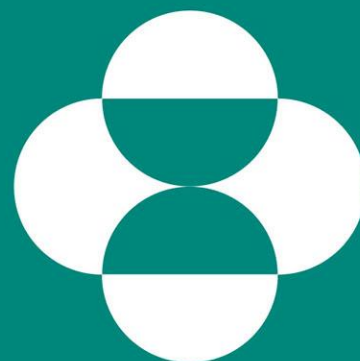


A Well Design QC Toolkit for Clinical Programming Compliance Checking



INVENTING
FOR LIFE

June 2021

Huei-Ling Chen, Sandeep Meesala, Xiaohui Wang
Merck & Co., Inc., Kenilworth, NJ, USA

Outline

- Introduction
- Clinical Programming Workflow
- Compliance Checking Items
- Quality Control Checking Macro Toolkit and Checking Steps
- Compliance Checking Score Card
- Conclusion

Introduction

- A statistical programming team in the pharmaceutical industry follows industry standards and regulatory guidelines for analysis and reporting to achieve regulatory compliance and high-quality results.
- Conventionally, every company has a checklist at hand to ensure the programming work follows the guidelines.
- This paper lists several **practical checking items** on whether a clinical study programming team followed these rules.
- A toolkit macro checking the checklist items can help teams quickly identify the rules they may have violated and improve their work quality.

Clinical Programming Workflow



Compliance Checking Items

1	All analysis datasets programs documented in the programming tracking sheet are developed in the setup program folder.
2	All TLF programs documented in the programming tracking sheet are developed in the analysis program folder.
3	All protocol-specific macro programs documented in the programming tracking sheet are in the macro folder.
4	All developed SAS programs should have corresponding outputs, logs, and listings. Every log/listing associated with the analysis datasets/TLFs should have consistent time stamps.
5	All TLFs documented in the TLF request list are developed in the output folder.
6	The validation for analysis datasets and TLFs programs is completed. The validation process executed has later timestamps than those of develop process.
7	The date/time stamps of TLF should be after the analysis dataset date/time stamps.
8	When there is a vertical dependency relationship between analysis datasets, the date/time of analysis datasets should follow this sequential order. For example, ADSL date/time should be before other ADaM datasets.

Quality Control Checking Macro Toolkit and Checking Steps

Steps:

1. Retrieve analysis dataset and TLF program list from programming tracking sheet. Retrieve TLF file names from TLF request list.
2. Retrieve analysis dataset and TLF programs, logs, listings, datasets, TLFs time stamp from working folder directory
3. Compare the programs with the programming tracking sheet and TLF request list.
4. Use ODS TAGSETS EXCELXP to print out the checking result

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 1. Retrieve analysis dataset and TLF program list from **programming tracking sheet**. Retrieve TLF file names from **TLF request list**.

```
%macro read0programtracker (tracker_file=,
                             tracker_sheetname=);

    PROC IMPORT OUT= WORK.tracker
                DATAFILE= "&tracker_file"
                DBMS=EXCEL REPLACE;
                RANGE="&tracker_sheetname.$a3:az1000";
                GETNAMES=YES;
    ....
    run;
    ....

    proc sort data=tracker out=tracker_pgmsetup nodupkey;
        by program_name;
        where program_subfolder='pgmsetup';
    run;
    ....
%mend read0programtracker;

%read0programtracker (tracker_file=%str(C:\Study001\documents\PDVT.xlsx),
                      tracker_sheetname=%str(Plan and Track));
```

	A	B	C	D
	Program Name	Description	Program Subfolder	run group
1				
2	adsl	Subject-Level Analysis Dataset	pgmsetup	
3	adrs	Analysis Dataset for Response	pgmsetup	adsl
4	adtlinv	Analysis Dataset of Target Lesions	pgmsetup	adsl
5	adintdt	Interim Dataset of Dates Used for	pgmsetup	adsl adrs
6	adtte	Data for the Time to Event Analyses	pgmsetup	adsl adrs adintdt
7				
8	apr0double0waterfall0plot	Double Waterfall Plot	macrolib	
9	apr0swim0plot	Swimmer Plot	macrolib	
10	apr0waterfall0plot	Waterfall Plot	macrolib	
11	apr0spider0plot	Spider Plot	macrolib	
12	kmplot	Kaplan-Meier Plot	pgmanal	
78				
79				
InstructionsPlan and TrackPathView UsersExceptionsRequired ActivitiesValidation				

