a PDF with the file name "acrf.pdf".

5

4

## TECHNICAL REQUIREMENTS

FDA'S PORTABLE DOCUMENT (PDF) SPECIFICATIONS



Peciption   Security Fonts   Custom   Advanced   PDF Producer: Acrobat Distiller 7.0.5 (Windows) PDF Version: 1.4 (Acrobat 5.x) Location: C:\Users\agarrett\Downloads\ File Size: 564.83 KB (578,382 Bytes) Page Size: 8.50 x 11.00 in Number of Pages: 63 Tagged PDF: No Fast Web View: No		Document	roperties	
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Tagged PDF: No	Fast Web View: No		
		ОК	Cancel

### **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

	Preferences
Categories:	Document Colors Options
Commenting	Replace Document Colors
Documents	O Use Windows Color Scheme
Full Screen	C Use windows Color Scheme
General Page Display	O Use High-Contrast colors High-contrast color combination:
3D & Multimedia	Custom Color: Page Background: Document Text:
Accessibility	✓ Only change the color of black text or line art.
Adobe Online Services	✓ Change the color of line art as well as text.
Email Accounts	
Forms	Override Page Display
Identity Internet	
JavaScript	Always use Page Layout Style Single Page
	Always use Zoom Setting
Measuring (2D)	
Measuring (3D)	
Measuring (Geo)	Other Accessibility Options 125% 150%
Multimedia (legacy)	✓ Use document structure for tab 200% plicit tab order is specified
Multimedia Trust (legacy)	✓ Enable assistive technology supj 400%
Reading Reviewing	Always display the keyboard sele
Search	1600%
Security	Always use the system selection 2400%
Security (Enhanced)	Show Portfolios in Files mode 3200%
Signatures	6400%  Screen reading and reading order options are available on the Reading panel. Multimedia accessibility options are available on the
Spelling	Multimedia panel. Other document color settings are found on the Forms, Full Screen, and Spelling preferences.
Tracker	
Trust Manager	
Units	
	OK Cancel

### **HOW TO PERSIST ZOOM**

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

Zoom settings should persist when navigating the document

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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
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		Notes to Readers
This is Version	1.0 of the Metadata S	Submissions Guidelines created by the CDISC Submission Data Standards
Metadata subt		
Revision I		

### Metadata Submission Guidelines (MSG)

Published by CDISC SDS Metadata Team, Dec 2011

#### SDTM aCRF Guideline

#### Guideline for SDTM annotations in Case Report Forms

#### Summary and Recommendations for Best Practice

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### SDTM aCRF Guidelines (Draft)

Published by German Speaking CDISC User Group, Sept 2019

### **INDUSTRY GUIDANCE** SUGGESTIONS FROM CDISC

The aCRF should be bookmarked in two ways – by visit and by form.

The aCRF must be complete — it contains all final unique CRF pages/modules. It should not contain any blank pages.

2

If more than one domain exists on a page, each domain annotation, and all of its variables, should be color-coded.

3

The aCRF should not have database annotations on it.

4

### **INDUSTRY GUIDANCE** SUGGESTIONS FROM CDISC (CONT'D)

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.

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.

6

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.

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### **INDUSTRY GUIDANCE** SUGGESTIONS FROM THE LITERATURE

Use conventions for annotations.

Use a separate annotation for each variable. Only combine variables that map to the same value.

When applicable, annotate the --CAT.

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When the variables prefix doesn't match the domain's prefix, include the domain name in the annotation

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Туре	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	(1) VSORRES where VSTESTCD = "SYSBP"
		(2) VS.VSORRES where VSTESTCD = SYSBP
	VARNAME1 where VARNAME2 = VALUE1 AND VARNAME3 = VALUE2	(3) FAORRES where FATESTCD = "ONSETDTC" and FAOBJ = "TRIAL DISEASE"
Unsubmitted data	[NOT SUBMITTED]	[NOT SUBMITTED]

