Clinical Data Dashboards for Centralized Monitoring Using SAS® and Microsoft® SharePoint®

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ABSTRACT

In recent guidance on risk-based monitoring practices, the Food and Drug Administration identified options for monitoring the data quality of a clinical investigation. Centralized monitoring is a practice in which clinical data management, statisticians, and/or clinical monitors[1] review the data on an ongoing basis and can easily identify the accuracy, completeness, and integrity of data. In this paper, we would like to describe the methods of developing an in-house tool using SAS® BASE (SAS® Institute, Cary, NC), GRAPH procedures (SAS® Institute, Cary, NC), and Microsoft® SharePoint® (Microsoft® Corporation, Redmond, WA) to achieve this goal. Centralized monitoring may decrease the cost of a clinical investigation and ensure identification of problems with the trial early on by maximizing the value of electronic data capture systems. Clinical dashboards created using SAS® BASE and GRAPH in conjunction with Microsoft® SharePoint® may provide cost savings, because most pharmaceutical/medical device companies frequently utilize these systems and no additional technology or human resources are required.

INTRODUCTION

Effective management of clinical trials is a cross-functional effort by clinical operations, clinical data management, programming and biostatistics and many more functional areas. In order to protect the safety of subjects, there is an increased need for regulatory oversight of clinical monitoring as the complexity of study designs increase with respect to the safety and efficacy of drugs/devices. At the same time, pharmaceutical and medical device companies are struggling with the overhead costs of clinical trials while ensuring the quality of data for a trial. In recent guidance by FDA regarding the approach for risk-based monitoring, an integrated approach with a combination of onsite monitoring and centralized monitoring was shown to improve the quality of data and protect the safety of subjects enrolled in a clinical trial. In a multicenter study, centralized monitoring may detect factitious data that may not otherwise found. (For instance, if there is a data fabrication with minimum or no variance and/or under/over reporting of the safety data.) Centralized monitoring also provides an opportunity to find the problems earlier during the trial and those deviations can be addressed early on to reduce the impact of a non-evaluable group at the end of study. This is an important concern in the conduct of a trial as a real-time look at the data distributions helps to evaluate the site performance and reinforces additional training requirement and feasibility of performing the trial by that particular investigator. Centralized monitoring also improves the team collaboration as a successful trial execution is a combined effort by various functional groups and the statistical monitoring helps to get the team involved early on from the study conduct and helps the team in understanding the complex longitudinal view of data compared to the discrete looks at data.

With the industry moving towards more of the electronic data capture techniques versus paper based trials, maximization of the benefits of electronic data capture can be realized when central monitoring techniques are used.

One of the most important steps in managing a risk-based approach for the monitoring of clinical trials is to identify the critical data. Critical data is the data which would ultimately support drawing the valid scientific conclusions and protecting the safety of subjects. With the advent of the new electronic data capture technologies with Onsite edit check process, much of the inconsistencies of the data with regard to the range checks, missing data and out of window visits can be easily identified. These checks work especially well at the level of individual subject data. In order to see the patterns of data, statistical approaches within and between sites is recommended.

METHODS

In this paper we would like to present a simple but elegant option in performing centralized monitoring using SAS and Microsoft Share Point. SAS is the number one choice in performing summaries for safety and efficacy reporting in Pharmaceutical/Medical Device/Biotech companies. Test data is simulated for a clinical trial to demonstrate the utility of clinical dashboards for the centralized monitoring. In developing this method, we have used Oracle Clinical RDC 4.6 as the electronic data capture methodology.

IDENTIFICATION OF DATA FOR CENTRALIZED MONITORING

Before implementation of this method, a cross functional team comprising clinical operations, data management and biostatistics is convened to identify the critical data points. The following items can be incorporated for the clinical dashboard. Aggregates (mean/median or counts) for each site and between sites were reported.

1. Enrollment numbers and completion status of the subjects
2. Safety Profile - # of Adverse Events, # of Related Adverse Events, # of Serious Adverse Events
3. Endpoint data – (Hypothetical) –
    a. Time to infection
    b. Number of complications post treatment
    c. Pain management
4. Protocol Deviations for the primary, secondary, exploratory and safety endpoint data
5. Data Management –
    a. Lag in data entry
    b. Source data verification
    c. # of data queries
    d. Resolution time for data queries
    e. Visit Calendar
    f. Missing CRF modules