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 1. Retrieve analysis dataset and TLF program list from **programming tracking sheet**. Retrieve TLF file names from **TLF request list**.

```
%macro read0argrid (argrid_file=,
                    argrid_sheetname=,
                    argrid_selection_criteria= );

    PROC IMPORT OUT= WORK.argrid
                DATAFILE= "&argrid_file"
                DBMS=EXCEL REPLACE;
                RANGE="&argrid_sheetname.$a1:az1000";
                GETNAMES=YES;
    .....
    RUN;
    .....

    proc sort data=argrid_ out=argrid_outtable nodupkey;
        by table;
    run;

    proc sort data=argrid_ out=argrid_pgmanal nodupkey;
        by pgmanal;
    run;
%mend read0argrid;

%read0argrid (argrid_file= %str(C:\Study001\documents\TLF_List.xlsx),
              argrid_sheetname=%str(TLFs LDS_EDS),
              argrid_selection_criteria=%str(where csr='Y' ) );
```

C	K	M	O	Z
TLF Title	Output Filename	Macro Program Name	Call program	CSR
Swimmer Plot: Time on Study Treatment and Time to Best Overall Response Based on Investigator Assessment per irRC (ASaT Population)	g0swim0plot0asat	apr0swim0plot	call0apr0swim0plot	Y
Swimmer Plot: Time on Study Treatment and Time to Best Overall Response Based on Investigator Assessment per irRC (ASaT Population)	g0swim0plot0asat0csr	apr0swim0plot	call0apr0swim0plot	Y
Swimmer Plot: Time on Study Treatment and Time to Best Overall Response Based on Investigator Assessment per irRC (ASaT Population)	g0swim0plot0asat0pid	apr0swim0plot	call0apr0swim0plot	Y
Swimmer Plot: Time on Study Treatment and Time to Best Overall Response Based on Investigator Assessment per irRC (ASaT Population)	g0swim0plot0asat0csr0pid	apr0swim0plot	call0apr0swim0plot	Y
Waterfall Plot of Maximum Percentage Change From Baseline in Index Lesions Based on Investigator Assessment per irRC (All Subjects with At Least One Post-baseline Index Lesion)	g0apr0waterfall0plot	apr0waterfall0plot	call0apr0waterfall0plot	Y
Waterfall Plot of Maximum Percentage Change From Baseline in Index Lesions Based on Investigator Assessment per irRC (All Subjects with At Least One Post-baseline Index Lesion)	g0apr0waterfall0plot0pid	apr0waterfall0plot	call0apr0waterfall0plot	Y
Spider Plot of Percent Change in Index Lesions From Baseline Based on Investigator Assessment per irRC (All Subjects with At Least One Post-baseline Index Lesion)	g0spider0plot0asat	apr0spider0plot	call0apr0spider0plot	Y
Spider Plot of Percent Change in Index Lesions From Baseline Based on Investigator Assessment per irRC (All Subjects with At Least One Post-baseline Index Lesion)	g0spider0plot0asat0csr	apr0spider0plot	call0apr0spider0plot	Y
Double Waterfall Plot of Maximum Index Lesion Change by Injected and Non-Injected Lesions Based on Site Assessment				
Instructions Trial Details TLFs LDS_EDS TLF Category Definitions PEM RWE HTA QP2 CSS Global ...				

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 2: Retrieve analysis dataset and TLF programs, logs, listings, datasets, TLFs time stamp from working folder directory

- SAS Component Language (SCL) Function

- FILENAME
- DOPEN
- DNUM
- DREAD
- FOPEN
- FINFO

```
data pgmsetup;  
    rc=filename ("filrf", "&studypath.\u0026pgmsetup");  
    did=dopen ("filrf");  
    if did > 0 then do ;  
        num=dnum(did);  
        call symput ('fnum', num);  
        do i=1 to num;  
            pgmsetup= scan(dread(did,i),1, '.');  
            fullname="&studypath.\u0026pgmsetup\u0026" || dread(did,i);  
            if scan(dread(did,i),-1) = 'sas' then do;  
                rc=filename ("onefile", fullname);  
                fid=fopen ("onefile");  
                moddate=input (finfo(fid, 'Last Modified'), datetime19.);  
                fidc= fclose(fid) ;  
                output;  
            end;  
        end;  
    end;  
run;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

- 1 All analysis datasets programs documented in the programming tracking sheet are developed in the setup program folder.

	A	B	C	D	E	F	G
1	Check 2.1: [PDVT: program name] (program subfolder=pgmsetup) has corresponding SAS codes						
2	in the CPI study folder \pgmsetup subfolder						
3	Good: setup files in PDVT can be found in CPI						
4	Warning: setup files in PDVT but not in CPI						
5	Maybe ok: need manually checking. Setup files in CPI but not in PDVT. This can be a utility sas code						
6							
7	pgmsetup	Subfolder 'pgmsetup' in Plan and Track	Program in CPI pgmsetup folder	flag			
8	adada	Yes	Yes	Good			
9	adae	Yes	Yes	Good			
10	adcm	Yes	Yes	Good			
11	adex	Yes	Yes	Good			
12	adexsum	Yes	Yes	Good			
13	adfacbrm	Yes	Yes	Good			
14	adintdt	Yes	Yes	Good			
15	adlesion	Yes	Yes	Good			
16	adpc	Yes	Yes	Good			
17	adrs	Yes	Yes	Good			
18	adsl	Yes	Yes	Good			
19	adtlinv	Yes	Yes	Good			
	check_1	check_2	check_3	check_4_1	check_4_2_a	check_4_2_b	check_5 ... (+)

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

- 1 All analysis datasets programs documented in the programming tracking sheet are developed in the setup program folder.

