SAS and the Intranet: How a Comments System Creates In-House Efficiencies
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ABSTRACT
A principal goal of SAS programming in a clinical setting is creating output that will be reviewed both internally and by external reviewing agencies. The Biometrics Department of Gilead Sciences, Inc. (GSI) has developed a Comments System that has streamlined the process of the internal review of tables, figures and listings (TFLs). GSI’s Comments System has created efficiencies, and further improvements to the system may be expected depending upon departmental analysis of available and future technologies.

INTRODUCTION
Gilead Sciences, Inc.’s (GSI) Comments System is designed to be used in conjunction with any planned analysis, not just analyses that are part of NDAs. In other words, any analysis that will become part of a clinical study report, which in turn will be reviewed by regulatory agencies for safety, efficacy, etc., is eligible for the Comments System. Even though the programming and biostatistics groups internally validate all analysis tables, figures and listings (TFLs), these outputs still must be evaluated by statistical, clinical (e.g., CRAs) and medical (e.g., physicians) reviewers. Their feedback is critical in moving the analysis to the final phase of completing the clinical study report. The Comments System is designed to ease the coordination involved among the various reviewers’ input of comments and the efforts of the programming staff to implement changes based on these comments.

HOW MEDICAL REVIEWERS PROVIDED COMMENTS PRIOR TO THE COMMENTS SYSTEM
GSI’s review process was mostly manual and quite cumbersome. During the pre-intranet era, TFLs were computer-generated, but huge amounts of paper were still needed in the review of SAS output.

Several issues were inherent in this process:
1. Limited copies available to be shared among the medical reviewers.
2. Physical space limitations in storing paper copies, especially when many versions of output were generated.
3. Time and effort expended by programming staff after the reviewers’ comments were submitted, including the interpretation of the reviewers’ meaning, especially when there were apparent contradictory comments or repetitive comments.
4. Inability to see prior reviewers’ comments.
5. Logistical issues in getting everyone, programmers and medical reviewers, in the same room to meet and discuss the comments on the output.
6. Logistical challenge of compiling all reviewers’ comments.
7. Difficulty in maintaining version control of the documents.

Figure 1 below illustrates the analysis review process prior to the advent of the Comments System:

Figure 1: Output Review Process Prior to Comments System

<table>
<thead>
<tr>
<th>Statistical Programming</th>
<th>Generate Paper Tables, Figures, Listings</th>
<th>Submit Output to Statistical Reviewers for Comments</th>
<th>Submit Output to Clinical Reviewers for Comments</th>
<th>Changes Required?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Submitted Output to Medical Reviewers for Comments</td>
<td>Programmers Interpret Statistical Reviewers Comments</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Programmers Interpret Clinical Reviewers Comments</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Programmers Interpret Medical Reviewers Comments</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Statistical Programming and Medical Reviewers Meet to Discuss Programming Changes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Incorporate Output into Clinical Study Report for FDA Review</td>
</tr>
</tbody>
</table>

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HOW GSI’S MEDICAL REVIEW PROCESS HAS CHANGED

Compare the flow chart above to Figure 2 below which maps the current review process:

Figure 2: Output Review Process With Current Comments System

Three tools are used in synchronization: the company intranet, a SQL server database and SAS. Together, these tools have formed a review process that created the following efficiencies:

1. Any reviewer with appropriate access privileges can view the output.
2. No or minimal paper, therefore eliminating physical storage as an issue.
3. Reviewers can verify output online, post comments, read one another’s comments and respond to previous reviewers’ comments.
4. Virtual elimination of comment redundancy and contradiction among reviewers – not only from seeing each other’s comments, but also from administrative rules of not being allowed to change comments once posted.
5. Logistical simplification – less of a need to have everyone meet to discuss reviewers’ comments. Programmers can view comments online and make changes as needed.
6. Audit trail: version, reviewer and date-time information for all comments can be seen online.
7. Easy to print out all comments in one table.

HOW GSI MIGRATES TABLES, FIGURES AND LISTINGS TO THE INTRANET

After programming of the study analysis TFLs is completed, the lead programmer is responsible for setting up the intranet directory folders that store the output and updating and executing the code that will post the output to the intranet.

