

Using the SAS® Information Delivery Portal in the Pharmaceutical sector

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ABSTRACT

This paper will demonstrate how the SAS® Information Delivery Portal can be used to assist the clinical trial reporting process and to speed up the data review process.

The solution presented here is the result of an investigation into how portal technology could benefit the data management and statistical programming functions in their efforts to present (interim) trial results to the various stakeholders in the field.

Topics are:

- Objectives;
- The portal;
- Content types;
- Portal structure;
- Study report;
- Validation;
- Security;
- Tips & next steps.

INTRODUCTION

This paper is meant to give an impression of what the portal can do for data review and clinical trial reporting. It will not cover all aspects of the SAS Information Delivery Portal but rather illustrate how the industry could benefit from it.

NOTE: All clinical information used within the paper and demonstration portal is dummy data, created by OCS Consulting for demonstration purposes only.

OBJECTIVES

The objective of this paper is to illustrate what the SAS Information Delivery Portal can do to assist in the clinical trial reporting process. For this purpose, OCS Consulting has developed a “proof of concept” demonstration of the SAS Information Delivery Portal presenting a broad range of examples to demonstrate the possible usage in the pharmaceutical sector.

THE PORTAL

WHAT IS A PORTAL?

A portal is a website that acts as a "doorway" to the Intranet or a portion of the Internet, targeted towards one particular person or group; An enterprise portal is designed to share collaboration in workplaces.

When breaking down a portal into elements the main element of the portal is a web site. This website has a navigation menu which points to different portal pages.

A portal page is a page within the portal that contains related information. For instance a page called "Validation" would contain information related to the topic "Validation".

The information on a portal page is stored in one or more "portlets". A portlet can be best described as a container for related information and can contain a broad range of items. Typically a portlet contains information such as a web page, an image, a hyperlink or an application. Applications can include news, weather reports, forums, and email.

Given the above a portal is therefore an environment that allows for a personalised virtual workspace to be created. Because a portal is available through a web browser, this workspace can be made available anytime, anywhere.

THE SAS® INFORMATION DELIVERY PORTAL

In addition to the functionality of a portal as described above, the SAS Information Delivery Portal provides a common front end to SAS software intelligence, providing a personalised virtual workspace which deploys the power of SAS software. The following image is a screenshot of the SAS Information Delivery Portal.

