

Meta-data Driven Automation of TLF Programs

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Outline

- Introduction
- Essential requirements for automation
- How automation can be implemented
- How automation can add benefit
- Summary

Introduction

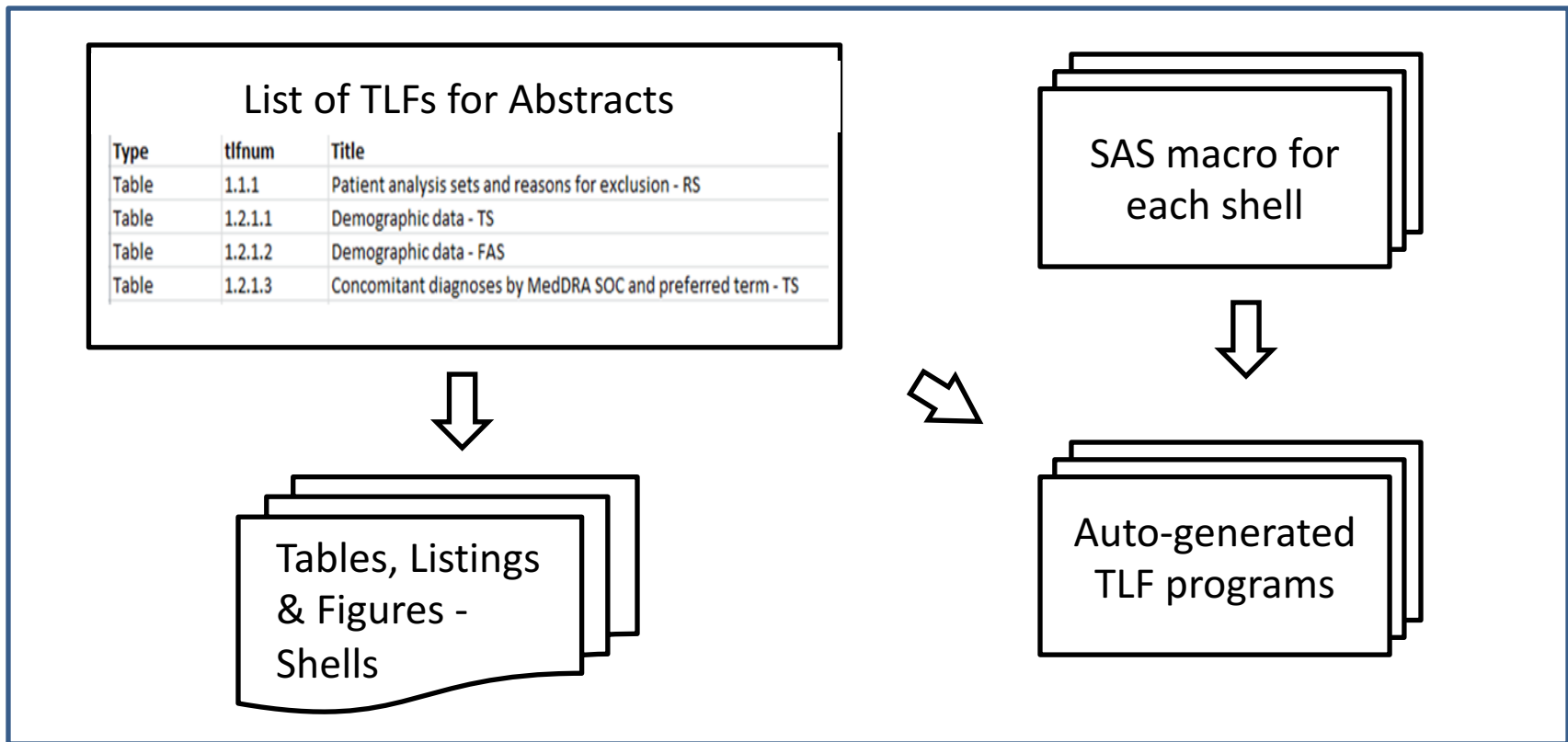
- As programmers we are all really busy
 - Number of TLFs are increasing
 - Timelines are reducing
- How can we reduce the burden on programming resource?
 - Reduce the number of outputs?
 - Increase resource?
- We need to work SMARTER!
 - Define standards
 - Automate

Essential requirements for automation

- Standards
 - Input: Data – SDTM/ADaM
 - Output: TLF – Standard table shells
 - Process: Standard macros for each TLF shell
- Meta-data
 - Structured data used to map the flow of data:

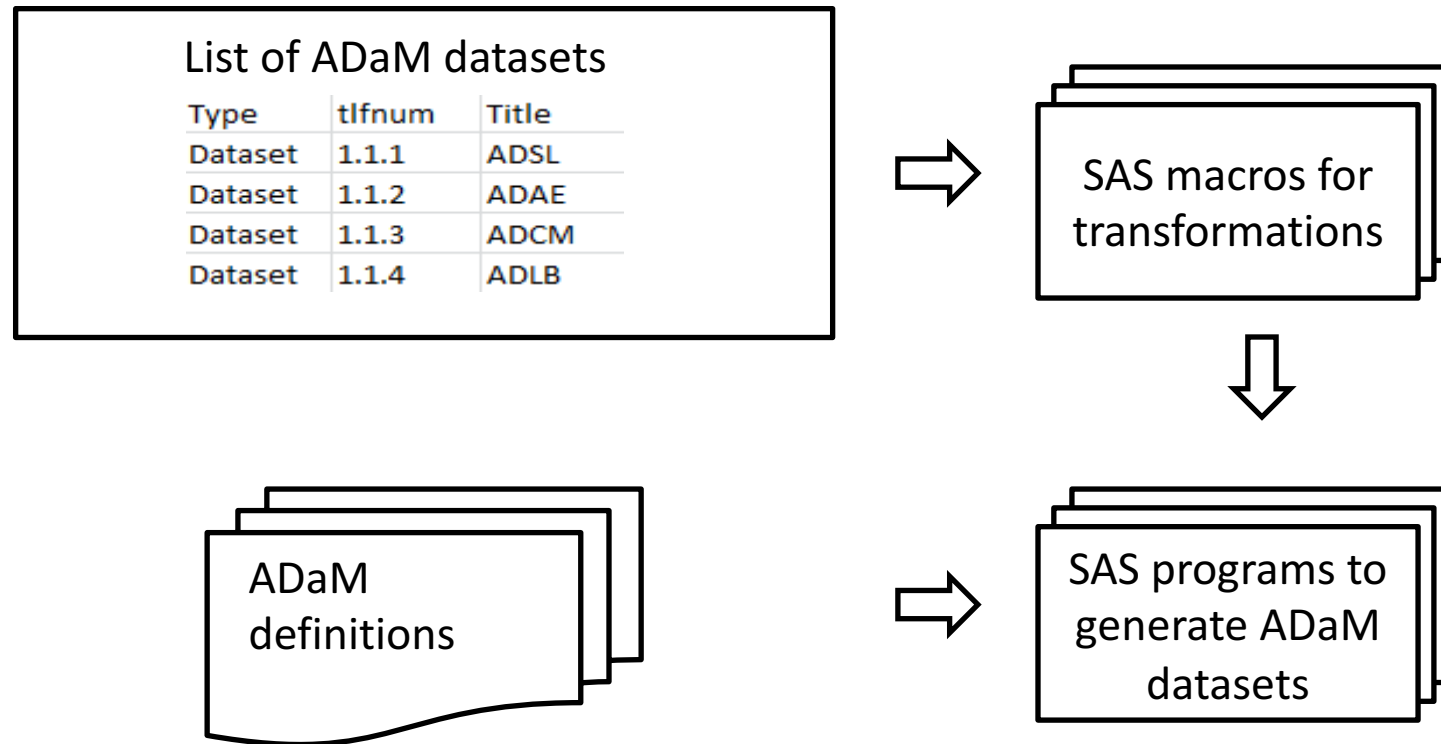
INPUT ➡ PROCESS ➡ OUTPUT

How automation can be implemented

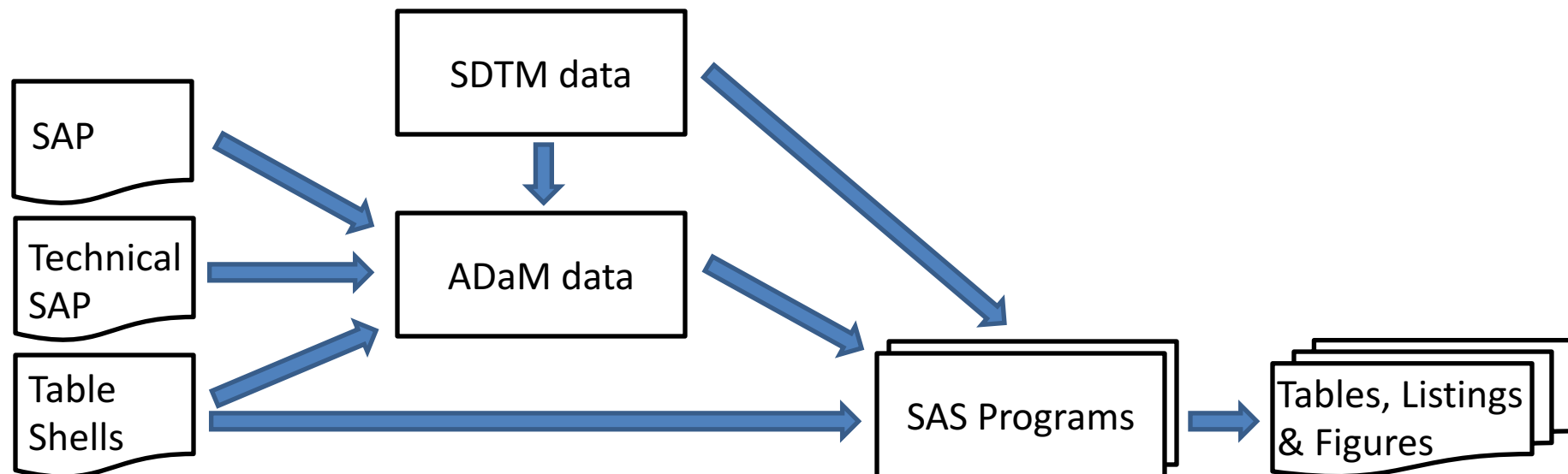


Metadata

Generating ADaM datasets in the same way



Current process



tlfnum	I	J	K	L	M	N	O
		Title	pgmlloc	pgmname	outno	outloc	outname
1.1.1		Patient analysis sets and reasons for exclusion - RS	pgm/ctr/tpopu.sas	tpopu.sas	T1	lst/tpopu_t1.lst	tpopu_t1.lst
1.2.1.1		Demographic data - TS	pgm/ctr/ct/demo.sas	demo.sas	T1	lst/demo_t1.lst	demo_t1.lst
1.2.1.2		Demographic data - FAS	pgm/ctr/ct/demo.sas	demo.sas	T2	lst/demo_t2.lst	demo_t2.lst
1.2.1.3		Concomitant diagnoses by MedDRA SOC and preferred term - TS	pgm/ctr/condiag.sas	condiag.sas	T1	lst/condiag_t1.lst	condiag_t1.lst
1.2.1.4		Concomitant therapies during screening by WHO INN - TS	pgm/ctr/conmed.sas	conmed.sas	T1	lst/conmed_t1.lst	conmed_t1.lst
1.2.1.5		New concomitant therapies during study part A by WHO INN - TS	pgm/ctr/conmed.sas	conmed.sas	T2	lst/conmed_t2.lst	conmed_t2.lst