Patient Profiles: Patient profiles of each subject for tracking of individual events within each patient. The following items are considered at each subject level.
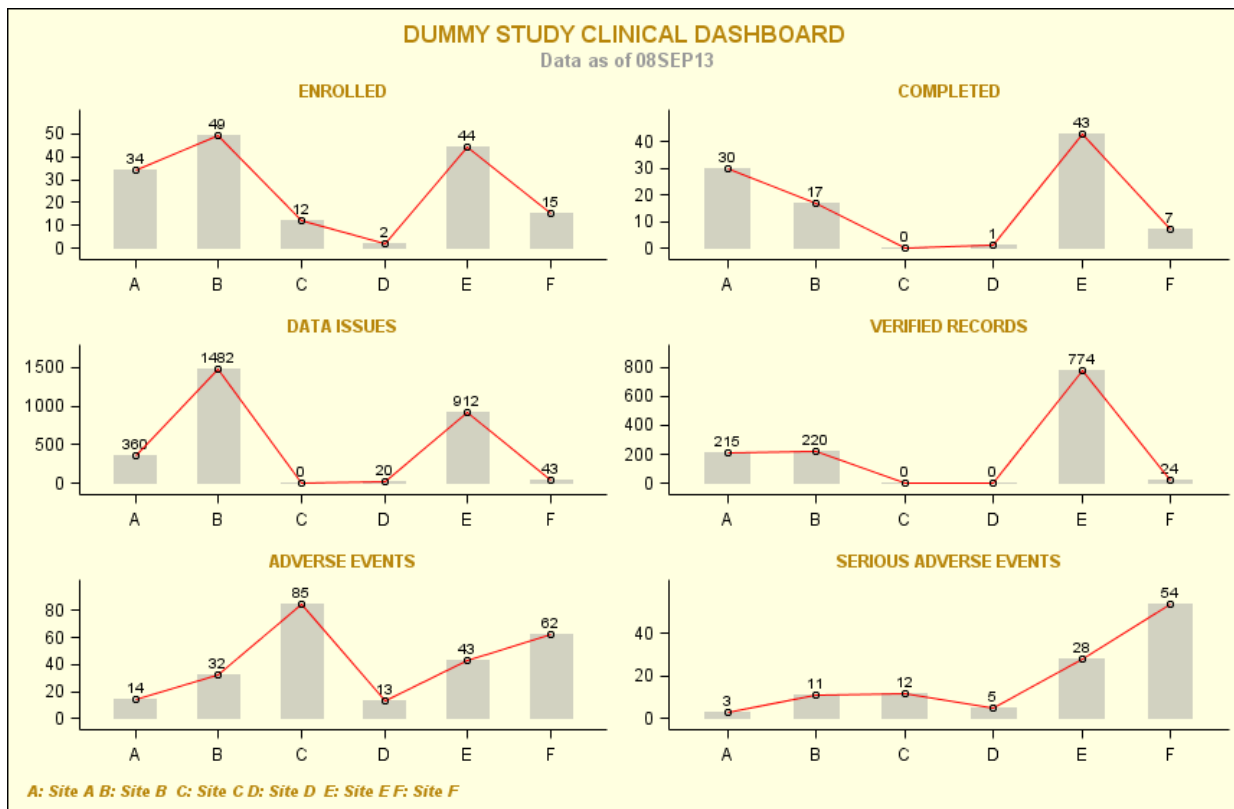
1. Demographic/Disposition information
2. Medical/Surgical History
3. Procedures related to Inclusion/Exclusion
4. Labs/Vitals
5. Adverse Events
6. Serious Adverse Events
7. Concomitant Medications

CREATING A DASHBOARD

Data needs to be arranged for the master dashboard page. We found it useful to have the data from various CRF pages to be pulled as an aggregate into one dataset for this purpose.

Sample data Structure for the main dashboard page:

sitec	pt	enrolled_patients	completed_study	adverse_events	serious_adverse_events	DISCREPRANCIES	VERIFIED_RECORDS	aehref	enhref	comhref	saehref	dathref	verhref
A	100	34	30	14	3	360	215	AE.htm	Enrolled.htm	Completed.htm	SAE.htm	disc.htm	ver.htm
B	100	49	17	32	11	1482	220	AE.htm	Enrolled.htm	Completed.htm	SAE.htm	disc.htm	ver.htm
C	100	12	0	85	12	0	0	AE.htm	Enrolled.htm	Completed.htm	SAE.htm	disc.htm	ver.htm
D	100	2	1	13	5	20	0	AE.htm	Enrolled.htm	Completed.htm	SAE.htm	disc.htm	ver.htm
E	100	44	43	43	28	912	774	AE.htm	Enrolled.htm	Completed.htm	SAE.htm	disc.htm	ver.htm
F	100	15	7	62	54	43	24	AE.htm	Enrolled.htm	Completed.htm	SAE.htm	disc.htm	ver.htm

CREATING SUBSEQENT DRILLDOWN

Additional data reports such as patient profiles, safety data displays and other relevant endpoints of the trial can be linked to the master dashboard page.