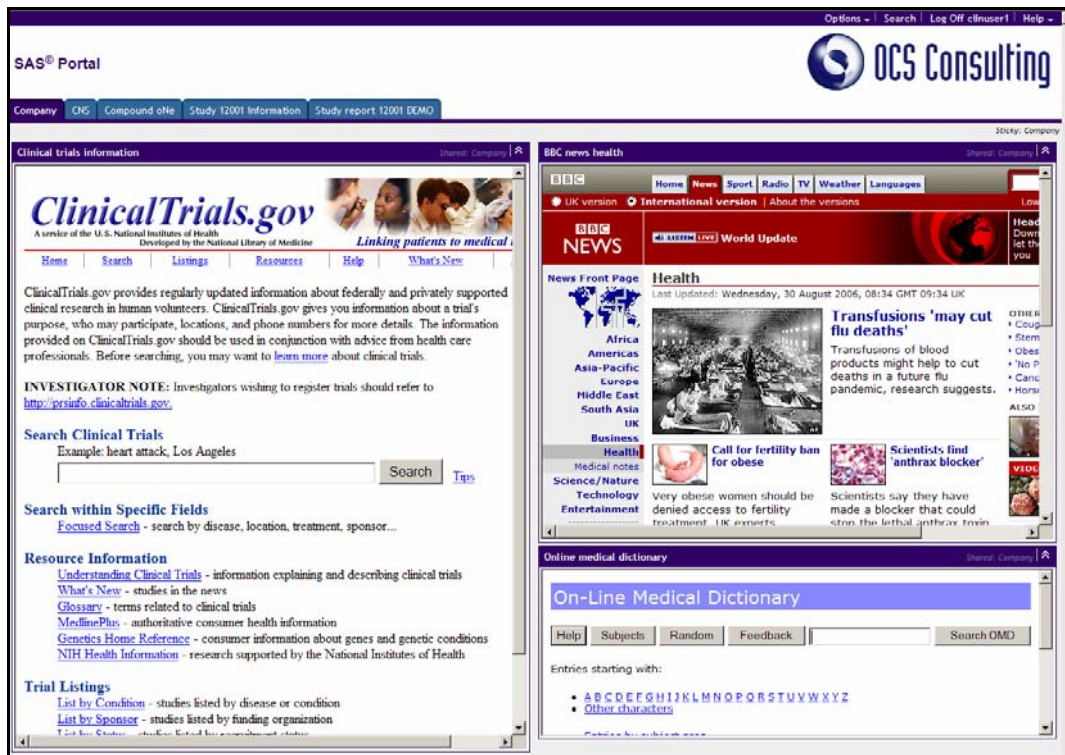


Image 1: The SAS® Information Delivery Portal

The appearance of the portal can be customised to represent the enterprises colours and logos. To illustrate this, the demonstration portal has been adapted to the colours and logos of OCS Consulting.

The portal exists of the following main screen components:

- Portal menu;
- Information header;
- Navigation menu;
- Portal page(s).

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PORTAL MENU

The default portal menu consists of the items: options, search, log off and help. The options menu allows the user to customise the portal, its content, the layout etcetera. Search allows to user to search for specific information within the portal. Log off will log off the current user. Help will open up the portal's help menu.



Image 2: Portal menu

INFORMATION HEADER

The information header contains information on what is currently displayed in the main portal screen. If, for instance, the result of a SAS program is displayed in the main portal window, the information header will present the name of the executed program.



Image 3: Information header

NAVIGATION

The navigation menu allows the user to navigate the portal content. Via the tabs the available portal pages can be accessed.



Image 4: Navigation

PORTAL PAGES

By means of the navigation menu the user can access the available portal pages. A portal page is a page that can contain one or multiple related portlets. The image below illustrates a part of the first portal page as presented in Image 1, with portlets, each showing an Internet site. The default content types available to the portlets are described in the next chapter.



Image 5: Portal page

CONTENT TYPES

Within a portal's portlet different types of content can be displayed. This chapter will give a short description of all content types used within the demonstration portlet. In addition to the types used within the demonstration portal, the SAS Information Delivery Portal contains other default content types. It can even be adapted to present custom content types. The following is an overview of all the default content types.

Types used within the demonstration portal:

- Stored process;
- Document;
- Link;
- Web application;
- Publication channel;
- Package;
- Syndication channel.

Types available but not used within the demonstration portal:

- Report;
- Information Map.

The content types not presented in the demonstration portal are used by other SAS software solutions such as Information Map Studio and Data Integration Studio and not solely by the SAS Information Delivery Portal; therefore it was decided to leave them out of the scope of this paper.

STORED PROCESSES

The stored processes, together with reports and information maps which are not part of the demonstration portlet, are the content type that differentiates the SAS Information Delivery Portal from a regular portal.

A stored process is a link to a SAS program which can be executed through the portal and has the ability to accept parameters, creating a possibility to develop a dynamic program. For instance, when a SAS program generates a listing on all subjects, it would be possible for the user to select the subject ID(s) to present in the listing.

The output created by the stored process can be a package (the results can then be published) or the output can be streaming which means that it will be displayed within the portal.

The execution of a stored process is real-time; the results are the latest available results at the moment of execution.

Within the demonstration portal several stored processes are presented and because this is a feature not available within a regular portal the example stored processes are described in this paper (see the chapter on study report).

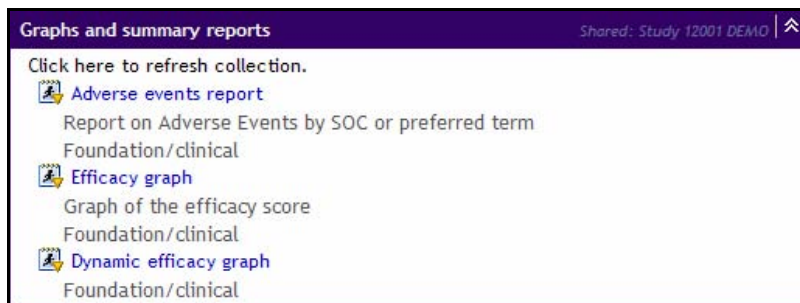


Image 6: Portlet with stored processes

DOCUMENT

Within a portlet it is possible to display links to documents. These documents can be either stored on a server, or in a "WEBDAV" repository, which is a storage available from the web.