The process is depicted in Figure 3:

Figure 3: Migrating Output from UNIX to the Intranet

Things to keep in mind:

1. Each step in the process above takes 5 minutes or less to perform.
2. The intranet directory structure should already mirror the production directory structure – e.g., /<compound name>/<study number>/task.
   What the lead statistical programmer adds is a folder that describes what the current version of the TFLs are (/version1, /draft1, etc.).
3. The code is DATA step driven, converts the output into .pdf and .html files and generates the menu which allows the end-user to directly open the output files in the intranet. The programmer basically has to update macro variables that contain the study and version information in w_intranet.sas for it to execute properly.
4. Permissions access is done in MS Windows Explorer using File-Properties – see Figure 4 below.
WHAT EXACTLY IS GSI’S COMMENTS SYSTEM?

The basic components of the Comments System are the TFLs, a database for comments storage linked to the TFLs, the corporate intranet for viewing the TFLs, software facilitating the entering and viewing comments online and reporting software.

The database is in Microsoft SQL Server. It basically consists of two tables of importance:

1. TFLIDs (i.e., tables/figures/listings identification) – one unique TFLID record per TFL
2. Comments – one record per comment, linked to the unique TFLIDs. There can be zero or many comments per TFLID

In addition, there is a SAS dataset stored on Unix that mirrors the TFLIDs table. It is used to help determine if a TFL is new to the system or already exists. If new TFLs are encountered, a SAS program exports those records to a flat file for subsequent import into the TFLIDs table. Data are imported to and exported from the database via flat text files.

As for the Comments System software, some active server pages (ASP) routines are used to facilitate the viewing and entry of comments on the intranet. The routines were originally from open source threaded bulletin board software that were adopted for this use. The software allows any user to view current comments, respond to a comment or start a new comment thread.
Figure 5 below depicts the process flow of GSI’s Comments System:

**Figure 5: Comments System Process**

![Figure 5: Comments System Process](image)

**IMPORTING TFL IDENTIFICATION (ID) RECORDS TO THE COMMENTS SYSTEM**

Before the reviewers’ comments are entered into the system, the database needs to be updated with the patient identification records from the TFLs. This is necessary in order for the comments to be appropriately linked to their respective TFLs.

In addition to the SAS-generated TFL output, there are also text files which get loaded into the Comments System. There is one TFL ID record per TFL registered in the system. The TFL ID records are generated as comma-delimited text files by the SAS program that prepares the html menus. Figure 6 below illustrates this:

**Figure 6: View of TFL ID Records**

![Figure 6: View of TFL ID Records](image)

SQL Server is then used to load the TFL ID records into a table which basically looks like text file above.

**ENTERING COMMENTS INTO THE COMMENTS SYSTEM**

Once the TFLs have been posted onto the intranet, the medical reviewers can view them and input their comments directly online; this information, in turn, is stored in the Comments System database.

Figures 7, 8 and 9 show how the reviewers enter their comments:
EXPORTING COMMENTS FROM THE COMMENTS SYSTEM
Reviewer comments must be exported from the Comments System database in order to execute a comments report for a given study. This is done with SQL Server and SAS working in tandem.

The comments database is simply extracted as a text file. A SAS program reads it, extracts the records of interest and prepares the report. Just as before with the process of migrating TFLs to the intranet, the programmer needs to update the macro variables containing study and version information so that the code properly executes DATA step and PROC REPORT routines that will generate a comments report. The report is produced in both text and .rtf format and is illustrated below in Figure 10:

CONCLUSION
Of course, the system can be further streamlined by taking advantage of new or existing technologies. But any potential implementation of such software must be balanced with cost considerations. For example, by using SAS/ACCESS software, comments could be directly loaded to and extracted from the database using SAS. For various reasons, including what we regard as undue additional expense, we continue to use this hybrid system of SQL Server, SAS and data import / export via flat text files.
Overall, GSI's Comments System has generated significant efficiencies in the review of clinical analysis output: (1) communication – reviewing output and entering comments online lessen the likelihood for misinterpretation; (2) resources saved – less paper; and (3) time saved – no waiting for limited hard copies of output and less need for face-to-face meetings to discuss the output.

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