QUALIANCE

Prototyping the Automation from SAP to Compiled Outputs

Copenhagen PhUSE SDE 2012

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Background

- ISS with 39 output templates – **2100+ outputs**
- A library of **standard module based macros** to reuse or update*
- **ISS SAP being adjusted** along the way with regular changes
- **Trial Derived Datasets** coming in the pool on a regular basis
- And **4 months to deliver** to validation team!

*: Building Block macro principle for Standard Program Library Design, Francis Dsa, PhUSE 2011

Goals

- Maximize **reuse of standard macros**
- Framework that **easily copes with changes** in Specs and addition of new trials to the pooled datasets
- **Keep work interesting** and focused on programming vs. repetitive and manual work
- **Acceptable performance** of full run that allows for quick feedback

Agenda

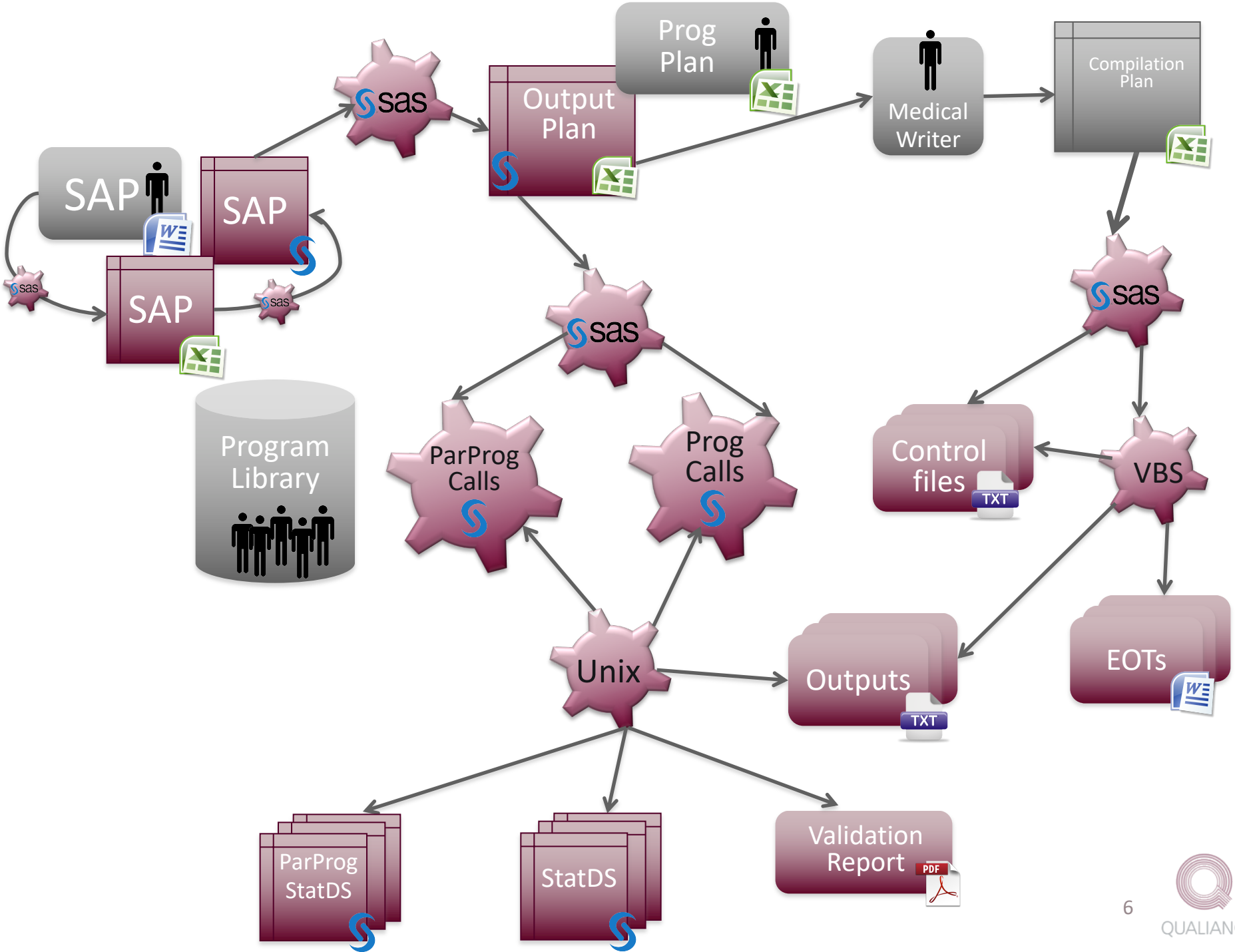
- Important decisions regarding validation
- Overall data flow
- Extracting SAP into SAS dataset
- Generating program calls
- Program design and validation
- Output information
- Conclusions

