Paper PP27

A Collaborative Approach to Analysis Standards

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ABSTRACT

When is a standard not a standard? When no one uses it! While that may be a bit exaggerated, to mitigate this possibility Janssen has developed a collaborative model for not only creating new analysis standards for the Janssen study teams but also for correcting and enhancing them. The standards include templates for select study documents, analysis dataset metadata and template code, and code to produce tables, listings and graphs. These are aligned with CDISC standards. The ongoing effort to keep these standards relevant and useable by our study teams involves the teamwork from representatives from three areas: the analysis standards team, statistical programming, and statistics. This paper will walk through the evolution of the collaboration of the three areas, share success stories of their efforts and consider the challenges facing them in the future.

INTRODUCTION

In this paper we will look at the people and processes used to develop and keep current the analysis standards used by Janssen's Statistical Programming and Analysis department.

WHO ARE THE PLAYERS?

There are three roles involved in the development of analysis standards: the analysis standards team, analysis standards Subject Matter Experts (SMEs) and the Statistical Programmers and Statisticians who work our clinical trials. The first two roles are somewhat dedicated to creating and maintaining standards while our associates working on trials are continuously vetting the standards by using them in their trial work.

ANALYSIS STANDARDS TEAM

This group consists of programmers and statisticians who have worked on clinical trials in the past but are now in a role in which they create and maintain the analysis standards used by trial teams. In addition to developing standards they also train the stat programmers and statisticians on the how to use the standards in clinical trials. They also actively participate in industry groups such as CDISC, PhUSE, PharmaSUG and keep the organization informed on updates to industry standards, such as ADaM.

SUBJECT MATTER EXPERTS (SME'S)

Our SMEs are statistical programmers and statisticians who work on trials but are lending their expertise in various topic areas such as Adverse Events, Pharmacokinetics (PK), and Labs. The goal is to have their input when standards are being developed or when questions are asked about current standards so that the deliverables are relevant and applicable to our studies. We try to "refresh" the individuals in the SME roles every 18 months or so. Since Janssen has five therapeutic areas (TA's), it's good to rotate associates in from a mixture of TA's so that the standards are relevant across our organization. For each topic area, one SME is designated the lead.

STATISTICAL PROGRAMMERS AND STATISTICIANS

From a standards perspective our stat programmers and statisticians work on the "front line" of the clinical trials from protocol development through to submission packages. They are working daily with the data to complete the

analyses required in submissions and in doing so they are figuring out how to meet the needs of complex trial designs.

WHAT ARE INCLUDED IN ANALYSIS STANDARDS?

The global analysis standards at a high level consist of document templates and SAS® code.

STATISTICAL REQUIREMENTS DOCUMENTS

The analysis standards team has worked with study statisticians to develop templates for creating Statistical Analysis Plans (SAP) and Data Presentation Specifications (DPS), the latter which contains the mock-ups and analysis/derivation rules. These document templates are purposely annotated in such a way that the study teams can identify which wording is optional and where the team must provide the trial-specific verbiage. The example below from the DPS template specifies by color what the author needs to do. They should review and update if needed where the text is highlighted in dark blue. The text that has light-blue highlighting is optional and can be eliminated if not needed for the analysis.

AETABLE: Number of Subjects With [Treatment-emergent Adverse Events] Through [Time Point] by System Organ Class and Preferred Term and Onset Time; [Analysis Set] (Study [Study ID])

	[Placebo]						[Treatment Group A]					
	Total	[Within 3 months]	[4 to 6 months]	[7 to 9 months]	[10 to 12 months]	[Beyond 13 months]	Total	[Within 3 months]	[4 to 6 months]	[7 to 9 months]	[10 to 12 months]	[Beyond 13 months]
Analysis set: [Analysis set]	###	###	###	###	###	###	###	###	###	###	###	###
Avg duration of follow-up ([units])	###						###					
Avg exposure ([units])	###						###					
Subjects with 1 or more [AEs]	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)
System organ class Preferred term												
System organ class	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)
Preferred term	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)	### (xx.x%)

GLOBAL METADATA AND ANALYSIS DATASET TEMPLATE CODE

The analysis standards team has developed global metadata and SAS template programs for creating analysis datasets, mainly safety datasets. There is one template program per dataset. For each analysis dataset, the metadata contains most of the possible variables, and the study teams remove or add variables to the metadata as needed for specific study needs. The template programs for the analysis datasets contain mostly macro calls, one for each variable. The study team removes any macro calls not needed and adds any study-specific code.