```
data check_1;
    length flag1 flag2 $3. flag $10.;
    merge tracker_pgmsetup(in=in1 rename=(program_name=pgmsetup) )
          pgmsetup(in=in2);
    by pgmsetup;
    if in1=1 then flag1='Yes';
    if in2=1 then flag2='Yes';

    label flag1="Subfolder 'pgmsetup' in Plan and Track"
          flag2='Program in CPI pgmsetup folder';
    keep pgmsetup flag1 flag2;

run;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

2 All TLF programs documented in the programming tracking sheet are developed in the analysis program folder.

	A	B	C	D	E
1	Check 2: [AR grid: call program] has 1-1 matching programs in [PDVT: program name] (program subfolder= pgmanal) and corresponding SAS codes in the CPI study folder \pgmanal subfolder				
2					
3	Good: call programs in AR grid and can be found in PDVT and CPI				
4	Warning: call programs in either AR grid or PDVT but not in CPI				
5	Maybe ok: need manually checking. Call programs in CPI but not in both AR grid PDVT. This can be a legacy sas code				
6					
7	pgmanal	Call Program In A&R Grid	Subfolder 'pgmanal' in Plan and Track	Program in CPI pgmanal folder	flag
8	call0apr0analysis0tte0vertical	Yes	Yes	Yes	Good
9	call0apr0bar0chart	Yes	Yes	Yes	Good
10	call0apr0cm	Yes	Yes	Yes	Good
11	call0apr0double0waterfall0plot	Yes	Yes	Yes	Good
12	call0apr0eff0listing	Yes	Yes	Yes	Good
13	call0apr0factbrm0sum0chg	Yes	Yes	Yes	Good
14	call0apr0ich0ae0listing	Yes	Yes	Yes	Good
15	call0apr0ich0demog0listing	Yes	Yes	Yes	Good
16	call0apr0line0overtime	Yes	Yes	Yes	Good
17	call0apr0onr0summary	Yes	Yes	Yes	Good
18	call0apr0spider0plot	Yes	Yes	Yes	Good
19	call0apr0sum0drug0exposure	Yes	Yes	Yes	Good

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

2 All TLF programs documented in the programming tracking sheet are developed in the analysis program folder.

```
data check_2;
    length flag1 flag2 flag3 $3. flag $10.;
    merge argrid_pgmanal(in=in1)
          tracker_pgmanal(in=in2 )
          pgmanal(in=in3);
    by pgmanal;
        if in1=1 and in2=1 and in3=1 then flag='Good';
    else if in1=0 and in2=0 then flag='Maybe ok';
    else                                flag='Warning';
    if in1=1 then flag1='Yes';
    if in2=1 then flag2='Yes';
    if in3=1 then flag3='Yes';
    label flag1='Call Program In A&R Grid'
          flag2="Subfolder 'pgmanal' in Plan and Track"
          flag3='Program in CPI pgmanal folder';
    keep pgmanal flag1 flag2 flag3 flag;

run;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

3 All protocol-specific macro programs documented in the programming tracking sheet are in the macro folder.

	A	B	C	D	E	F
1	Check 2.3: [PDVT: program name] (program subfolder=macrolib) has corresponding SAS codes in the CPI					
2	study folder \macrolib\protocol-macros subfolder					
3	Good: macro in PDVT can be found in CPI					
4	Warning: macro in PDVT but not in CPI					
5	Maybe ok: need manually checking. macro in CPI but not in PDVT. This can be a legacy sas code					
6						
7	macro	Subfolder 'macrolib' in Plan and Track	Program in CPI macrolib\protocol-macros folder	flag		
8	apr0analysis0tte0vertical	Yes	Yes	Good		
9	apr0bar0chart	Yes	Yes	Good		
10	apr0cm	Yes	Yes	Good		
11	apr0double0waterfall0plot	Yes	Yes	Good		
12	apr0eff0listing	Yes	Yes	Good		
13	apr0factbrm0sum0chg	Yes	Yes	Good		
14	apr0ich0ae0listing	Yes	Yes	Good		
15	apr0ich0demog0listing	Yes	Yes	Good		
16	apr0line0overtime	Yes	Yes	Good		
17	apr0onr0summary	Yes	Yes	Good		
18	apr0spider0plot	Yes	Yes	Good		
check_1 check_2 check_3 check_4_1 check_4_2_a check_4_2_b check_5 ... + :						

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

3 All protocol-specific macro programs documented in the programming tracking sheet are in the macro folder.

