

Paper 016-2012

Automated Process for Routine Clinical and Safety Data Monitoring Reports: An Integration of EDC Database, Microsoft Outlook, and SAS®

Songtao Jiang, MA, MS and H. Terry Liao, PhD, Boston Scientific Corporation, Marlborough, MA

ABSTRACT

In the pharmaceutical or the medical device industry, routinely reporting clinical and safety data is required to meet the ICH Guideline for Good Clinical Practice. However, the repeated report production per se is sometimes time-consuming and requires a significant amount of resources. Therefore, an innovation for improving the current reporting process is always a demand. An automated process leveraging the integrating features of an electronic data capture (EDC) database, Microsoft Outlook, and SAS is proposed. Specifically, a completely data-driven process for generating routine reports by using Visual Basic Application (VBA) codes incorporated with moderate SAS coding is deemed cost-effective. The process can be applied to any industry where a programming professional is equipped with Microsoft Outlook and SAS as a working platform.

INTRODUCTION

In the pharmaceutical or device industry, there are many regulatory requirements and guidelines for monitoring clinical trials. According to the ICH guidelines for Good Clinical Practice (GCP): *“ICH E6 (R1) 1.38 Monitoring: The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).”*

To support GCP, there are many monitoring reports required by regulatory agencies, trial sponsors and investigators such as: clinical monitoring, safety monitoring, progress report, and many more. A huge amount of time and resources are spent on these reports. Here are some common characteristics of these monitoring reports that we will be focusing on in this paper:

- Happen daily, weekly, biweekly or monthly
- Quick report delivery
- SAS programs well developed, minimal modification required
- Time consuming but tedious to rerun

Given the nature of these reports, to improve efficiency, and to save time and resources, an automated process without human intervention became highly desired. However, before we could set up an automated process, we have to overcome a few technique hurdles.

PREVIOUS PROCESS

Reports are scheduled to be rerun on a regular basis. To get the data, a recurring data extract in EDC database is scheduled. All following tasks are manually done.

- Log into the FTP site and download the zipped SAS data sets generated from EDC.
- Get other data – mostly come from email attachments in MS Outlook.
- Prepare data – create folders, move data, unzip the data sets, etc.
- Prepare programs – move, copy, modify SAS codes accordingly.
- Run programs and check results and log
- Send out reports

Many of above activities are time consuming and tedious work. The process is not data-driven. Since the SAS programs are already well developed and minimal or none modification required, it is not very efficient to have human involvement in the process. Human factor is the major bottleneck and most likely creates errors during the reporting

Automated Process for Routine Clinical and Safety Data Monitoring Reports: An Integration of EDC Database, Microsoft Outlook, and SAS®, continued

process. Given the power of SAS system, there should be a better or more elegant way to get these kinds of jobs done.

AUTOMATED PROCESS

WORKING PLATFORM

The process is tested under the following working environment:

- A electronic data capture (EDC) database
- MS Outlook 2010
- SAS v9.2 on Windows XP

The EDC database hosts most of the clinical trial data. The data are electronically captured from every study site. We extract data by logging into the database. The data type is the zipped file containing SAS data sets. There are two options to get the data. One option is to extract the data to an FTP site. Then you can log into the FTP site to download the data. The other option is to let the EDC database email the data as an attachment.

Other sources of data may come in as an email attachment via MS Outlook system. In this situation, any kind of file types is possible as the data sources for reports, such as: xls, csv, SAS transport file, etc.

PC-based SAS v9.2 is our statistical software to create reports. Windows XP is the operating system.

IDEA FOR INTEGRATING THREE MAJOR COMPONENTS

As described in previous section, we have EDC database, MS Outlook attachments as data sources, and SAS system as the reporting tool. A natural question for us is that “can we unify these two data sources”? Since EDC can send the data via email as attachment, it seemed we have found a way to unify them by using email attachment as the only data source. But another immediate question is “can we automatically download the attachments and save them in a working folder?”

As many of you may know, MS Outlook provides a function called “Rules and Alerts”. By using this function, you can start an application under some specified conditions. This function could be used to realize the true data-driven process.

By now, everything points to MS Outlook. If we could find a way to download the email attachment data in MS Outlook, we should be on the right track to overcome the two technique hurdles and integrate these three major components of our working platform into a working system.

TECHNIQUE HURDLES

There are two major technique hurdles ahead of the proposed automated process.

- To get data from EDC database or email attachment automatically.
- How to make it a true data-driven process.

There are some other minor issues which can be solved using moderate or advanced SAS programming techniques.