Within the demonstration portal there are links to documents stored on a server. There are no links to documents which are stored in a WEBDAV repository. From the end-user point of view this makes no difference.

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LINK

Another method of distributing information is through links. A link can be to a document: Word, PDF, Excel, ... or to another website, to an image, etcetera. The demonstration portal displays links to documents: PDF and word.

WEB APPLICATION

Through a portlet that is capable of displaying a web site or a web application, the content of this site can be accessed and used. Since these are presented in a portlet, this portlet then functions as a mini-web browser.

The demonstration portlet contains several examples. On the main page two web sites and a web application (on-line medical dictionary) are presented and in the compound section a recruitment overview for studies conducted with this compound is displayed.

PUBLICATION CHANNEL

A publication channel is a channel to which reports can be “published”. A published report is a static report; it represents the status at the time of publishing. Therefore it could be used to distribute a snapshot of the data.

Users have the option to subscribe to channels they have access to. When subscribing the user will have access to a publication portlet, in which the publication channel subscriptions will be presented.

Within the demonstration portlet two publication channels have been created. One channel is called “Data review”, where subscribers would typically be data-management or medical personnel. The other is called “Report review”, where the subscribers would typically be statisticians, medical writers or medical personnel.

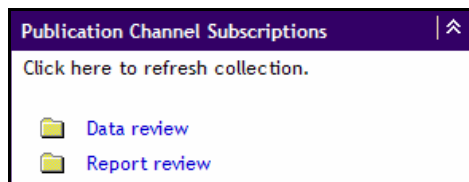


Image 7: Publication portlet

PACKAGE

A package is a collection of structured and unstructured content produced by the publication framework.

SYNDICATION CHANNEL

A syndication channel, also known as RSS feeds, provides a way for users to passively receive newly released content from a content provider. Typically a content provider publishes a “feed link” on their site to which end-users can subscribe. The content of this is controlled by the content provider. Example of syndication channels are for instance news channels, where the user receives “headlines” of the latest news, and when the link is clicked, the website presenting the article is shown. These channels are stored as a link in a portlet, so that multiple channels can reside in one portlet. When the link is accessed, the content (headlines) of the channel is presented on a result screen.

The demonstration portal uses both internal and external syndication channels. The external channel presents the latest news from “Science Daily” on the topic “Central Nervous System”. The internal channel presents the latest updates related to the study (Example topics are Protocol amendment, Next team meeting, Meeting minutes, etcetera.) providing a method of distributing study related topics to the study team.

PORTAL STRUCTURE

When developing the portal, it is important to define a solid structure to organise the information. As the portal can contain a large amount of different information, it is easy to lose track. For the demonstration portal a structure was defined that would assist a company to organise its information.

The main structure is defined as:

- Company;
 - └ Therapeutic area;
 - └ Compound;
 - └ Study;

This structure accounts for multiple therapeutic areas, multiple compounds and even compounds that reside in multiple therapeutic areas.

COMPANY

The highest level is Company. All pages within this level can contain information which the company staff is allowed to have access to. For example these pages can contain the company inter/intranet site, Internet news, company guidelines, rules and regulations etcetera.

THERAPEUTIC AREA

The second level is Therapeutic area. All users who are working within this therapeutic area can have the right to access all pages on this level. These pages can function as an information resource for the area by means of syndication channels on the topic, company documentation, discussion forums and an overview of studies which are available within this therapeutic area.

For the demonstration portal the therapeutic area CNS (Central Nervous System) was selected.

COMPOUND

The third level is Compound; this should be accessible to all users working on the compound within the therapeutic area. These pages can function as an information resource, like the therapeutic area pages, but on a more detailed level. Next to the compound information, the pages could contain a graphical overview of the recruitment by country for the studies conducted for this compound.

For the demonstration portal the dummy compound "Compound oNe" is used.