Important Decisions re Validation

- **Custom vs. standard programs, different effort**. It was not possible to update standard programs and revalidate them within the timeframe, parallel programming was the only viable option

- Parallel programming and **comparison had to be automated** due to the number of outputs

- **Cross-trial validation** was also carried out by an independent team once all trial derived datasets were available


Prog Plan
sas
Output Plan
Medical Writer
Compilation Plan
SAP
SAP
SAP
sas
sas
sas
sas
Program Library
ParProg Calls
Prog Calls
Control files
TXT
VBS
Unix
Outputs
TXT
EOTs
ParProg StatDS
StatDS
Validation Report
PDF

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Extracting SAP into a SAS dataset (1)

Copying the MS Word SAP to computer clipoard

1.3.1 Table: Adverse Events by SOC/PT

```
* Opening SPS in MS Word and copying it
  to PC clipboard;
%let rc=%sysfunc(system(start winword));

* Waiting 2 sec to give a chance to MS Word
  to open before continuing;
DATA _NULL_;
    T=SLEEP(2);
RUN;

filename word DDE 'Winword|System';

data _null_;
    file word;
    put '[FileOpen .Name = "' "&ISS_path." '"]';
    put "[EditSelectAll]";
    put "[EditCopy]";
    put '[FileClose]';
run;
```

Reference: Importing Data from MS Word into SAS, Jay Zhou, PharmaSUG 2009

1.3 Ad-hoc Data Handling

1.3.1 Table: Adverse Events by SOC/Preferred Term

	Treatment 1				Comparator				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Safety Analysis Set	xxx				xxx				xxx			
Total Exposure (yrs)	xxx.x				xxx.x				xxx.x			
All Adverse Events	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
SOC 1	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
Preferred term 1	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
Preferred term 2	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
Preferred term 3	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
.												
SOC 2	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
Preferred term 1	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
Preferred term 2	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
Preferred term 3	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x	xxx	(xx.x)	xxxx	xxxx.x
.												

N= Number of Subjects with adverse events, %= Proportion of subjects in analysis set having adverse events, E= Number of adverse events, R= Number of events/100 patient years for events multiplied by 100
Total Exposure (yrs)= Total Exposure in years for Safety Analysis Set
<Therapeutic Area>/<Clinical Programme>/<project>/<trials>/<instance>
<date> - <programme name>/<output name>

Table to be repeated for table:

Table to be repeated for table:

	Trial Group 1			
	Population 1	Population 2	Population 3	Population 4
Treatment emergent	• TRT1 vs Comparator • TRT2 vs Comparator	• TRT1 vs Comparator • TRT2 vs Comparator	• TRT1 vs Comparator • TRT2 vs Comparator	• TRT1 vs Comparator • TRT2 vs Comparator
Severe	• TRT1 vs Comparator • TRT2 vs Comparator	• TRT1 vs Comparator • TRT2 vs Comparator	• TRT1 vs Comparator • TRT2 vs Comparator	• TRT1 vs Comparator • TRT2 vs Comparator

Note:

Note:

