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Quality Assurance within Statistical Programming:

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ABSTRACT

This paper is a discussion of how Quality Assurance (QA) can be used to improve the Quality Control (QC) process within Statistical Programming. QC in this paper is defined to mean independent programming, meaning two programmers use the same Protocol, Statistical Analysis Plan, and other related documents to generate the results as specified in the Table, Listing and Figure (TFL) templates for a specific analysis. Ideally, as QC is independent and the documentation clear, the results between programmers will be identical. That said, when was the last time you QC'd the results of a study and everything was 100% correct, the very first time it was programmed? This is why we will talk about Quality Assurance, which in this paper is defined as using the raw data to generate data that is used to create the same TFLs as the two independent programmers. One of the major benefits of this process sis that it bypasses any issues that may have resulted in having standard SDTM/ADaM data matching in error for any number of reasons (again – when was the last time QC resulted in 100%, accurate results the very first time the QC program was used). Specific process and key documentation/guidance are identified which have resulted in using selective QA (almost always on a pivotal phase III study or other deliverables intended for regulatory review). The content of this paper is based on many years of experience and past formal training of the authors and of both current and prior project team members.

INTRODUCTION

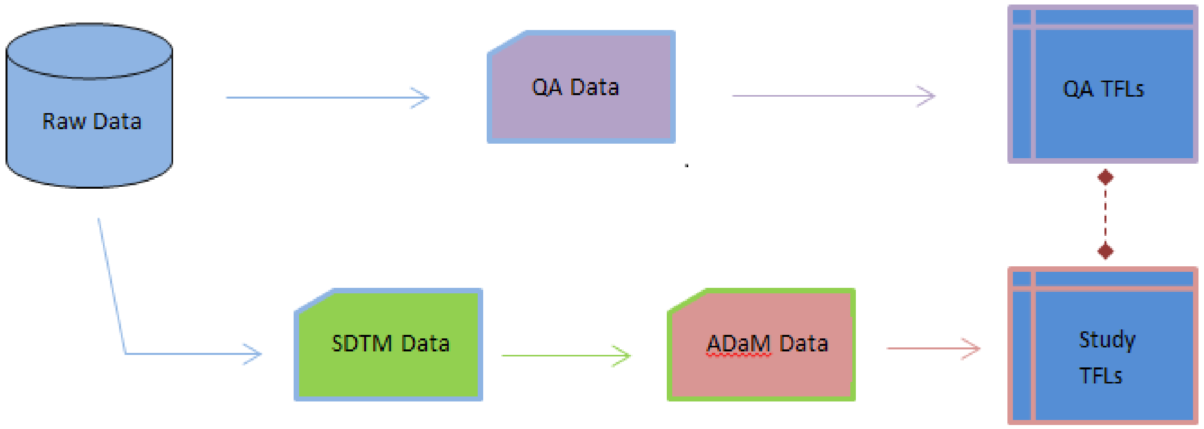
This paper demonstrates the advantages that QA adds to improve the Quality of Statistical Programming deliverables, specifically the Tables, Listings and Figures (TFLs). When a programmer independent of the project team uses the same Protocol, Statistical Analysis Plan, and other related study documents to generate the TFLs it maintains integrity by bypassing any issues the study team, working together on a daily basis, may miss in their discussions of how algorithms are generated and evolve. The reader will gain valuable insights into how TFLs can be generated from raw data, the benefits of having an independence programmer on pivotal and/or critical studies and other inherent benefits, such as being able to use open source programming languages and working with junior team members and interns.

WHAT IS QA?

Quality Assurance in this paper is defined as Independent Review / Programming from raw data to TFLs. Some of the most important goals of QA are:

1. Confirm that "high priority", "high risk", or "novel" deliverables receive a "triple-check" of their accuracy.
2. Confirm that the study team's TFL deliverables and study's SAP(Methods), Protocol, Specifications, & tables shells are in alignment and conform to Standards and;
3. Explore open source programming languages as beneficial tools.

Figure 1. Quality Assurance Process Visualization



WHY QA?

As described above, the benefits of QA are many, including:

1. Improve data integrity.
2. Third level of independent review for key studies.
3. Identify and proactively address any potential issues and risks.
4. Ensure higher quality outcomes.
5. Review documents to ensure definitions are clear, accurate, reliable and align with standards.
6. Ensure consistency within and across studies and disease/therapeutic areas.
7. Leverage appropriate programming language for the relevant task.

WHEN TO QA?

The study team should ensure the following criteria are met prior to engaging with the QA team:

1. Confirm the protocol, Statistical Analysis Plan (SAP), Case Report Form (CRF) and TFL templates are steady.
2. Resolve raw data issues or document them for the QA team's awareness.
3. Generate study datasets and TFLs for at least one dry run that pass Quality Control (1st layer of independent review).

HOW TO QA?

How to perform QA is the focus of the remainder of this paper. The QA process involves in-depth work from the study team, the QA team and both teams working together to establish transparent goals and finally, the specific tasks involved in QA.

We will start with the study team, where all the development and QC are performed. Many companies end with QC, satisfied that independent programming will catch any and all critical issues related to quality, which is the case in the vast, vast majority of studies. But what about that one potential time where a critical TFL can go out the door and there is a question about the result? It's those cases we think about when performing QA (and deciding which studies to perform QA on).