```
data check_3;
    length flag1 flag2 $3. flag $10.;
    merge tracker_macrolib(in=in1 )
          macrolib(in=in2);
    by macro;
        if in1=1 and in2=1 then flag='Good' ;
    else if in1=1 and in2=0 then flag='Warning';
    else if in1=0 and in2=1 then flag='Maybe ok';

    if in1=1 then flag1='Yes';
    if in2=1 then flag2='Yes';
    label flag1="Subfolder 'macrolib' in Plan and Track"
          flag2='Program in CPI macrolib\protocol-macros folder';
    keep macro flag1 flag2 flag;

run;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

- 4 All developed SAS programs should have corresponding outputs, logs, and listings. Every log/listing associated with the analysis datasets/TLFs should have consistent time stamps.

	A	B	C	D	E	F	G	H
1	Check 4.2.a: [PDVT: program name] (program_subfolder=pgmanal) should have corresponding outputs, logs, and listings.)							
2	Every log/listing associated with the output TLF should have consistent time stamps.							
3	Ensure corresponding outputs were created after SAS programs.							
4								
5	Good: call program and TLF in AR grid has corresponding SAS code, TLF, log, and listings in CPI. Every log/listing/TLF has consistent time stamps and all are created after SAS code.							
6	Warning: not meeting the 'Good' criteria							
7								
8	pgmanal	TLF output name	Log/List file name	pgmtir	logtir	listtir	tbltir	flag
9	call0apr0analysis0tte0vertical	e0apr0tte0vertical0irc	e0apr0tte0vertical0irc	12MAY2020:02:24:41	25AUG2020:12:22:35	25AUG2020:12:22:35	25AUG2020:12:22:35	Good
10	call0apr0analysis0tte0vertical	e0apr0tte0vertical0os	e0apr0tte0vertical0os	12MAY2020:02:24:41	25AUG2020:12:22:37	25AUG2020:12:22:37	25AUG2020:12:22:37	Good
11	call0apr0analysis0tte0vertical	s0apr0tte0vertical0ae35	s0apr0tte0vertical0ae35	12MAY2020:02:24:41	25AUG2020:12:22:38	25AUG2020:12:22:38	25AUG2020:12:22:37	Good
12	call0apr0bar0chart	g0facbrm0bar0chart0m12	g0facbrm0bar0chart0m12	06AUG2020:11:53:28	25AUG2020:12:21:59	25AUG2020:12:21:58	25AUG2020:12:21:59	Good
13	call0apr0bar0chart	g0facbrm0bar0chart0m7	g0facbrm0bar0chart0m7	06AUG2020:11:53:28	25AUG2020:12:22:00	25AUG2020:12:21:59	25AUG2020:12:22:00	Good
14	call0apr0cm	d0prior0med	d0prior0med	14JUL2020:14:05:19	24AUG2020:18:12:16	24AUG2020:18:12:13	24AUG2020:18:12:16	Good
15	call0apr0double0waterfall0plot	g0double0waterfall0plot	g0double0waterfall0plot	21JUL2020:10:26:34	25AUG2020:14:54:06	25AUG2020:14:54:05	25AUG2020:14:54:06	Good
16	call0apr0eff0listing	l0apr0eff0listing0cf	l0apr0eff0listing0cf	20JUL2020:03:33:21	25AUG2020:12:22:48	25AUG2020:12:22:47	25AUG2020:12:22:48	Good
17	call0apr0factbrm0sum0chg	e0factbrm0sum0chg0m12	e0factbrm0sum0chg0m12	24AUG2020:10:56:01	25AUG2020:12:22:50	25AUG2020:12:22:48	25AUG2020:12:22:50	Good
18	call0apr0factbrm0sum0chg	e0factbrm0sum0chg0m7	e0factbrm0sum0chg0m7	24AUG2020:10:56:01	25AUG2020:12:22:52	25AUG2020:12:22:50	25AUG2020:12:22:52	Good
19	call0apr0ich0ae0listing	l0apr0ich0ae0listing	l0apr0ich0ae0listing	21JUN2020:18:27:15	24AUG2020:18:39:34	24AUG2020:18:39:34		Warning
20	call0apr0ich0demog0listing	l0apr0ich0demog0listing	l0apr0ich0demog0listing	21JUN2020:18:37:48	24AUG2020:18:15:42	24AUG2020:18:15:42		Warning
21	call0apr0line0overtime	g0factbrm0line0overtime	g0factbrm0line0overtime	24AUG2020:15:37:13	25AUG2020:12:22:07	25AUG2020:12:22:06	25AUG2020:12:22:07	Good
22	call0apr0orr0summary	e0apr0orr0summary	e0apr0orr0summary	09AUG2020:22:23:43	25AUG2020:14:39:10	25AUG2020:14:39:10	25AUG2020:14:39:10	Good