SOLUTION

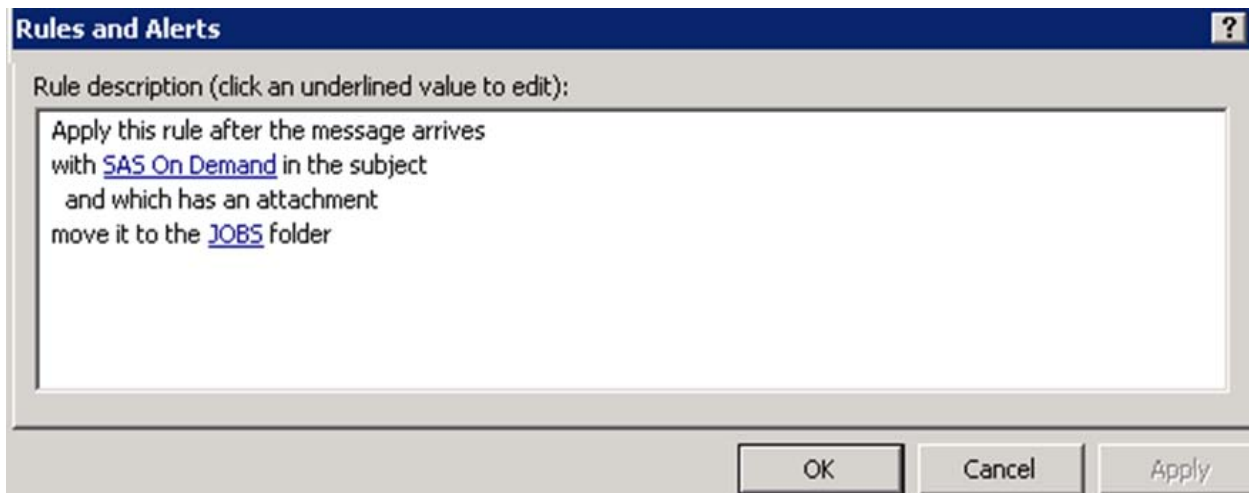
The solution is to use some very simple Visual Basic Application (VBA) code and the “Rules and Alerts” function in MS Outlook. Combining MS Outlook Rules with VBA code, we are able to save email attachment files to some specified folders. Then using MS Outlook Rules, we are able to make this process a true data-driven automated process without human intervention.

IMPLEMENTATION

- Schedule a recurring data extract in EDC database; specify the data to be sent to your email account as an attachment on a regular basis.

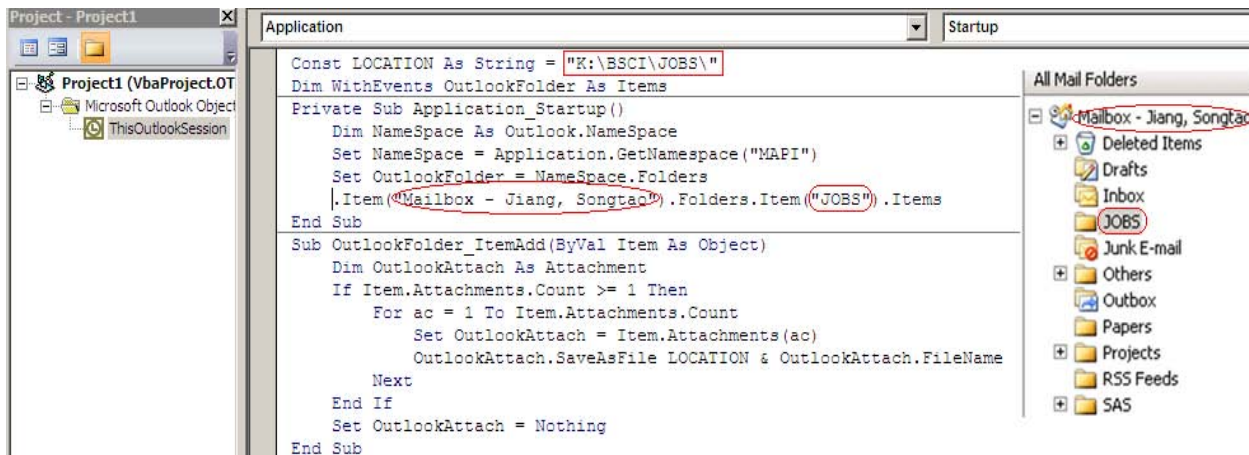
Automated Process for Routine Clinical and Safety Data Monitoring Reports: An Integration of EDC Database, Microsoft Outlook, and SAS®, continued

- Create an MS Outlook Rule which can move the specific emails to a mailbox folder. For example in the following screen shot (Display 1), we set the rules to move emails with “SAS on Demand” in subject field and an attachment into an email folder called “JOBS”.