- Treatment columns must be displayed by increasing dose

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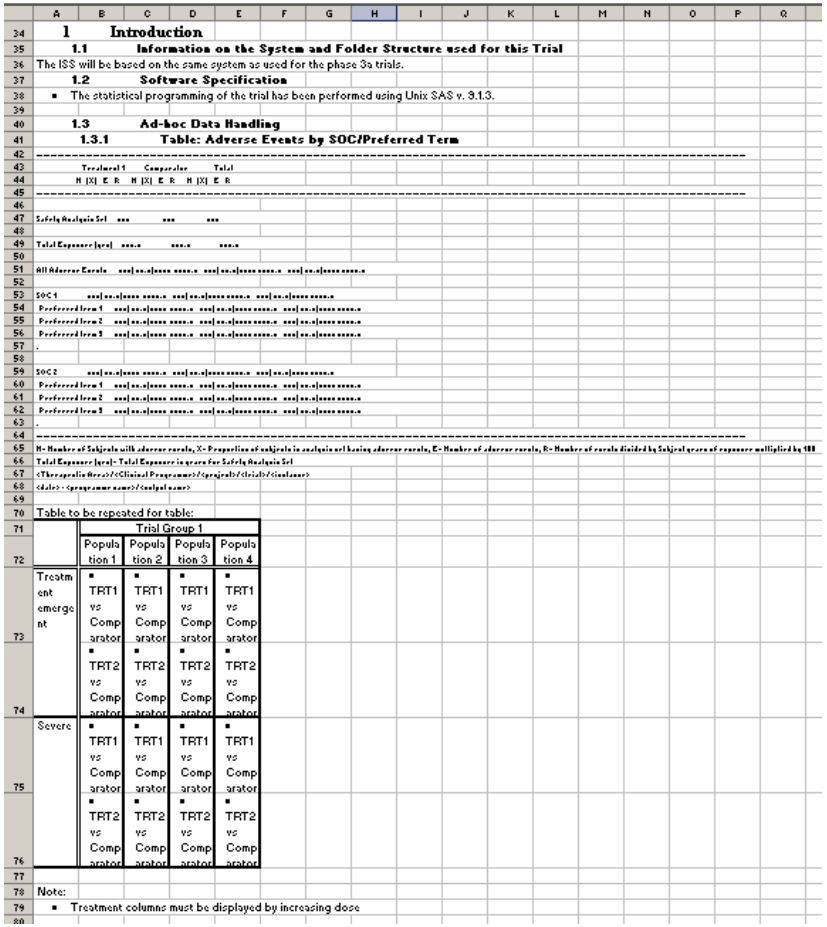
Extracting SAP into a SAS dataset (2)

Pasting into a temporary MS Excel file

```
* Waiting 2 sec to give a chance to MS Excel
  to open before continuing;
DATA _NULL_;
    T=SLEEP(2);
RUN;

filename excel dde 'Excel|System';

data _null_;
    file excel;
    put '[Error(false)]';
    put '[Paste]';
    put '[SAVE.AS("C:\temp\myiss.xls")]';
    put '[Select.Last.Cell()]';
    put '[Copy]';
    put '[Quit]';
run;
```



34 **1 Introduction**

35 **1.1 Information on the System and Folder Structure used for this Trial**

36 The ISS will be based on the same system as used for the phase 3a trials.

37 **1.2 Software Specification**

38 ▪ The statistical programming of the trial has been performed using Unix SAS v. 9.1.3.

39

40 **1.3 Ad-hoc Data Handling**

41 **1.3.1 Table: Adverse Events by SOC/Preferred Term**

42 ----------

43 Treatment 1 Comparator Total

44 N (%) E R N (%) E R N (%) E R

45 ----------

46

47 Safety Analysis Set xxx xxx xxx

48

49 Total Exposure (yrs) xxx.x xxx.x xxx.x

50

51 All Adverse Events xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

52

53 SOC 1 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

54 Preferred Term 1 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

55 Preferred Term 2 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

56 Preferred Term 3 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

57 .

58

59 SOC 2 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

60 Preferred Term 1 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

61 Preferred Term 2 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

62 Preferred Term 3 xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x xxx (xx.x) xxxx xxxx.x

63 .

