

# Best Practices for Annotated CRFs

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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 to the corresponding variables or discrete variable values contained within the SDTM datasets.” Creating a high-quality aCRF is important for reviewers and study teams – both parties used the aCRF as a reference document independently and in combination with the define.xml. Follow regulatory requirements and industry recommendations to help streamline your process.

## Technical Conformance Guide<sup>1</sup>, § 4.1.4.6 (see paper for more details)

- ▶ It should include the variable names and coding for each CRF item.
- ▶ It should be provided as a PDF with the file name “acrf.pdf”.
- ▶ 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.



## Portable Document (PDF) Specifications<sup>2</sup> (see paper for more details)

- ▶ Acceptable versions of PDF are 1.4 - 1.7, PDF/A-1, PDF/A-2.
- ▶ Text should be searchable.
- ▶ Include a Table of Contents with hyperlinks to bookmarked pages.
- ▶ Use a standard font: Times New Roman, Arial, Courier
- ▶ The left (top) margin should be at least 3/4 inch. All others, at least 3/8 inch.

## Suggestions from CDISC<sup>3,4</sup> (see paper for more suggestions)

- ▶ 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.
- ▶ If more than one domain exists on a page, each domain annotation, and all of its variables, should be color-coded.
- ▶ The aCRF should not have database annotations on it.
- ▶ Each domain on a page should have its own annotation on the upper left side of the CRF with the 2-letter domain code and domain name.



## Suggestions from the Literature

- ▶ Use conventions for annotations<sup>5</sup>. (see paper for table of conventions)
- ▶ When applicable, annotate the --CAT.
- ▶ Use a separate annotation for each variable. Only combine variables that map to the same value.
- ▶ When the variables prefix doesn't match the domain's prefix, include the domain name in the annotation

## Creation

- ▶ Manual methods still prevail (85% of users report manual creation)
- ▶ Automation methods exist but are not widely adopted
- ▶ Bookmarks can be created in an automation way<sup>6</sup>



## Verification & Validation

- ▶ **Verification:** Perform programmatic comparisons between the aCRF and the define.xml and/or mapping specifications to verify metadata matches<sup>7</sup>.
- ▶ **Validation:** Visually inspect the aCRF against a validation checklist. (See paper for sample checklist)

1 FDA. STUDY DATA TECHNICAL CONFORMANCE GUIDE (2019).

2. FDA. PORTABLE DOCUMENT FORMAT (PDF) SPECIFICATIONS (2016).

3. CDISC SDS Metadata Team. Study Data Tabulation Model Metadata Submission Guidelines (2011)

4 CDISC German Speaking User Network. SDTM annotated Case Report Form (aCRF) Guideline (2019).

5. Joy, G., & Couturier, A. (2015). SDTM Annotations: Automation by implementing a standard process. In *Proceedings of the PharmaSUG US Annual Conference*.

6. Zhou, Y. (2019). Adding Table of Contents (TOC) for the Annotated CRF Automatically. In *Proceedings of the PharmaSUG US Annual Conference*.

7. Zeng, X., & Zhang, S. (2016). Define.xml Content Validation – CRF Page Check. In *Proceedings of the PharmaSUG China Annual Conference*.