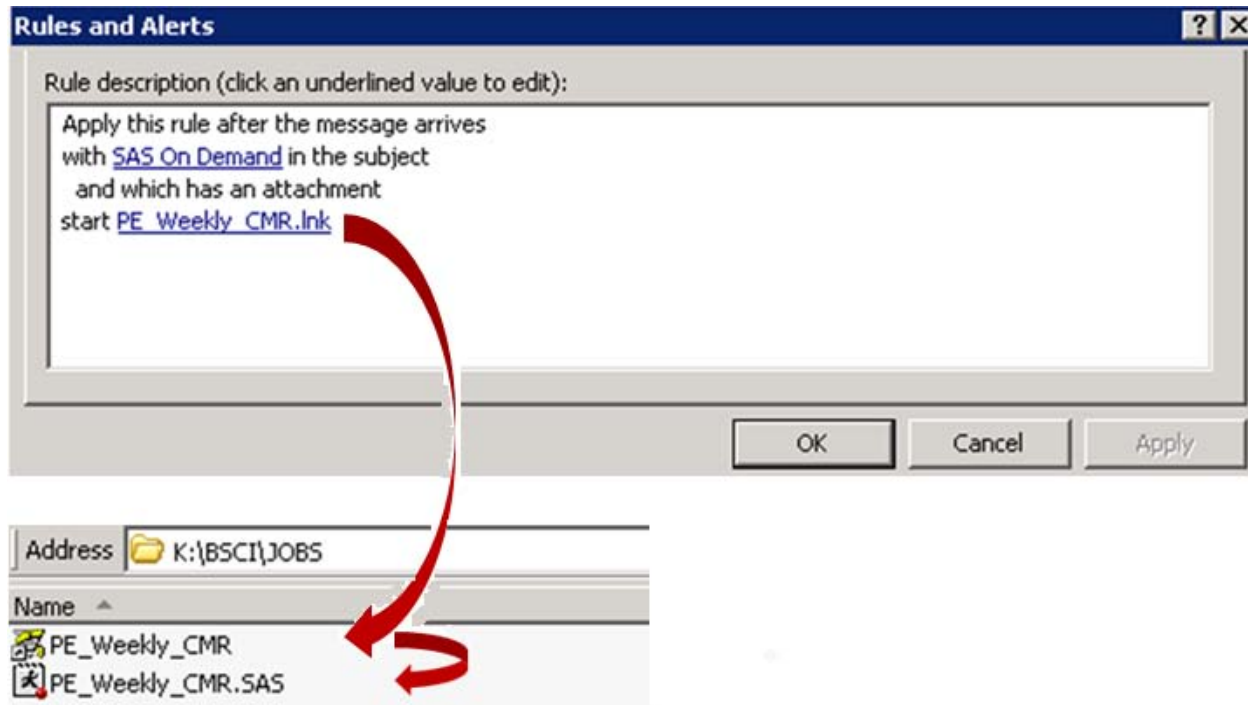
Display 1. MS Outlook Rules and Alerts – Receiving Data

- A piece of simple VBA code automatically extracts email attachments and saves them to any indicated location (Display 2). In the MS Outlook window, use ALT+F11 to activate the VBA editor and type in the VBA code. In this case, the VBA code detects if a new email has arrived in the “JOBS” folder with an attachment. If there is a new email with an attachment in the “JOBS” folder, the piece of VBA code will save the attachment to the location K:\BSCI\JOBS.



Display 2. MS Outlook VBA Code – Saving Data

- To implement the true data-driven process and launch the SAS system upon the event of receiving data in the emails, another MS Outlook Rule has to be set up. Once the data has been saved on a hard drive or network folder in previous steps, the SAS batch mode will be activated through MS Outlook Rule. In Display 3, the Rule starts an application. In our case, it is the SAS with batch mode. It loads the SAS program “PE_Weekly_CMR.sas”. This is the entry point. This SAS program will be serving as a control center of all your related work.