64 ----------

65 N= Number of Subjects with adverse events, X= Proportion of subjects in analysis set having adverse events, E= Number of adverse events, R= Number of events divided by Subject years of exposure multiplied by 100

66 Total Exposure (yrs) - Total Exposure in years for Safety Analysis Set

67 <Therapeutic Area>/<Clinical Programme>/<project>/<trial>/<analyses>

68 <date> - <programmer name>/<analyst name>

69

70 Table to be repeated for table:

71 | | Trial Group 1 | | | |

72 | | Population 1 | Population 2 | Population 3 | Population 4 |

73 | Treatment emergent | ▪ TRT1 vs Comparator | ▪ TRT1 vs Comparator | ▪ TRT1 vs Comparator | ▪ TRT1 vs Comparator |

74 | | ▪ TRT2 vs Comparator | ▪ TRT2 vs Comparator | ▪ TRT2 vs Comparator | ▪ TRT2 vs Comparator |

75 | Severe | ▪ TRT1 vs Comparator | ▪ TRT1 vs Comparator | ▪ TRT1 vs Comparator | ▪ TRT1 vs Comparator |

76 | | ▪ TRT2 vs Comparator | ▪ TRT2 vs Comparator | ▪ TRT2 vs Comparator | ▪ TRT2 vs Comparator |

77

78 Note:

79 ▪ Treatment columns must be displayed by increasing dose

Reference: Importing Data from MS Word into SAS, Jay Zhou, PharmaSUG 2009

Extracting the SAP into a SAS dataset (3)

Loading into SAS, transposing and parsing…

1.3.1 Table: Adverse Events by SOC/PT

```
* Importing from C:\temp\myfile.xls to SAS;
proc import out=temp
            datafile= "C:\temp\myiss.xls"
            replace;
    getnames=no;
    mixed=yes;
run;

* Deleting C:\temp\myfile.xls;
filename fd "C:\temp\myiss.xls";
%let rc=%sysfunc(fdelete(fd));
filename _all_ clear;
```

	sort_row	Col0	Col1	Col2	Col3	sort_col	section
1	73	Trial group 1	Treatment emergent	Population 1	· TRT1 vs Comparator	2	1.3.1
2	73	Trial group 1	Treatment emergent	Population 2	· TRT1 vs Comparator	3	1.3.1
3	73	Trial group 1	Treatment emergent	Population 3	· TRT1 vs Comparator	4	1.3.1
4	73	Trial group 1	Treatment emergent	Population 4	· TRT1 vs Comparator	5	1.3.1
5	74	Trial group 1	Treatment emergent	Population 1	· TRT2 vs Comparator	2	1.3.1
6	74	Trial group 1	Treatment emergent	Population 2	· TRT2 vs Comparator	3	1.3.1
7	74	Trial group 1	Treatment emergent	Population 3	· TRT2 vs Comparator	4	1.3.1
8	74	Trial group 1	Treatment emergent	Population 4	· TRT2 vs Comparator	5	1.3.1
9	75	Trial group 1	Severe	Population 1	· TRT1 vs Comparator	2	1.3.1
10	75	Trial group 1	Severe	Population 2	· TRT1 vs Comparator	3	1.3.1
11	75	Trial group 1	Severe	Population 3	· TRT1 vs Comparator	4	1.3.1
12	75	Trial group 1	Severe	Population 4	· TRT1 vs Comparator	5	1.3.1
13	76	Trial group 1	Severe	Population 1	· TRT2 vs Comparator	2	1.3.1
14	76	Trial group 1	Severe	Population 2	· TRT2 vs Comparator	3	1.3.1
15	76	Trial group 1	Severe	Population 3	· TRT2 vs Comparator	4	1.3.1
16	76	Trial group 1	Severe	Population 4	· TRT2 vs Comparator	5	1.3.1

40	1.3 Ad Hoc Data Handling		
41	1.3.1 Table: Adverse Events by SOC/Preferred Term		
42			
43	Comparator	Treatment 1 Total	
44	E R N (%) E R	N (%) E R N (%)	
45			
46			
47	Safety Analysis Set xxx xxx xxx		
48			
49	Total Exposure (yrs) xxx.x xxx.x xxx.x		
50			
51	All Adverse Events xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
52			
53	SOC 1 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
54	Preferred term 1 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
55	Preferred term 2 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
56	Preferred term 3 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
57	.		
58			
59	SOC 2 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
60	Preferred term 1 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
61	Preferred term 2 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
62	Preferred term 3 xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x xxx(xx.x)xxxx xxxx.x		
63			
64			
65	N= Number of Subjects with adverse events, %= Proportion of subjects in analysis set having adverse events, E= Number of adverse events, R= Number of events divided by Subject years of exposure multiplied by 100		
66	Total Exposure (yrs)= Total Exposure in years for Safety Analysis Set		
67	<Therapeutic Area>/<Clinical Programme>/<project>/<trial>/<instance>		
68	<date> - <programme name>/<output name>		
69			
70	Table to be repeated for table:		
71		Trial Group 1	
72		Population 1	Population 2
73	Treatment emergent	· TRT1 vs Comparator	· TRT1 vs Comparator
74		· TRT2 vs Comparator	· TRT2 vs Comparator
75	Severe	· TRT1 vs Comparator	· TRT1 vs Comparator
76		· TRT2 vs Comparator	· TRT2 vs Comparator
77			
78	Note:		
79	Treatment columns must be displayed by increasing dose		