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

- 4 All developed SAS programs should have corresponding outputs, logs, and listings. Every log/listing associated with the analysis datasets/TLFs should have consistent time stamps.

```
data check_4;
    . . .
    if . < logtime < pgmtime then flag5='X';
    if . < listtime < pgmtime then flag6='X';
    if . < datatime < pgmtime then flag7='X';
    if abs(intck ('minutes',logtime,datatime))>1 then flag8='X';
    if abs(intck ('minutes',logtime,listtime))>1 then flag9='X';
    if flag1='Yes' and flag2='Yes' and flag3='Yes' and flag4='Yes' and
        flag5=' ' and flag6=' ' and flag7=' ' and flag8=' ' and flag9=' '
        then flag='Good';
    else flag='Warning';
    output;
end;
    . . .
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

5 All TLFs documented in the TLF request list are developed in the output folder.

	A	B	C	D	E
1	Check 5.2: [AR Grid: Output Filename] has corresponding rtf files in the CPI study folder \outtable				
2					
3	Good: output filename in AR grid can be found in CPI				
4	Warning: output filename in AR grid but not in CPI				
5	Maybe ok: need manually checking. TLF in CPI but not in AR grid. This can be a leftover output				
6					
7	table	TLF in A&R Grid	TLF in CPI outtable folder	flag	
9	d0an0summary0listing	Yes		Warning	
10	d0an0summary0range		Yes	Maybe ok	
11	d0base0char0asat	Yes	Yes	Good	
12	d0disposition0asat	Yes	Yes	Good	
13	d0investigator0by0site	Yes	Yes	Good	
14	d0prior0med	Yes	Yes	Good	
15	e0apr0onr0summary	Yes	Yes	Good	
16	e0apr0tte0vertical0irc	Yes	Yes	Good	
17	e0apr0tte0vertical0os	Yes	Yes	Good	
18	e0factbrm0sum0chg0m12	Yes	Yes	Good	
19	e0factbrm0sum0chg0m7	Yes	Yes	Good	
20	e0sum0t2r0dor0asat	Yes	Yes	Good	
21	g0apr0waterfall0plot	Yes	Yes	Good	
22	g0double0waterfall0plot	Yes	Yes	Good	
23	g0double0waterfall0plot0csr		Yes	Maybe ok	
24	g0facbrm0bar0chart0m12	Yes	Yes	Good	
25	g0facbrm0bar0chart0m7	Yes	Yes	Good	
26	g0factbrm0line0overtime	Yes	Yes	Good	
27	g0km0os0asat0er	Yes	Yes	Good	

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

5 All TLFs documented in the TLF request list are developed in the output folder.

```
data check_5;
  length flag $10.;
  merge argrid_outtable(in=in1 ) outtlf(in=in2 );
  by table;
  if in1=1 then flag1='Yes';
  if in2=1 then flag2='Yes';
  if flag1='Yes' and flag2='Yes' then flag='Good';
  else if flag1='Yes' and flag2='' then flag='Warning';
  else flag='Maybe ok';
  label flag1='TLF in A&R Grid'
        flag2='TLF in CPI outtable folder';
  keep table flag1 flag2 flag;
run;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