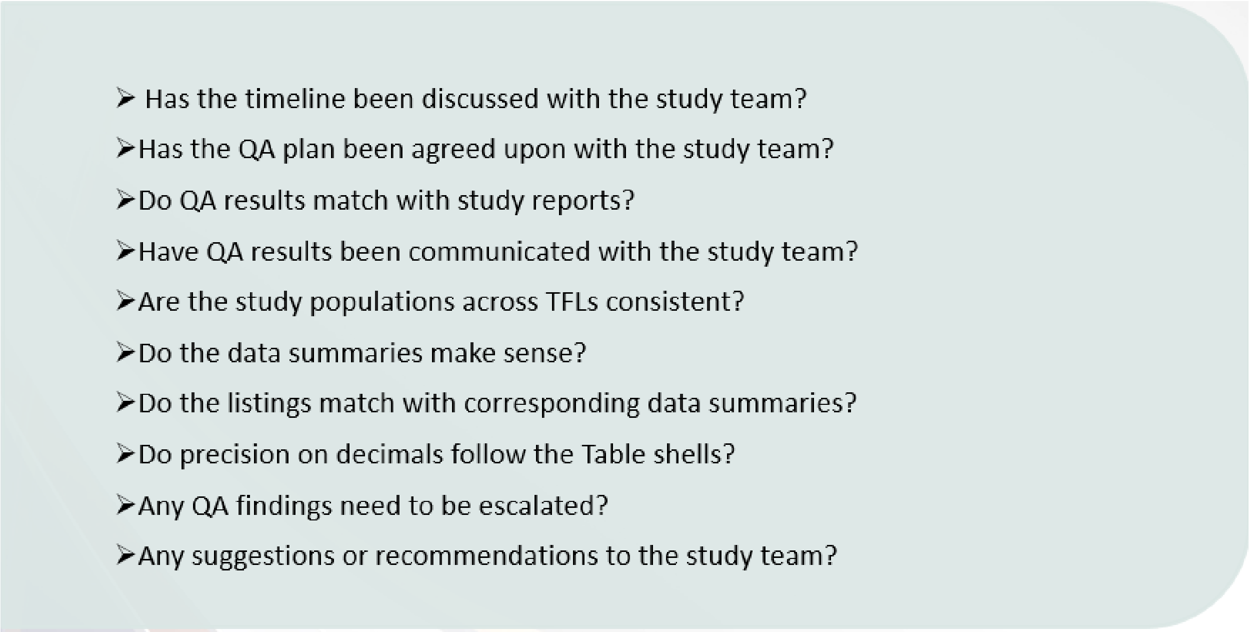
The critical task a study needs to complete in collaboration with the QA team are twofold: a knowledge transfer which includes a study overview from the team's perspective as well as key elements of the study (primary efficacy endpoint, key secondary endpoints, any novel safety analysis, etc.).

The critical task the QA team needs to receive and incorporate into their work is also twofold – since there is a learning curve the QA team needs to rapidly catch up on, it's extremely important that the familiarize themselves with all key documents (Protocol, SAP, CRF, etc.) as well as details that are not in those documents and may only exist in the ADaM specs, or sometimes may not be 100% complete (if everything is 100% complete the QC Programmer would always come up with the same results as the development programmer so there needs to be room for interpretation).

We present below the 'How' a QA team works in order to achieve the highest quality results:

1. Collaborate closely, early and only as much as necessary with the Study Team.
2. Establish clear QA communication channel.
    a. Ad hoc meetings / Emails.
    b. Instant messages / phone calls.
    c. Escalate any issues to the statistician if necessary.
3. Set up a separate QA work folder under each study's reporting folder.
4. Maintain QA documents. - QA checklist (Figure 2).
    a. QA Findings tracker.
    b. Issues & Resolution tracker.
    c. Timeline tracker.
5. Present at the monthly programming meeting for the common QA findings.
6. Work with Statistical Programming Leadership team by the end of each year to set up the QA Calendar for the next year.

Figure 2. Quality Assurance Checklist



- ➢ Has the timeline been discussed with the study team?
- ➢Has the QA plan been agreed upon with the study team?
- ➢Do QA results match with study reports?
- ➢Have QA results been communicated with the study team?
- ➢Are the study populations across TFLs consistent?
- ➢Do the data summaries make sense?
- ➢Do the listings match with corresponding data summaries?
- ➢Do precision on decimals follow the Table shells?
- ➢Any QA findings need to be escalated?
- ➢Any suggestions or recommendations to the study team?

CONCLUSION

In conclusion, Quality Assurance can be a powerful process to ensure nearly perfect quality – not only in the Tables, Listings and Figures that are programmed from raw data (bypassing SDTM and ADaM), but also in ensuring data quality and any mapping issues from SDTM and/or algorithms derived in ADaM datasets. We strongly recommend teams to think about using QA for their pivotal Phase III/submission studies and any other studies where there is zero tolerance for any gaps in documentation, potential for uncertainty where algorithms cannot be spelled out in SAS code (we don't recommend spelling out algorithms in SAS code since that can be copied by anyone, resulting in all results being the same) or randomly to ensure teams are adhering to the highest possible quality standards.

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