Table to be repeated for table:

Note:

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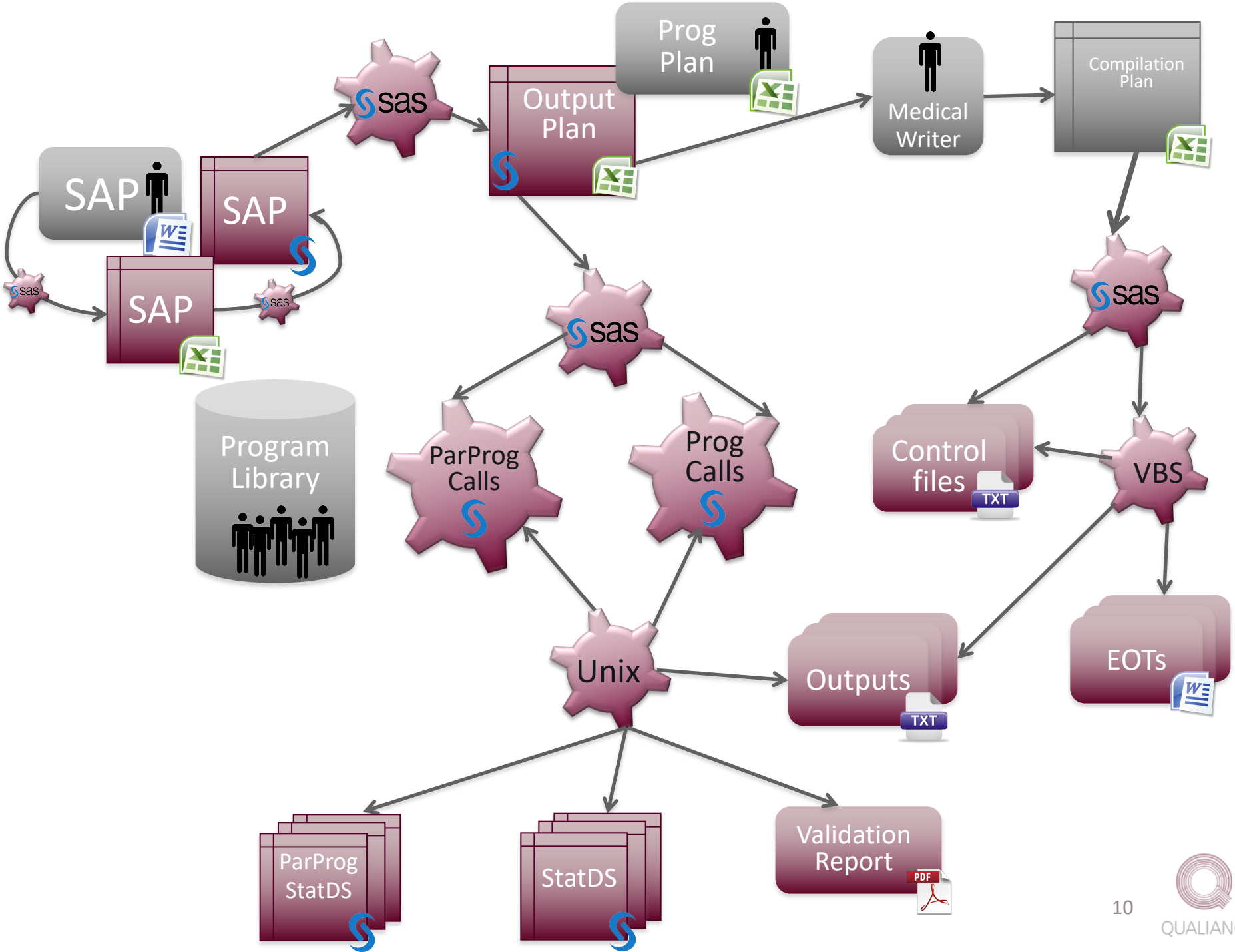
Prog Plan
sas
Output Plan
Medical Writer
Compilation Plan
SAP
SAP
SAP
sas
sas
sas
sas
Program Library
ParProg Calls
Prog Calls
Control files
TXT
VBS
Unix
Outputs
TXT
EOTs
ParProg StatDS
StatDS
Validation Report
PDF