- 6 Validation for analysis datasets and TLFs programs is completed. Validation process executed has later time stamps than those of develop process.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	Check 2.6.1: [PDVT: program name] with [program validation category] filled with number 1,2 has SAS code, log file, listing file, dataset or rtf file in the CPI validate\xxx\dbl-pgm\ folder.													
2	All [1,2] programs should have corresponding outputs, logs, and listings in dbl-pgm folder													
3	In dbl-pgm folder: Every log/listing/output should have consistent time stamps. Ensure corresponding outputs were created after SAS programs.													
4														
5	Good: PDVT: Validation Cat (1,2) has pgm, log, lst, output in the CPI validate\xxx\dbl-pgm\ folder. Every log/lst/output has consistent time stamps and all are created after SAS programs.													
6	Warning: not meeting the 'Good' criteria													
7														
8	filename	dbl-pgm sas code available	dbl-pgm log available	dbl-pgm list available	dbl-pgm sas dataset available	dbl-pgm sas code Modified DateTir	dbl-pgm log Modified DateTir	dbl-pgm listing Modified DateTir	dbl-pgm rtf Modified DateTir	dbl-pgm sas dataset Modified DateTir	Log time stamp before program	List time stamp before program	Data time stamp before program	flag
9	bsplus	Yes	Yes	Yes	Yes	08JUL2020:18:53:27	08JUL2020:18:53:31	08JUL2020:18:53:31	.	08JUL2020:18:53:30				Good
10	isplus	Yes	Yes	Yes	Yes	08JUL2020:18:58:03	08JUL2020:18:58:06	08JUL2020:18:58:06	.	08JUL2020:18:58:06				Good
11	adsl	Yes	Yes	Yes	Yes	19AUG2020:09:11:31	19AUG2020:09:14:18	19AUG2020:09:14:18	.	19AUG2020:09:14:17				Good
12	adex	Yes	Yes	Yes	Yes	14MAY2020:13:55:57	19AUG2020:09:45:23	19AUG2020:09:45:23	.	19AUG2020:09:45:22				Good
13	adexsum	Yes	Yes	Yes	Yes	14MAY2020:14:11:25	19AUG2020:10:01:32	19AUG2020:10:01:32	.	19AUG2020:10:01:31				Good
14	adae	Yes	Yes	Yes	Yes	14MAY2020:13:51:36	19AUG2020:09:26:21	19AUG2020:09:26:21	.	19AUG2020:09:26:20				Good
15	adttae	Yes	Yes	Yes	Yes	21JUL2020:16:18:42	19AUG2020:11:07:47	19AUG2020:11:07:47	.	19AUG2020:11:07:47				Good
16	adcm	Yes	Yes	Yes	Yes	19AUG2020:09:35:29	19AUG2020:09:36:09	19AUG2020:09:36:09	.	19AUG2020:09:36:09				Good
17	adrs	Yes	Yes	Yes	Yes	04AUG2020:11:34:23	19AUG2020:11:44:29	19AUG2020:11:44:29	.	19AUG2020:11:44:29				Good
18	adtliv	Yes	Yes	Yes	Yes	14MAY2020:17:04:12	20AUG2020:08:10:40	20AUG2020:08:10:40	.	20AUG2020:08:10:39				Good
19	adintdt	Yes	Yes	Yes	Yes	05AUG2020:22:44:51	19AUG2020:12:18:46	19AUG2020:12:18:46	.	19AUG2020:12:18:45				Good
20	adtte	Yes	Yes	Yes	Yes	12JUL2020:23:34:10	20AUG2020:03:58:11	20AUG2020:03:58:11	.	20AUG2020:03:58:11				Good
21	adfacbm	Yes	Yes	Yes	Yes	20AUG2020:07:58:54	20AUG2020:08:01:07	20AUG2020:08:01:07	.	20AUG2020:08:01:06				Good
22	adlesion	Yes	Yes	Yes	Yes	21AUG2020:12:09:31	21AUG2020:12:11:00	21AUG2020:12:11:00	.	21AUG2020:12:10:59				Good
23	adada	Yes	Yes	Yes	Yes	19AUG2020:11:26:23	19AUG2020:11:27:08	19AUG2020:11:27:08	.	19AUG2020:11:27:08				Good
24	adpc	Yes	Yes	Yes	Yes	19AUG2020:11:23:30	19AUG2020:11:23:37	19AUG2020:11:23:37	.	19AUG2020:11:23:37				Good
25	apr0double0waterfa ll0plot	Yes	Yes	Yes	Yes	21JUL2020:14:55:49	24AUG2020:11:05:44	24AUG2020:11:05:44	.	24AUG2020:11:05:44				Good