Display 3. MS Outlook Rules and Alerts – Activating SAS Program

- Prepare programs and data, set parameters or macro variables, and make logic checks if necessary in the entry program. In our case, we make all necessary preparation in the “PE_Weekly_CMR.sas”. The following are some SAS codes that are typical in this program. The X command is used to create a new folder, unzip data files and copy existing programs.

```
x "mkdir L:\PE\Biostatistics\Data\20111025";
x "unzip -P pwdforpe -o K:\BSCI\JOBS\sjiang_PE*.zip -d L:\PE\Biostatistics\Data\20111025";
x "mkdir L:\PE\Biostatistics\CMR\20111025";
x "mkdir L:\PE\Biostatistics\CMR\20111025\SASCode";
x "copy L:\PE\Biostatistics\CMR\20111018\SASCode\*. * L:\PE\Biostatistics\CMR\20111025";
```

The SAS FILENAME statement and DOPEN function are used to check if certain data is ready.

```
filename indir "L:\PE\Biostatistics\Data\20111025";
data _filenames_;
  length filename $200.;
  did=dopen("indir");
  filename=dread(did,i);
  rc=dclose(did);
run;
```

- Call other programs to create your reports. We use the SAS %INCLUDE statement. For example:

```
%include "L:\PE\Biostatistics\CMR\20111018\SASCode\0040_followup_status.sas";
```

- Check the log for errors and warnings by using SAS to scan the log file, or for any other keywords you want to identify after you run the report programs. Quality should never be compromised especially when we use the automated process. If possible, you should set up checkpoints within your programs to check any possible programming or data issues.
- Send out the reports to project team via emails or a warning letter to yourself depending on the check results based on previous step. If the reports passed quality check, they can be sent out automatically via email attachment to the project team. If they did not pass, a warning letter should be sent to yourself stating that a manual review is required. The code is as following :

Automated Process for Routine Clinical and Safety Data Monitoring Reports: An Integration of EDC Database, Microsoft Outlook, and SAS®, continued

```

options emailsys=smtp emailhost=bscmail.bossci.com;
filename demo email;
data _null_;
  file demo
    to=('peprojectteam@bsci.com')
    subject='PE CMR Reports'
    attach='L:\PE\Biostatistics\CMR\20111025\Report\PE_CMR.doc';
  put "Dear Project Team,";
  put " ";
  put "Attached Please find the PE CMR Report.";
  put " ";
  put "Regards,";
  put "Songtao";
run;

```

A CASE STUDY

In this study, we compare two processes that both run on a clinical monitoring report (Table 1). They are automated process and manual process on left and right, respectively. The total time used to create a report in the automated process is 118 minutes compared with more than 148 minutes used in the manual process. There is no human and computer interaction time spent for the automated process. The human-computer interaction time is about 45 minutes for the manual process, which included downloading data, unzipping data, creating folder, copying and preparing SAS programs (there may be some waiting period during this time). For the automated process, all the actions performed are outside of the regular working hours. But for the manual process, it is about 145 minutes of regular working hours. Because the automated process does not need human intervention, and it can start at any time, reports would be ready sooner and could be delivered earlier. In some situations, this could be very important.

Action (Automated)		Action (Manual)	
EDC Scheduled Extract to Email	0:01AM	0:01AM	EDC Scheduled Extract to FTP
Email Received with Data	0:09AM	0:09AM	Data Ready on FTP
Process Started	0:09AM		
Report Created	1:58AM		
Report Sent	1:59AM		
		9:00AM+	Start to Download and Prepare Data
		9:40AM+	Run SAS Programs
		11:20AM+	Report Created
		11:20AM+	Manual Review Started
		11:25AM+	Report Sent
Time to Create Report	118 mins	148 mins+	
Time with Human Interaction	0 mins	45 mins+	
Regular Work Hours Used	0 mins	145 mins+	

Table 1. Comparison on two processes

CONCLUSION

Given the huge amount of clinical data monitoring reports, a data-driven, human-free automated reporting process is highly desired. The proposed process can largely reduce the burden of these routine tasks. With less human intervention, more data-driven, and virtually longer working hours, the process can save a lot of time and human resources, and provide quicker report delivery. Thus, you can have more time and focus on other important work.

Automated Process for Routine Clinical and Safety Data Monitoring Reports: An Integration of EDC Database, Microsoft Outlook, and SAS®, continued

Furthermore, this process makes the non-stop project support possible with peace of mind. This process can also be applied to other industries with similar requirements.

REFERENCES

ICH HARMONISED TRIPARTITE GUIDELINE: GUIDELINE FOR GOOD CLINICAL PRACTICE E6 (R1), Current Step 4 Version, 1996

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Name: Songtao Jiang
Enterprise: Boston Scientific Corporation
Address: 100 Boston Scientific Way
City, State ZIP: Marlborough, MA 01752-1234
Work Phone: 508-683-4432
Fax: 508-683-5191
E-mail: jiangs@bsci.com
Web: <http://www.bostonscientific.com>

SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc. in the USA and other countries. ® indicates USA registration.

Other brand and product names are trademarks of their respective companies.