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Generating program calls (1)

Merging progplan with SAP info

```
data dummy_progplan;
* Progplan information that would
  be extracted from excel file;
    length prog_init prog_date val_init
           val_date macro_name $100
           section $6;
    macro_name="table_ae_v01";
    prog_init="JMFE";
    prog_date="29MAY2012";
    val_init="PHJK";
    val_date="30MAY2012";
    section="1.3.1";
    output;
run;
```

```
data progcalls;
    * Merge all progplan information
      and output metadata extracted from SAP;
    merge dummy_progplan sap_transpose;
    by section;
    length output_title output_name filename
    * Construction of output title;
    output_title=catx("",'Adverse event table (',Col1,')',Co2, Col3);
    * Construction of program call/output filename;
    output_name=catx('_',"ID",sort_row,sort_col);
    * Construction of program call full path;
    filename = catx('',"E:\ISS\progcalls\",output_name,".sas");
run;
```

	prog_init	prog_date	val_init	val_date	macro_name	section	sort_row	output_title	Col0	Col1	Col2	Col3	sort_co	output_name	filename
1	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	73	Adverse event table (Treatment emergent) Population 1 · TRT1 vs Comparator	Trial group 1	Treatment emergent	Population 1	· TRT1 vs Comparator	2	ID_73_2	E:\ISS\progcalls\ ID_73_2 .sas
2	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	73	Adverse event table (Treatment emergent) Population 2 · TRT1 vs Comparator	Trial group 1	Treatment emergent	Population 2	· TRT1 vs Comparator	3	ID_73_3	E:\ISS\progcalls\ ID_73_3 .sas
3	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	73	Adverse event table (Treatment emergent) Population 3 · TRT1 vs Comparator	Trial group 1	Treatment emergent	Population 3	· TRT1 vs Comparator	4	ID_73_4	E:\ISS\progcalls\ ID_73_4 .sas
4	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	73	Adverse event table (Treatment emergent) Population 4 · TRT1 vs Comparator	Trial group 1	Treatment emergent	Population 4	· TRT1 vs Comparator	5	ID_73_5	E:\ISS\progcalls\ ID_73_5 .sas
5	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	74	Adverse event table (Treatment emergent) Population 1 · TRT2 vs Comparator	Trial group 1	Treatment emergent	Population 1	· TRT2 vs Comparator	2	ID_74_2	E:\ISS\progcalls\ ID_74_2 .sas
6	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	74	Adverse event table (Treatment emergent) Population 2 · TRT2 vs Comparator	Trial group 1	Treatment emergent	Population 2	· TRT2 vs Comparator	3	ID_74_3	E:\ISS\progcalls\ ID_74_3 .sas
7	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	74	Adverse event table (Treatment emergent) Population 3 · TRT2 vs Comparator	Trial group 1	Treatment emergent	Population 3	· TRT2 vs Comparator	4	ID_74_4	E:\ISS\progcalls\ ID_74_4 .sas
8	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	74	Adverse event table (Treatment emergent) Population 4 · TRT2 vs Comparator	Trial group 1	Treatment emergent	Population 4	· TRT2 vs Comparator	5	ID_74_5	E:\ISS\progcalls\ ID_74_5 .sas
9	JMFE	29MAY2012	PHJK	30MAY201	table_ae_v01	1.3.1	75	Adverse event table (Severe) Population 1 · TRT1 vs Comparator	Trial group 1	Severe	Population 1	· TRT1 vs Comparator	2	ID_75_2	E:\ISS\progcalls\ ID_75_2 .sas

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Generating program calls (2)