Sample Patient Enrollment Drill down Page:

Enrolled Patients
Please click on the Patient Number for drill down

Investigational Site=A

Unique Subject Identifier	Date of Informed Consent
A_1	01JAN2013
A_2	01JAN2013
A_3	01JAN2013
A_4	01JAN2013
A_5	01JAN2013

Enrolled Patients
Please click on the Patient Number for drill down

Investigational Site=B

Unique Subject Identifier	Date of Informed Consent
B_1	01JAN2013
B_2	01JAN2013
B_3	01JAN2013
B_4	01JAN2013
B_5	01JAN2013

CONCLUSION

The technique presented in this paper is an application of SAS Graph and SAS Base with the ODS output destination (html) to present the data in an easy and consumable form for the entire project team. This way provides an easy understanding of the complex data in comparison to the review of several hundred pages of line listings to check the quality of data. Collaboration in reviewing the data quality between the functional groups can be improved with this technique as it would provide real-time access to the data for everyone in the team and no functional role dependencies. Dashboards can be customized to the user needs and addition of drill down pages for many of the ad hoc reports is an easy add-on. The program to generate can be a scheduled job every night to refresh the data and can be run as needed for updated data. This would serve as an efficient tool for assessing the risk on an ongoing basis and appropriate actions can be taken to improve the data quality.

REFERENCES

US Food and Drug Administration. Guidance for Industry Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring (Aug 2011)