### **ANNOTATION CONVENTIONS**

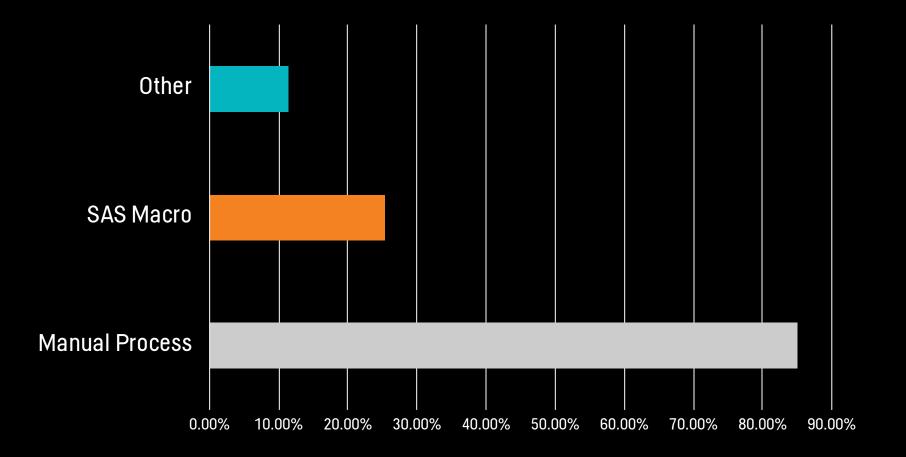
Adapted from *SDTM Annotations: Automation by Implementation of a Standard Process*, 2015, Geo Joy & Andre Couturier

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 8<sup>th</sup> - Jan 15<sup>th</sup> 2020



4.682

276.270

8 5649.71

711.109

82 805



584.662

630 95

270

### 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

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### 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

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- All annotations do not contain typos and are searchable
- Annotation text does not contain pseudo-code

### EXAMPLES WHAT NOT TO DO

DM=Demographi	ics		
		Enrollment F	orm
Enroll the	subject by en	tering the 3-digit S	ite # and the 5-digit Subject ID#
	Site #		SITEID
	[]		1
	Subject ID#		SUBJID
SC=Subject Char	acteristi	CS	
	Subject Initials		SCORRES when SCTESTCD = SUBJINIT

### EXAMPLES WHAT NOT TO DO

SV=Subjec	ts Visits	Study Site Visit Name	SCREENING	Patient No	

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### EXAMPLES WHAT NOT TO DO

DM=Demographics	SC=Subject Characteristics	DS=Disposition

Date of Birth:// BRTHDTC	
SEX	
Gender: Male Female	
Ethnicity: Hispanic or Latino Not Hispanic or Latino	
Race: Check all that apply <b>RACE</b> , when more than one selected,	
White RACE=MULTIPLE and individual responses are RACE1, RACE2, etc. in SUPPDM	
American Indian or Alaska Native	
Black or African American	
Native Hawaiian or Other Pacific Islander	
Asian	
Other::	
FamilyStatus: Never Married   Married Divorced   Legally Separated Widowed	
Education:       Some High School       College Graduate         High School Graduate/GED       Graduate Degree & Beyon	
□ Some College □ Other::	
INFORMED CONSENT DSDECOD	
DSSTDTC	
Date consent form signed:/// /YYYY	





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### CONCLUSION

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### 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

### **Good Data Validation Practice**

- Good Data Validation Practice
- Introducing P21 Community 3.0
- How to Automate Validation with Pinnacle 21 Command Line Interface and SAS<sup>®</sup>
- 7 Habits of Highly Effective (Validation Issue) Managers
- Diagnostics of Technical Errors in define.xml File
- Best Practice for Explaining Validation Results in the Study Data Reviewer's Guide
- Updates on validation of ADaM data
- Strategy to Evaluate the Quality of Clinical Data from CROs
- Common Pinnacle 21 Report Issues: Shall we Document or Fix?
- Exploring Common CDISC ADaM Conformance Findings
- Common Programming Errors in CDISC data
- Best Practices for Annotated CRFs

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# THANK YOU;)

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