IMPLEMENTING THE SDRG

Reflections from the Reviewer Community

Helena Sviglin[1], Eileen Navarro[1], Crystal Allard[1], Lilliam Rosario[1]

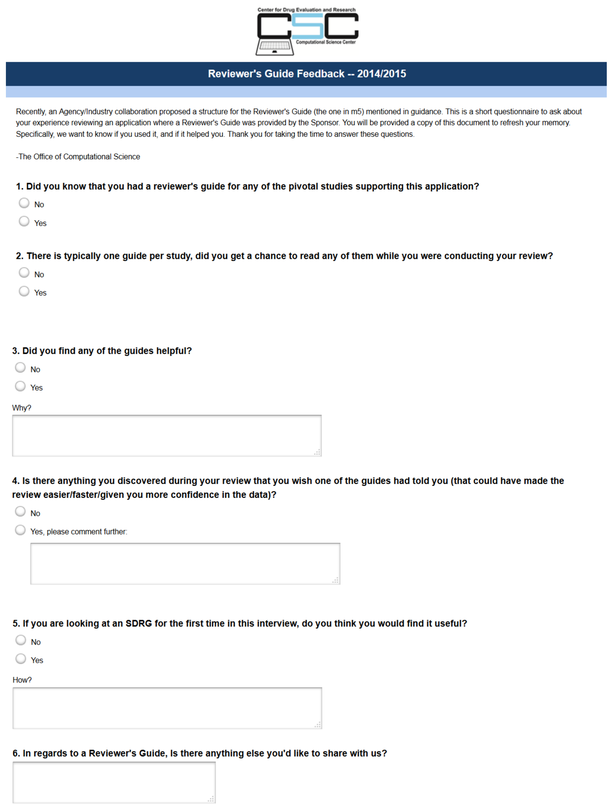
ABSTRACT:

The FDA Guidance: Providing Regulatory Submissions in Electronic Format – Submissions under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act, refers to a study guide that should accompany the data in submissions to the Agency. In 2013 a suggested template for this document (named Study Data Reviewer Guide or SDRG) was developed in collaboration with Industry[3]. Last year, the OCS reported internally on reviewer feedback on the SDRG from JumpStart sessions – which are conducted at the beginning of a review. This year OCS has been evaluating SDRG helpfulness by interviewing reviewers that have completed a review that was supported by a SDRG. Further evaluations are being considered.

BACKGROUND:

Study data has a life cycle that begins well before submission to an Agency. The Study Data Reviewer Guide (SDRG) serves as the roadmap to the study data in ways that the Define.xml does not adequately document. Some of data documentation gaps that the SDRG addresses are:

- SDTM mapping decisions *(does an event get captured as an AE or as a sign and symptom in the CE domain?)*
- Sponsor-defined (custom) domains *(are all the MRI interpretations in the Physical Exam (PE) domain or are they separated into their own dataset?)*
- Sponsor-defined controlled terminology *(Did the sponsor use MedDRA or their own dictionary?)*
- Does the analysis data come from the SDTM data or was it derived separately? *(This can have an impact on the reconciliation of analysis data to the tabulation data and the CSR)*



Reviewer's Guide Feedback -- 2014/2015

Recently, an Agency/Industry collaboration proposed a structure for the Reviewer's Guide (the one in m5) mentioned in guidance. This is a short questionnaire to ask about your experience reviewing an application where a Reviewer's Guide was provided by the Sponsor. You will be provided a copy of this document to refresh your memory. Specifically, we want to know if you used it, and if it helped you. Thank you for taking the time to answer these questions.

-The Office of Computational Science

1. Did you know that you had a reviewer's guide for any of the pivotal studies supporting this application?
- No
- Yes

2. There is typically one guide per study, did you get a chance to read any of them while you were conducting your review?
- No
- Yes

3. Did you find any of the guides helpful?
- No
- Yes

Why?

4. Is there anything you discovered during your review that you wish one of the guides had told you (that could have made the review easier/faster/given you more confidence in the data)?
- No
- Yes, please comment further:

5. If you are looking at an SDRG for the first time in this interview, do you think you would find it useful?
- No
- Yes

How?

6. In regards to a Reviewer's Guide, is there anything else you'd like to share with us?

CONCLUSION:

The SDRG was developed to complement the define.xml to enable the reviewers to understand the data representations included in a submission. Uptake of the SDRG has been robust and there are many SDRG documents that serve as best practices in implementation. We summarize the issues that limit the usefulness of the SDRG; these issues generally result in information requests to the sponsor, and can impact review time. When an application does not have an SDRG, reviewers are encouraged to advocate for an SDRG in their future applications.

METHODS:

A systematic inventory of all CDER electronic applications in 2014 was beyond OCS resources. Instead, several two week samples of submissions throughout late 2013 until 2014 were manually examined for the presence of an SDRG-type document. Applications where an SDRG-type was identified were then researched to see which of these reviews had been completed. Clinical reviewers from these completed applications were then contacted and asked about their experience using the SDRG during their review.

RESULTS AND DISCUSSION:

- CDER approximates that 450 NDAs were received in 2013 and 2014 (BLAs not included in this count). Each application has multiple sequence folders in the eCTD structure.
- 15 weeks of submissions from late 2013 through 2014 to the CDER Electronics Document Room (EDR) were randomly selected to evaluate for the presence of an SDRG-type document in each study data folder.
- Within those 15 weeks, 550 eCTD study data folders were manually evaluated for an SDRG-type document located in the same folder as the datasets in m5.
- 98/550 folders had an SDRG-type document
- 52/98 of these folders supported with an SDRG-type document had a completed review (indicated by a regulatory decision posted in the Document Archiving, Reporting, and Regulatory Tracking System (DARRTS).
- 10/52 SDRG-type documents had a Clinical reviewer who was available and willing/able to answer 6 questions about their experience.
- 44/98 of SDRG-type documents were loosely based on the recommended SDRG template. The format for the rest of the documents differed widely.
- All Reviewers had located the SDRG in the m5 folder and had read and referred to the document in the course of their review. The usefulness of the SDRG-like documents varied depending on their quality.

[1] U.S. Food and Drug Administration/CDER/OTS/OCS

[3] http://www.phusewiki.org/wiki/index.php?title=Study_Data_Reviewer's_Guide.