STUDY

The lowest level is the level of Study. All users working on this study should have the right to access these pages. These pages can be divided into two areas: study information and study report.

Study information can contain information such as the study protocol, the statistical analysis plan, procedures, news from the study team etcetera. Also an overview of outstanding questions regarding study data can be presented, so that when a possible data issue has been encountered, it can be verified whether this has already been identified by data management.

The study report contains the SAS stored procedures which assist in reviewing and create (part of) the study report. The stored procedures which are part of the demonstration portal are described in the next chapter "Study report".

For the demonstration portal the dummy study "12001 DEMO" is used.

STUDY REPORT

The study report page is the page of the demonstration portal where the stored processes are presented. These stored processes were created to give an impression on how they can be of added value to a pharmaceutical company. Therefore these examples can be seen as a “proof of concept” to build upon.

The examples demonstrate the usage for both data review purposes as well as report review purposes. Also the advantage of creating dynamic results, because the result can be outputted to web browser, is demonstrated.

All stored processes described in this section are real-time; this means that the latest known status of the data at the moment of execution will be presented.

PATIENT PROFILES

The patient profile portlet has three types of patient profile listings. The first one is a listing of the patient profile where all patients are presented sequentially. The second one will produce the same overview, but before the listing is created the user will be presented a parameter selection screen allowing the user to select the patients to be included in the listing, with a minimum of 1 patient.

The last type is the graphical version of the patient profile. This table is created as an HTML table and can therefore benefit from both graphic and dynamic functionalities. It contains the domains Adverse Events, Drug accountability and Vital Signs. To assist the reviewing process, the user has the ability to expand and collapse the different domains allowing two domains to be displayed directly underneath each other.

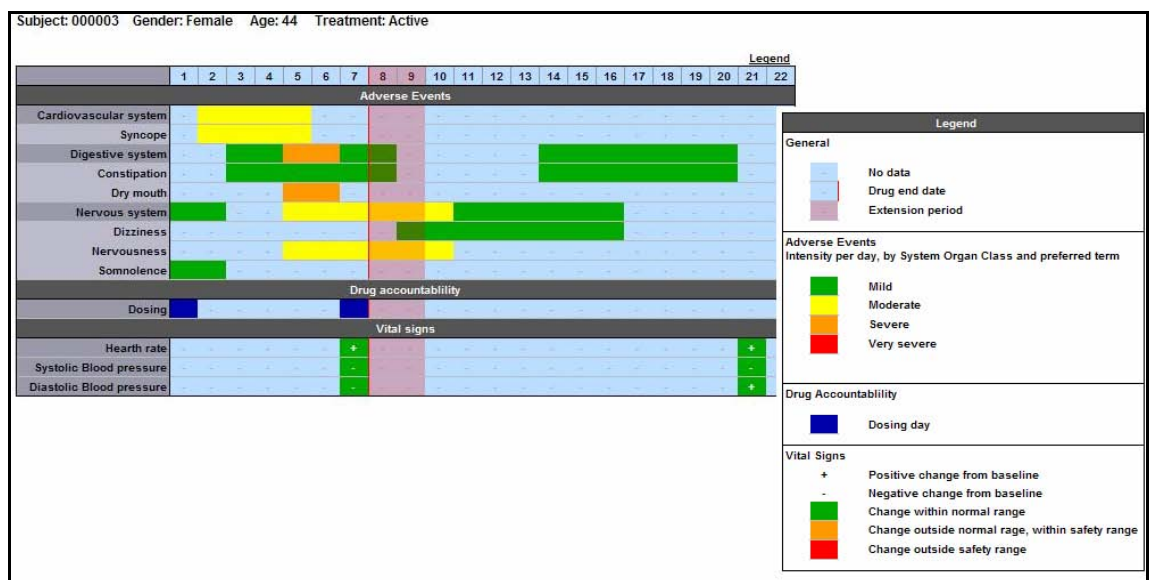


Image 8: Graphical patient profile

The Adverse Events section contains all Preferred Terms listed per System Organ Class. The System Organ Class shows the maximum severity of the Preferred Terms occurred within this class. The user can also collapse or expand the System Organ Classes, hiding the detailed Preferred Term. The red line indicates drug end day and the reddish area indicates the extension period.