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

6 Validation for analysis datasets and TLFs programs is completed. Validation process executed has later time stamps than those of develop process.

```
data check_6_dev;
  merge
    file
    dev_pgm (keep=sas moddate)
    dev_out (keep=log lst rtf sas7bdat logtime lsttime datatime rtftime);
. . .
data check_6_dbl;
  merge
    file
    dbl_pgm (keep=sas moddate)
    dbl_out (keep=log lst rtf sas7bdat logtime lsttime datatime rtftime);
. . .
proc sql;
  create table check_6 as
  select a.file, a.logtime as devlogtime, b.logtime as dbllogtime,
        'Warning' as flag
  from check_6_dev as a, check_6_val as b
  where a.file = b.file and a.logtime > b.logtime;
quit;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

7 The date/time stamps of TLF should be after analysis dataset date/time stamps.

	A	B	C	D	E	F	G	H
1	Check 3.1: CPI study folder \outtable subfolder rtf tables time stamp are after \dataanalysis subfolder analysis dataset time stamp							
2								
3	Warning: TLF created before \lptda analysis dataset. Need manual check.							
4								
5	table	tlf	modda	Analysis Dataset	Analysis Dataset Modified DateTir	flag		
6	g0km0os0asat0gr	F	21JUL2020:15:22:43	adfcbm	06AUG2020:09:55:45	Warning		
7	g0km0pfs0asat0gr	F	21JUL2020:15:22:42	adfcbm	06AUG2020:09:55:45	Warning		
8	g0spider0plot0asat	F	21JUL2020:15:22:55	adfcbm	06AUG2020:09:55:45	Warning		
9	g0spider0plot0asat0csr	F	21JUL2020:15:22:56	adfcbm	06AUG2020:09:55:45	Warning		
10	g0swim0plot0asat	F	21JUL2020:15:22:48	adfcbm	06AUG2020:09:55:45	Warning		
11	g0swim0plot0asat0csr	F	21JUL2020:15:22:46	adfcbm	06AUG2020:09:55:45	Warning		
12	d0an0summary0range	T	21JUL2020:15:20:30	adfcbm	06AUG2020:09:55:45	Warning		
13	d0base0char0asat	T	21JUL2020:15:20:40	adfcbm	06AUG2020:09:55:45	Warning		
14	d0disposition0asat	T	21JUL2020:15:20:18	adfcbm	06AUG2020:09:55:45	Warning		
15	d0investigator0by0site	T	21JUL2020:15:20:24	adfcbm	06AUG2020:09:55:45	Warning		
16	d0prior0med	T	21JUL2020:15:20:48	adfcbm	06AUG2020:09:55:45	Warning		
17	e0apr0on0summary	T	21JUL2020:15:22:26	adfcbm	06AUG2020:09:55:45	Warning		
18	e0apr0tte0vertical0irc	T	21JUL2020:15:22:22	adfcbm	06AUG2020:09:55:45	Warning		
19	e0apr0tte0vertical0os	T	21JUL2020:15:22:23	adfcbm	06AUG2020:09:55:45	Warning		

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

7 The date/time stamps of TLF should be after analysis dataset date/time stamps.

```
proc sql;
  create table check_7 as
  select table, tlf, a.moddate format=datetime19. , dataanalysis,
         b.moddate as lastadam, 'Warning' as flag
  from outtlf a, lastadam b
  where a.moddate < b.moddate;
quit;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

- 8 When there is a vertical dependency relationship between analysis datasets, the date/time of analysis datasets should follow this sequential order. For example, ADSL date/time should be before other ADaM datasets.

	A	B	C	D	E	F	G	H
1	Check 3.2: [Prog Tracking Sheet] __program_name has run group value for the setup programs.							
2	The setup programs in the CPI have been run in the right order (e.g. ADSL before other ADaM datasets).							
3								
4	Warning: \ptda timestamp is not following [PDVT: Run Group]. Need manual check.							
5								
6	last	next	run group - l	run group - ne	Modified Datetime - l	Modified Datetime - ne	flag	
7	adsl	adlesion	1	2	08APR2020:16:33:44	08APR2020:15:47:55	Warning	
8	adsl	adtlinv	1	2	08APR2020:16:33:44	08APR2020:15:47:47	Warning	
9	adsl	adtte	1	4	08APR2020:16:33:44	08APR2020:15:47:39	Warning	
10	adsl	adintdt	1	3	08APR2020:16:33:44	08APR2020:15:47:32	Warning	
11	adsl	adrs	1	2	08APR2020:16:33:44	08APR2020:15:47:23	Warning	
12	adsl	adexsum	1	3	08APR2020:16:33:44	08APR2020:15:47:21	Warning	
13	adsl	adex	1	2	08APR2020:16:33:44	08APR2020:15:47:18	Warning	
14	adsl	adttae	1	3	08APR2020:16:33:44	08APR2020:15:47:15	Warning	
15	adsl	adae	1	2	08APR2020:16:33:44	08APR2020:15:47:06	Warning	
16	adlesion	adtte	2	4	08APR2020:15:47:55	08APR2020:15:47:39	Warning	
17	adlesion	adintdt	2	3	08APR2020:15:47:55	08APR2020:15:47:32	Warning	
18	adlesion	adexsum	2	3	08APR2020:15:47:55	08APR2020:15:47:21	Warning	
19	adlesion	adttae	2	3	08APR2020:15:47:55	08APR2020:15:47:15	Warning	
20	adtlinv	adtte	2	4	08APR2020:15:47:47	08APR2020:15:47:39	Warning	
21	adtlinv	adintdt	2	3	08APR2020:15:47:47	08APR2020:15:47:32	Warning	
22	adtlinv	adexsum	2	3	08APR2020:15:47:47	08APR2020:15:47:21	Warning	
23	adtlinv	adttae	2	3	08APR2020:15:47:47	08APR2020:15:47:15	Warning	
24	adrs	adexsum	2	3	08APR2020:15:47:23	08APR2020:15:47:21	Warning	
25	adrs	adttae	2	3	08APR2020:15:47:23	08APR2020:15:47:15	Warning	