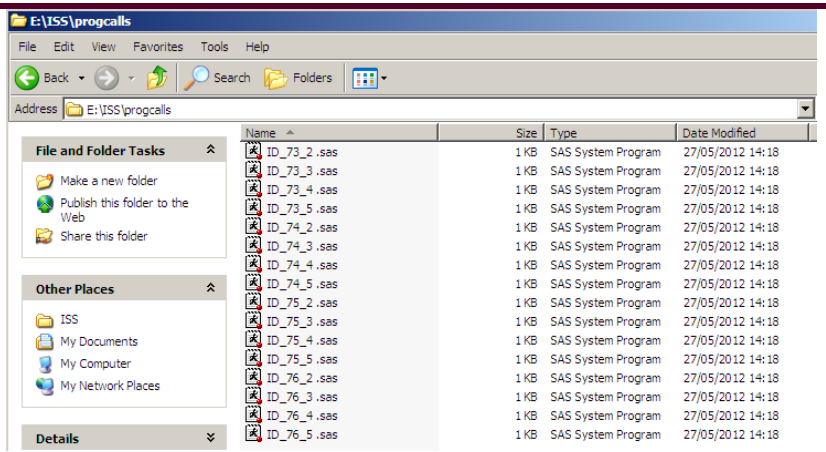
Write all program calls with headers

```
%global project trial instance;
%let project=CPHSDE2012;
%let trial=LastPresentation;
%let instance=current;

%macro print_progheader();
    put '/*************************************************************';
    put "Project: &project.";
    put "Trial: &trial.";
    x0 = catx(' ','Title:',output_title);                    put x0;
    x1 = cats('Program name:',output_name,'.sas');           put x1;
    x2 = cats('Output: ',output_name,'.txt');                put x2;
    x3 = cats('Macro: %',macro_name);                        put x3;
    put            "                    DDMMMYYYY";
    x4 = catx(' ','Programmer :',prog_init,prog_date);       put x4;
    x5 = catx(' ','Validator  :',val_init,val_date);         put x5;
    put            'Changes    :';
    put            'Comments   :';
    put '*************************************************************/';
    put "%access(project=&project.,trial=&trial.,instance=&instance.);";
    put ' ';
%mend print_progheader;

%macro print_macrocall();
    x10 = cats('%',macro_name,'(');              put x10;
    x11 = cats('trial_grp=',Col0);               put x11;
    x12 = cats(',ae_type=',Col1);                put x12;
    x13 = cats(',pop=',Col2);                    put x13;
    x14 = cats(',treat=',Col3);                  put x14;
    put ');';
%mend print_macrocall;

data _null_;
* Write all programs with headers in one datastep;
    set progcalls;
    file notitle filevar=filename flowover ls=500;
    %print_progheader;
    %print_macrocall;
run;
```




```
/*************************************************************
Project: CPHSDE2012
Trial: LastPresentation
Title: Adverse event table ( Treatment emergent ) Population 1