DISPLAY SAS DATASETS

This stored process allows the user to view the SAS datasets which are used for study reporting. When the stored process is executed a parameter selection screen is generated. On this screen the user can select the dataset to display from all datasets available *at that moment* which are listed in the drop-down box. When desired the user can define a “where clause” filtering the dataset. For example selecting only subjects “where age >35”. Because this screen is custom made, it is of course possible to create an extensive data-driven selection filter, but for proof of concept the manual input of the “where clause” suffices.

Image 9: Custom parameter screen

When the user clicks on the “execute” button the content of the dataset will be displayed within the portal.

sid	age	weight	height	gender	race	Treatment group	center	birthd
000003	44	74.5	191	Female	Caucasian	Active	Berlin	23OCT1955
000007	38	75.0	172	Male	Black	Active	Dortmund	28SEP1961
000008	37	75.5	171	Female	Caucasian	Active	Dortmund	28NOV1963

Image 10: Partial listing of the basechar dataset

LISTINGS

To demonstrate some of the possibilities of listings, the demonstration portal contains two different example listings: The Vital Signs listing and the Adverse Events listing.

For the Vital Signs listing it was chosen to generate the result immediately, bypassing a parameter screen. This means that the listing will be presented as is; No additional parameters can be set. Thus when the user clicks on the link, a Vital Signs listing will be displayed on the screen.

For the Adverse Events listing the parameter screen is bypassed as well. To illustrate how output reviewing could be performed, the Adverse Events listing contains a method for reviewing. For this process two types of users are recognised within the portal: *Study viewer* and *study reviewer*.

The *study reviewer* has the ability to attach comments to the Adverse Events listing. When a *study reviewer* opens the listing, three columns are shown: “View Comment”, “Post Comment” and “Remove Comment”.

Subject number	System organ class	Preferred term	Start date (day)	End date (day)	Intensity	Relationship to study drug	Action taken	View Comment	Post comment	Remove comment
000001	Body as a whole	Headache	05JAN1999 (3)	10JAN1999 (8)	mild	unlikely	none			
	Nervous system	Dizziness	05JAN1999 (3)	10JAN1999 (8)	mild	unlikely	none			

Image 11: Partial Adverse Events listing with Add comment window

By clicking on the “Post Comment” icon in the row where the *reviewer* wants to attach the comment, the *reviewer* will be prompted for the comment to be added. Once a comment has become obsolete, the *reviewer* can remove the comment by clicking on the “Remove Comment” icon.

The *study viewer* will see the Adverse Events listing with one extra column called “View comment”. If a comment has been applied to a row, a “View Comment” icon is displayed in the “View comment” column. When the study viewer hovers the mouse-pointer over a “View Comment” icon, the comment will appear.

Subject number	System organ class	Preferred term	Start date (day)	End date (day)	Intensity	Relationship to study drug	Action taken	View comment	Post comment	Remove comment
000007	Body as a whole	Face edema	27JAN1999 (3)	03FEB1999 (10)	moderate	unlikely	none			
	Digestive system	Constipation	11FEB1999 (18)	13FEB1999 (20)	mild	unlikely	none			
000008	Body as a whole	Headache	01FEB1999 (3)	06FEB1999 (8)	mild	unlikely	none			
	Nervous system	Dizziness	11FEB1999 (13)	20FEB1999 (22)	moderate	possibly	decreased			

Image 12: Partial Adverse Events listing for the study viewer

SUMMARY REPORTS

The last example table is the Adverse Events summary report and demonstrates several report settings. For example purposes it is possible to override the default title or choose whether to generate this report by Preferred Term or System Organ Class. Finally the user can select the output type to illustrate that portal output can be exported to different document types. This example uses the output types: Word document, PDF document and HTML.

Number (%) of subjects with AE, by System Organ Class

System organ class	Active treatment (N=16)	Placebo (N=14)
Body as a whole	6 (37.5)	7 (50.0)
Cardiovascular system	2 (12.5)	1 (7.1)
Digestive system	11 (68.8)	8 (57.1)
Nervous system	7 (43.8)	9 (64.3)

Image 13: Adverse Events summary report

When the HTML report is selected, the report displayed has drill-down capabilities. When clicking on one of the figures in the table, a new window is opened, displaying the records from the Adverse Events dataset which are used to calculate the figure. The image below shows the detailed information for “Body as a whole” for the “Active treatment” group displaying 7 events for 6 subjects.