GLOBAL SAS MACROS AND TABLE, LISTING, GRAPH (TLG) CODE

The global SAS macros and TLG code differ from the analysis dataset templates in that they're designed to be used as-is. The logic in global macros can be manipulated by use of parameters when the macro is called. This way the study teams can "customize" how the macro executes without changing any of the code to meet their study needs.

The TLG code will produce the outputs specified in the DPS.

EXAMPLES OF COLLABORATIONS

We've met the players and a sampling of the analysis standards deliverables that they must collaborate on. So how does the process work? Below are some common situations and the processes that guide the team towards their solutions.

NEW ANALYSIS STANDARD

When a new standard is developed, most frequently a new table or graph, it's typically a disease-area or therapeutic area standard that's been adopted by other therapeutic areas. The governance rules state that a standard that's adopted by more than one TA gets "elevated" to global designation and subsequently is maintained by the analysis standards team. You could say that the collaboration has already taken place as evidenced by its use across TA's.

QUESTION ABOUT AN EXISTING ANALYSIS STANDARD

This is the most common scenario. When a question arises about a standard, that question is posted to an intranet portal known as "The Red Desk". The user is asked to select the topic area under which the question falls. When the question is posted it automatically generates emails to all standards team members plus all SME's for the topic area chosen by the user posting the question. Note in the diagram below the handoff from analysis standards to the SMEs. For the more complex questions it's the SMEs, who are representative of the associates who use the standards daily, who get the final say. Practically speaking, there are live discussions and email exchanges between analysis standards and SME's for those questions and consensus is reached. But per the process, it's the SMEs' final decision.

If it's determined that there is an issue with one of the standards and a change is needed, then the Change Request process (see next section below) is executed.

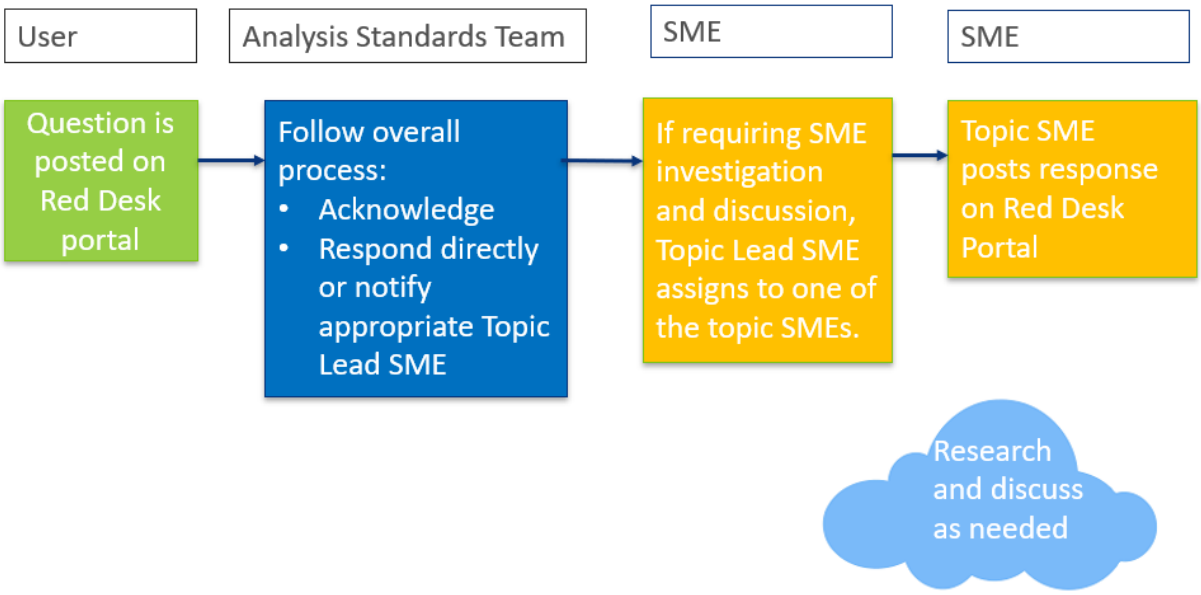

Figure 1

REQUEST A CHANGE TO AN EXISTING STANDARD

A change request can result from a question posted to our Red Desk portal or the change can be requested directly as a result of an error found or a suggestion for an enhancement to an existing standard. The latter occurs most frequently with the standard macro code when one of our stat programmers suggests an improvement or bug fix to the code.