CONTACT INFORMATION

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Sample code

```
proc template;
  define Style Styles.dash;
      parent = styles.printer;
          replace fonts /
                    'docFont'            =("Arial",10pt)
                    'headingFont'        =("Arial",10pt)
                    'FixedFont'          =("Courier",8pt)
                    'BatchFixedFont'     =("Courier",8pt)
                    'FixedStrongFont'    =("Courier",8pt)
                    'FixedHeadingFont'   =("Courier",8pt)
                    'FixedEmphasisFont'  =("Courier",8pt)

                    'EmphasisFont'       =("Arial",8pt)
                    'HeadingEmphasisFont'=("Arial",8pt,Bold)

                    'StrongFont'         =("Arial",8pt)

                    'TitleFont'          =("Arial",8pt,Bold)
                    'TitleFont2'         =("Arial",8pt,Medium)
                    ;
            style table from table /
                    frame           =box
                    rules           =all
                    protectspecialchars=off
                    font            =fonts('docFont')
                    borderwidth     =.1pt
                    cellpadding     =1pt
                       cellspacing     =1pt
                    ;
      end;
run;

data cd;
      do sitec="A","B","C","D","E","F";
            do pt=100;
                    enrolled_patients=floor(uniform(383939)*pt);
                        completed_study=floor(uniform(383939)*enrolled_patients);
                        adverse_events=floor(uniform(8329329)*pt);

      serious_adverse_events=floor(uniform(32883)*adverse_events);

      discreprancies=floor(uniform(32883)*enrolled_patients)*floor(uniform(37733)*50)
*floor(uniform(37377)*5);

      verified_records=floor(uniform(32883)*completed_study)*floor(uniform(3323)*50);
        output;
      end;
end;
run;

data cd;
      set cd;
      aehref="http:\\portal.company.com\department/folder\Test
Study/Reports/AE.htm";
      enhref="http:\\portal.company.com\department/folder\Test
Study/Reports/Enrolled.htm";
      comhref="http:\\portal.company.com\department/folder\Test
Study/Reports/Completed.htm";
      saehref="http:\\portal.company.com\department/folder\Test
Study/Reports/SAE.htm";
```

```
        dathref="http:\\portal.company.com\department/folder\Test
Study/Reports/disc.htm";
        verhref="http:\\portal.company.com\department/folder\Test
Study/Reports/ver.htm";
run;

filename odsout '\\portal.company.com\Folder/DUMMY STUDY';
filename odsout1 '\\portal.company.com\Folder/DUMMY STUDY/Reports';
%let hardcoded_drilldown=\\portal.company.com\Folder/DUMMY STUDY/Reports;

ods graphics on/imagemap=on;
options nodate nonumber;
title;

proc template;
define statgraph sgdesign;
dynamic _sitec _enrolled_patients _sitec2 _completed_study _sitec3
        _discreprancies _sitec4 _verified_records _sitec5
        _adverse_events _sitec6 _serious_adverse_events
         _enhref _aehref _comhref _saehref _dathref _verhref
         _sitec7 _enrolled_patients2 _sitec8 _completed_study2 _sitec9
        _discreprancies2 _sitec10 _verified_records2 _sitec11 _adverse_events2 _sitec12
_serious_adverse_events2;

        begingraph / designwidth=860 designheight=561 border=true
BACKGROUNDCOLOR=cxFFFFE0 ;
        entrytitle halign=center 'DUMMY STUDY CLINICAL DASHBOARD ' /
textattrs=(color=cxB8860B size=12  weight=bold family='webdings');
        entrytitle halign=center "Data as of &SYSDATE." / textattrs=(color=gray99
size=10 family='webdings' weight=bold);
        entryfootnote halign=left 'A: Site A B: Site B  C: Site C D: Site D  E: Site E
F: Site F' / textattrs=(color=cxB8860B family='webdings'
        size=8 style=italic weight=bold );

        layout lattice /  rowdatarange=data columndatarange=data rows=3 columns=2
rowgutter=10 columngutter=10 columnweights=(0.49 0.51);
        layout overlay / wallcolor=CXFFFFFF walldisplay=none xaxisopts=( display=(LINE
TICKVALUES TICKS))
        yaxisopts=( display=(TICKS TICKVALUES LINE));
        barchart x=_SITEC y=_ENROLLED_PATIENTS / url=_ENHREF name='bar'
        datatransparency=0.56 display=(FILL) barlabel=true  barwidth=0.5
        discreteoffset=0.0  fillattrs=(color=gray99 );   ;
        entry halign=center 'ENROLLED' / valign=top location=outside
textattrs=(color=cxB8860B family='webdings' style=normal weight=bold );
        seriesplot x=_SITEC7 y=_ENROLLED_PATIENTS2 / name='series'
        display=(markers) connectorder=xaxis lineattrs=(color=CXFF0000 )
markerattrs=(symbol=CIRCLE );
        endlayout;
        layout overlay / wallcolor=CXFFFFFF walldisplay=none xaxisopts=( display=(TICKS
TICKVALUES LINE)) yaxisopts=( display=(TICKS TICKVALUES LINE));
        barchart x=_SITEC2 y=_COMPLETED_STUDY / url=_COMHREF name='bar2' barlabel=true
        datatransparency=0.56 display=(FILL) barlabel=true  barwidth=0.5
        discreteoffset=0.0  fillattrs=(color=gray99 );
        entry halign=center 'COMPLETED' / valign=top location=outside
textattrs=(color=cxB8860B family='webdings' style=normal weight=bold );
        seriesplot x=_SITEC8 y=_COMPLETED_STUDY2 / name='series2'
        display=(markers) connectorder=xaxis lineattrs=(color=CXFF0000 )
markerattrs=(symbol=CIRCLE );