Selected subset of the Adverse event report

subject number	system organ class	preferred term	start date (day)	end date (day)	intensity	relationship to study drug	action taken
000006	Body as a whole	Asthenia	30JAN1999 (10)	01FEB1999 (12)	mild	unlikely	none
	Body as a whole	Flu syndrome	09FEB1999 (20)	. (.)	moderate	possibly	none
000007	Body as a whole	Face edema	27JAN1999 (3)	03FEB1999 (10)	moderate	unlikely	none
000014	Body as a whole	Face edema	22FEB1999 (9)	22FEB1999 (9)	mild	probably	none
000017	Body as a whole	Face edema	20FEB1999 (4)	27FEB1999 (11)	moderate	unlikely	none
000027	Body as a whole	Face edema	18MAR1999 (5)	19MAR1999 (6)	moderate	unlikely	none
000029	Body as a whole	Headache	30MAR1999 (8)	30MAR1999 (8)	mild	unlikely	none

Image 14: Adverse Events summary report detailed information

Of course it would be possible to create a link in the listing above that would display for instance the patient profile for the subject clicked on, but for proof of concept the example suffices.

GRAPHS

The last stored processes within the study report session are the graphs. There are two types of graphs presented: a static and a dynamic graph. The static graph in this example will produce an image of the Efficacy parameter. The dynamic graph presents the same graph, but because it is presented in a web browser, the user can change the type of the graph (such as bar chart, pie chart, etcetera.), the colours and many other settings.

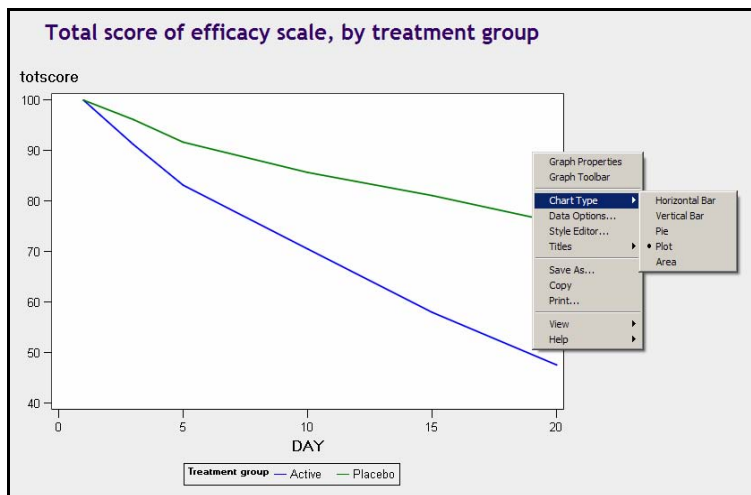


Image 15: Dynamic graph

VALIDATION

An important topic in the pharmaceutical industry is validation. To get a clear understanding of the impact on validation, it is important to understand the main difference between a regular SAS program, and a stored process.

The following lines of code are a snapshot of a regular SAS program generating a Vital Signs listing.

```
%*****;
%* Output the listing *;
%*****;
options ls=126;
title "Vital Signs";

proc report data=work.vitlis headskip split = '~' spacing=4 nowindows;
  column sid vitstr hrtxt bp;
  define sid      / order  'Subject no.'          Spacing=0      width=7 ;
  define vitstr   / display 'Start date (day)'      width=16;
  define hrtxt    / display 'Heart rate'           left              width=5 ;
  define bp       / display 'Blood pressure~(systolic/diastolic)' width=25;

  break after sid / skip;
run;
```

The changes to be made to this program, so that it can function as a stored process, are minimal.