        ·   TRT1 vs Comparator
Program name:ID_73_2.sas
Output:ID_73_2.txt
Macro: %table_ae_v01
                    DDMMMYYYY
Programmer : JMFE 29MAY2012
Validator  : PHJK 30MAY2012
Changes    :
Comments   :
*************************************************************/
%access(project=CPHSDE2012,trial=LastPresentation,instance=current);

%table_ae_v01(
trial_grp=Trial group 1
,ae_type=Treatment emergent
,pop=Population 1
,treat=·   TRT1 vs Comparator
);
```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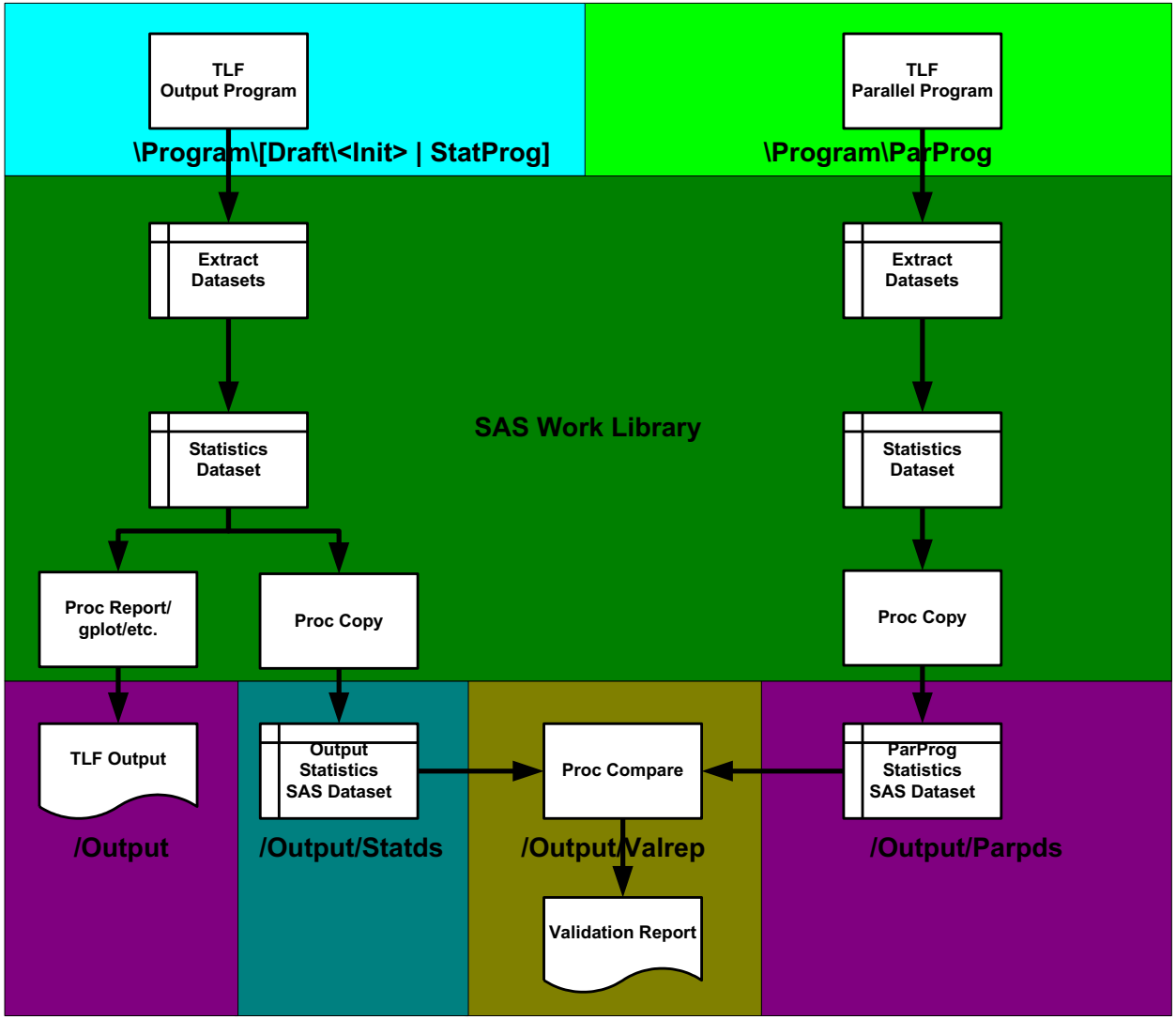
Program Design and Validation



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Output Information

	Source	Target
Statistical Information		
Output template	SAP	Output Plan
Statistical Parameters	SAP	Program call
Title	Derived	Program call & header
Operational Information		
Output ID	Derived	Program call
Output filename	Derived	Program call &header
Template Program & Parallel program	Prog & Output Plan	Program call & header
Author/Reviewer/Dates	ProgPlan	Program call header
Program & Parallel program path	Derived	Program call
Layout Information	Embedded or Derived	Template program (when defaulted) or program call
Compilation Information		
Document, Section, Order	Compilation Plan	Compilation VBS code

Conclusions

- Automation enabled **quick adaptation to changes**
- Specifications **extracted from the source**
- **Traceability** between outputs, programs and specs
- Terminology in SAP **translated into database usable** terms through parsing
- **Word/Excel** – A (too?) user-friendly environment
- **Naming conventions** and **streamlining of processes** were key to success
- Programmers could **focus on their programming** while manual processes were handled by code

THANK YOU!

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