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 3: Compare the programs with the programming tracking sheet and TLF request list

- 8 When there is a vertical dependency relationship between analysis datasets, the date/time of analysis datasets should follow this sequential order. For example, ADSL date/time should be before other ADaM datasets.

```
proc sql;
  create table check_8_ as
  select run_group, moddate format=datetime19., dataanalysis
  from tracker_pgmsetup a, dataanalysis b
  where a.program_name = b.dataanalysis and a.run_group ne ''
  ;
quit;

proc sql;
  create table check_8 as
  select a.dataanalysis as dataanalysis, b.dataanalysis as pre,
         a.run_group as pre_required_list label='pre-required list',
         a.moddate as moddate label='Data Datetime',
         b.moddate as moddate_pre label='Pre-Data Datetime',
         'Warning' as flag, findw(a.run_group,b.dataanalysis) as ind
  from check_8_ a, check_8_ b
  where a.dataanalysis ne b.dataanalysis and
         findw(a.run_group,trim(left(b.dataanalysis)))>0 and
         a.moddate < b.moddate
  ;
quit;
```

Quality Control Checking Macro Toolkit and Checking Steps (cont.)

Step 4: Use ODS TAGSETS EXCELXP to print out checking result

```
ods _all_ close;
ods tagsets.excelxp path("&outputpath\" file "&outfilename"
                    style=Printer
options(autofit_height='yes'
        pages_fitwidth='1'
        fittopage='yes'
        autofilter='all'
        embedded_titles="yes"
        autofit_height='yes');

%if &check_1=Y %then %do;
  title1; title2; title3; title4; title5; title6; title7;
  ods tagsets.excelxp
    options(sheet_name = "check_1"
            frozen_headers="7"
            absolute_column_width='15');
  proc print data=check_1 noobs label;
    var pgmsetup flag1 flag2 flag
      / style={background=$flagcolor.} ;
  ...
  run;
%end;

...
ods tagsets.excelxp close;
ods listing;
```

Compliance Checking Score Card

A	B	C	D	E	F	G	H	I
	mk9999-P001		mk9999-P002		mk9999-P003		mk9999-P004	
Major Compliance Checking Items	Check Box	Score	Check Box	Score	Check Box	Score	Check Box	Score
All analysis datasets programs documented in the programming tracking sheet are developed in the setup program folder.	Yes	1	Yes	1	Yes	1	Yes	1
All TLF programs documented in the programming tracking sheet are developed in the analysis program folder.	Yes	1	Yes	1	No	0	Yes	1
All protocol specific macro programs documented in the programming tracking sheet are in the macro folder.	Yes	1	Yes	1	Yes	1	Yes	1
All developed SAS programs should have corresponding outputs, logs, and listings. Every log/listing associated with the analysis datasets/TLFs should have consistent time stamps.	Yes	1	Yes	1	Yes	1	Yes	1
All TLFs documented in the TLF request list are developed in the output folder.	Yes	0	Yes	1	Yes	1	Yes	1
Validation for analysis datasets and TLFs programs is completed. Validation process executed has later time stamps than those of develop process.	Yes	1	Yes	1	No	0	No	0
The date/time stamps of TLF should be after analysis dataset date/time stamps.	No	0	Yes	1	Yes	1	Yes	1
When there is a vertical dependency relationship between analysis datasets, the date/time of analysis datasets should follow this sequential order. For example, ADSL date/time should be before other ADaM datasets.	No	0	Yes	1	Yes	1	Yes	1
Total Score		62.5%		100.0%		75.0%		87.5%

Conclusion

- The macro toolkit conducts the quality control process and checks whether a clinical study programming team following guidelines for analysis and reporting.
 - The macro toolkit is a demo work for the quality control process.
 - Reference: PHUSE US 2020 conference paper, “How to Build Compliance Mindset into A Team Habit”.
- Who use this macro toolkit
 - Trial programmers do self-checking to ensure the compliance and quality.
 - The project leads or compliance SME can also conduct regular checking.

Reference

- Matthews, C., and Shilling, B. 2008. “*Validating Clinical Trial Data Reporting with SAS*”, SAS Press.
- “Best Practices for Quality Control and Validation”, PHUSE White Paper
- Wang, X. 2020. “How to Build Compliance Mindset into A Team Habit”
Proceedings of the PHUSE US 2020 Conference, Paper SP07. Available at <https://www.lexjansen.com/phuse-us/2020/sp/SP07.pdf>
- “SAS® Component Language 9.4: Reference”, Third Edition

THANK YOU



MERCK