Notice that instead of a hand-off between Analysis Standards and SME's there is an interactive discussion. That's because a change request may be acceptable to analysis standards but not the SME's. And vice-versa! Frequently the SME's provide a "reality check" as to whom will benefit from a change. For example, if a change is requested to a macro which will benefit a small fraction of studies, it may be deemed not worth pursuing.

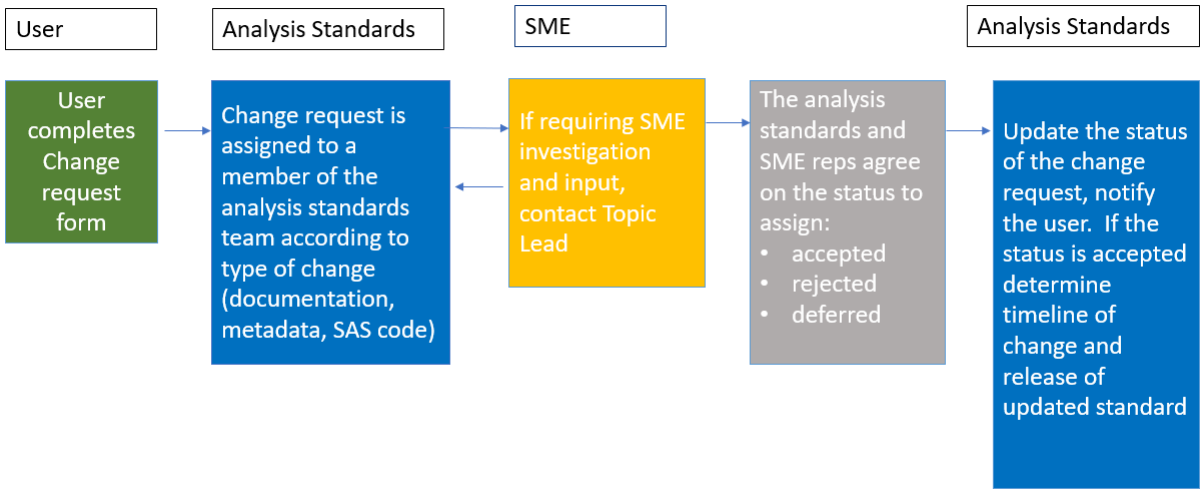

Figure 2

BUT THE STANDARDS DON'T FIT MY STUDY

The needs of a study will always take precedence over the use of global standards. But with the complexity of study designs ever increasing plus the diversity of analyses from one disease area to another the analysis standards team felt the need to collaborate with study teams on developing more customized standards. That is how the evolution of disease-area standards evolved. Working with study teams from select disease areas, we've developed SAP and DPS templates that are aligned with the common disease-specific analyses performed in their studies. This results in disease-specific CRF's that capture the appropriate information needed for those analyses. And the last piece is disease-specific standard code that produces the tables and graphs needed for the analyses.

MEASURE THE VALUE OF USING ANALYSIS STANDARDS

Applying metrics to the improvements that result from the use of analysis standards had been somewhat elusive. What is measurable? Number of days to FDA approval? Those of you reading this paper are likely smirking at that last statement. We can't control what the FDA does, but we can control internal process quality such as consistency across studies of our deliverables. We must make assumptions about the use of our associates' time, for example when a stat programmer can use existing standard code to develop 60-70% of their table and graph deliverables then presumably that frees them up to create code that is study-specific. That results in faster completion of all study deliverables. We continue to work with our study teams for their ideas on what metrics to capture.

CONCLUSION

So what is the future for developing and using analysis standards at Janssen? Without a doubt we'll continue with more disease-area standards as that collaboration has been a great success and addresses concerns about a less-than-optimal fit between standards and studies. With our study teams having a lot of "skin in the game" there is more enthusiastic use of the standards when they are customized to specific compounds.

CONTACT INFORMATION

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