        endlayout;
        layout overlay / wallcolor=CXFFFFFF walldisplay=none xaxisopts=(
display=(TICKS TICKVALUES LINE)) yaxisopts=( display=(TICKS TICKVALUES LINE));
        barchart x=_SITEC3 y=_DISCREPRANCIES / url=_DATHREF name='bar3'
        datatransparency=0.56 display=(FILL) barlabel=true  barwidth=0.5
```

```
        discreteoffset=0.0  fillattrs=(color=gray99 );;
        entry halign=center 'DATA ISSUES' / valign=top location=outside
textattrs=(color=cxB8860B family='webdings' style=normal weight=bold );
        seriesplot x=_SITEC9 y=_DISCREPRANCIES2 / name='series3'
        display=(markers) connectorder=xaxis lineattrs=(color=CXFF0000 )
markerattrs=(symbol=CIRCLE );
        endlayout;
        layout overlay / wallcolor=CXFFFFFF walldisplay=none xaxisopts=(
display=(TICKS TICKVALUES LINE)) yaxisopts=( display=(TICKS TICKVALUES LINE));
        barchart x=_SITEC4 y=_VERIFIED_RECORDS / url=_VERHREF name='bar4'
        datatransparency=0.56 display=(FILL) barlabel=true  barwidth=0.5
        discreteoffset=0.0  fillattrs=(color=gray99 );;
        entry halign=center 'VERIFIED RECORDS' / valign=top location=outside
textattrs=(color=cxB8860B family='webdings' style=normal weight=bold );
        seriesplot x=_SITEC10 y=_VERIFIED_RECORDS2 / name='series4' display=(markers)
connectorder=xaxis
        lineattrs=(color=CXFF0000 ) markerattrs=(symbol=CIRCLE );
        endlayout;
        layout overlay / wallcolor=CXFFFFFF walldisplay=none xaxisopts=(
display=(TICKS TICKVALUES LINE)) yaxisopts=( display=(TICKS TICKVALUES LINE));
        barchart x= SITEC5 y= ADVERSE EVENTS / url= AEHREF name='bar5'
datatransparency=0.56 display=(FILL) barlabel=true  barwidth=0.5
        discreteoffset=0.0  fillattrs=(color=gray99 );
        entry halign=center 'ADVERSE EVENTS' / valign=top location=outside
textattrs=(color=cxB8860B style=normal family='webdings' weight=bold );
        seriesplot x=_SITEC11 y=_ADVERSE_EVENTS2 / name='series5' display=(markers)
connectorder=xaxis
        lineattrs=(color=CXFF0000 ) markerattrs=(symbol=CIRCLE );;
        endlayout;
        layout overlay / wallcolor=CXFFFFFF walldisplay=none xaxisopts=(
display=(TICKS TICKVALUES LINE)) yaxisopts=( display=(TICKS TICKVALUES LINE));
        barchart x= SITEC6 y= SERIOUS ADVERSE EVENTS / url= SAEHREF name='bar6'
        datatransparency=0.56 display=(FILL) barlabel=true  barwidth=0.5
        discreteoffset=0.0  fillattrs=(color=gray99 );;
        entry halign=center 'SERIOUS ADVERSE EVENTS' / valign=top location=outside
textattrs=(color=cxB8860B style=normal family='webdings' weight=bold );
        seriesplot x=_SITEC12 y=_SERIOUS_ADVERSE_EVENTS2 / name='series6'
display=(markers)
        connectorder=xaxis lineattrs=(color=CXFF0000 ) markerattrs=(symbol=CIRCLE );;
        endlayout;
        endlayout;
endgraph;
end;
run;

ods listing close;
ods html path=odsout body="clinical_dashboard.htm" (title="clinical dashboard ")
style=dash;

proc sgrender data=cd template=sgdesign;
        dynamic _sitec="sitec" _enrolled_patients="'enrolled_patients'n"
_sitec2="sitec"
        _completed_study="'completed_study'n" _sitec3="sitec"
_discreprancies="discreprancies"
        _sitec4="sitec" _verified_records="'verified_records'n" _sitec5="sitec"
_adverse_events="'adverse_events'n"
        _sitec6="sitec" _serious_adverse_events="'serious_adverse_events'n"
        _enhref="enhref" _aehref="aehref" _comhref="comhref" _saehref="saehref"
_dathref="dathref" _verhref="verhref"
        _sitec7="sitec" _enrolled_patients2="'enrolled_patients'n" _sitec8="sitec"
_completed_study2="'completed_study'n"
        _sitec9="sitec" _discreprancies2="discreprancies" _sitec10="sitec"
_verified_records2="'verified_records'n"
```

```
        _sitec11="sitec" _adverse_events2="'adverse_events'n" _sitec12="sitec"
        _serious_adverse_events2="'serious_adverse_events'n";
run;

ods html close;


/*SUBSEQUENT REPORTS*/

data dm;
label sitec="Investigational Site"
        subjid="Unique Subject Identifier"
        infcondt ="Date of Informed Consent"
    ;
        format infcondt date9.;
  do sitec="A","B","C","D","E","F";
   do pt=1 to 5;
   subjid=catx("-",sitec,pt);
   infcondt='01JAN2013'd;
  output;
    end;
end;
run;

data icf_format;
 set DM; _subjid=tranwrd(subjid,"-","_");
 label="<a
href="||"&hardcoded_drilldown"||'PATIENT_PROFILE_'||strip(_SUBJID)||".html>"||strip(_S
UBJID)||"</a>";
 fmtname="$patfmt";
 type="C";
 start=subjid;
run;

proc format library=work cntlin=icf_format;
run;

ods html close;
ods html path=odsout1 body="enrolled.htm" (url=none)  style=dash;;

title1 "Enrolled Patients";
title2 "Please click on the Patient Number for drill down";

proc sort data=dm;
 by sitec subjid;
run;

proc report data=dm headskip missing split="~" style(header)={just=left};
     column     subjid infcondt
     ;
     by sitec;
     define subjid   / center  order order=internal format=$patfmt.;;
run;

ODS HTML CLOSE;


%macro _profiles;
%local i;

%do i=1 %to &totpat;

ods listing close;
ODS HTML path=odsout1 nogtitle image_dpi=100 body="PATIENT_PROFILE_&&pat&i...html"
```

```
style=dash;
/*CODE FOR CREATING PATIENT PROFILES*/
ods listing;
ods html close;

%end;
%mend;
```

```
style=dash;
/*CODE FOR CREATING PATIENT PROFILES*/
```