Before the program starts outputting (proc report), the SAS reserved macro call “%STPBEGIN;”, which comes with the SAS System version 9 architecture, must be inserted in the program. When the program stops outputting (run of proc report), the SAS reserved macro call “%STPEND;” must be inserted in the code. This tells the SAS System that the output is the output of a stored process, and works similar to the BASE SAS procedure “proc printto”. The snapshot of the code when changed to a stored process is listed below.

```
%*****;
%* Output the listing *;
%*****;
options ls=126;
title "Vital Signs";

%stpbegin; /* Re-direct the output */

proc report data=work.vitlis headskip split = '~' spacing=4 nowindows;
  column sid vitstr hrtxt bp;
  define sid      / order  'Subject no.'          Spacing=0      width=7 ;
  define vitstr   / display 'Start date (day)'      width=16;
  define hrtxt    / display 'Heart rate'           left              width=5 ;
  define bp       / display 'Blood pressure~(systolic/diastolic)' width=25;

  break after sid / skip;
run;
%stpend; /* Close re-direction*/
```

Given the example above, the difference in validating a “regular” SAS program and a stored process is minimal. In general you could state that all output created with a SAS program producing static output, will require minimal changes to be transformed into a stored process, and therefore the impact on validation is minimal. When desired the portal is capable of creating a SAS log of the executed process.

Of course the portal offers a multitude of possibilities for creating dynamic output, some of which are described in the “study report” chapter (e.g. summary report with drill-down capabilities and the dynamic graph). This would require alternative validation to receive the status of validated program. Since these programs are used to gain insight into the data and assist with reviewing rather than for reporting to authorities, validation is less of an issue.

SECURITY

Due to the confidential nature of most clinical data, security is an important topic as well. For this paper two types of security will be differentiated: access to the portal and access within the portal. Because the portal is available through a web browser, it could be made accessible anytime, anywhere. How this can be secured has more to do with accessing secure sites (https) than with the portal itself, therefore this will not be discussed within the paper.

ACCESS WITHIN THE PORTAL

Access to the portal itself is granted via a logon procedure. The user has to specify username and password which are verified by the same procedure as when the user would log on to the company network. The portal makes use of Single Sign On, this means that once logged on no credentials are requested until the session ends when the user logs off or by means of a session time-out.

One of the advantages of the SAS Information Delivery Portal is that the security within the portal is regulated through the SAS metadata architecture. This makes maintenance easy, and assists in solving the issue of access to data and securing the execution of SAS programs.

The security is based on users and user groups. This security is applied to all portal elements such as: portal pages, portlets and portlet content. If a user has no access rights to a specific item, the item is not visible for this user. This means that the content of the same portal page can differ between users.

For the demonstration portal user groups were created reflecting the structure defined in the chapter "portal structure": Company, Therapeutic area CNS, Compound oNe, Study 12001 demo. This means that when a user is a member of the "Company" group, all items accessible to user group "Company", are available to this user, when the user is also a member of the "Therapeutic area CNS" all these items within "Therapeutic area CNS" are available etcetera.

Typically a user working on study "12001 DEMO" would be a member of all four groups mentioned above.

To differentiate users working on a study, two alternate user groups are defined: study viewer and study reviewer. This information is used to differentiate the roles within the study team. An example is illustrated in the topic "listings" in the "study report" chapter.

TIPS & NEXT STEPS

When implementing the portal environment the following tips could be of assistance:

- With regard to the basic structure of the portal; the basic content and security could be derived from existing Standard Operation Procedures as the portal is just a means to execute existing procedures;
- Demonstrating a “proof of concept” portal before the actual development assists future users in creating a better understanding of the possibilities which results in improved user requirements;
- When security is based on user groups instead of single users the maintenance becomes easier;
- When generating stored processes, make a clear differentiation between programs used to create the actual study report and programs that create dynamic output for reviewing purposes only. This will decrease the validation effort required.

CONCLUSION

The SAS® Information Delivery Portal can deliver added value to the daily process of the pharmaceutical sector. It delivers a front-end to the power of SAS software where security is integrated through the SAS metadata server. Furthermore, access through the browser allows the portal to be accessed anytime, anywhere (if desired) and creates the possibility to create flexible output which will speed up the reviewing process. When the portal is used to create traditional output, the validation does not differ much from the validation when the portal would not be used to generate this output.

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RECOMMENDED READING

<http://support.sas.com/rnd/web/portal/index.html>

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