1.2.1.6		New concomitant therapies during study part B by WHO INN - TS2	pgm/ctr/conmed.sas	conmed.sas	T3	lst/conmed_t3.lst	conmed_t3.lst
1.2.1.7		Use of ASA, antihypertensives, lipid lowering drugs or P-gp and CYP 3A4 inhibitors during screening - TS	pgm/ctr2/cttass.sas	cttass.sas	T1	lst/cttass_t1.lst	cttass_t1.lst
1.2.1.8		New use of ASA, antihypertensives, lipid lowering drugs or P-gp and CYP 3A4 inhibitors	pgm/ctr2/cttass.sas	cttass.sas	T2	lst/cttass_t2.lst	cttass_t2.lst
1.2.1.9		New use of ASA, antihypertensives, lipid lowering drugs or P-gp and CYP 3A4 inhibitors	pgm/ctr2/cttass.sas	cttass.sas	T3	lst/cttass_t3.lst	cttass_t3.lst

Excel is often used to capture TLF meta-data

Type	tlfnum	Title
Table	1.1.1	Patient analysis sets and reasons for exclusion - RS
Table	1.2.1.1	Demographic data - TS
Table	1.2.1.2	Demographic data - FAS
Table	1.2.1.3	Concomitant diagnoses by MedDRA SOC and preferred term - TS

pgmloc	pgmname	outno	outloc	outname	logname
pgm/ctr/tpopu.sas	tpopu.sas	T1	lst/tpopu_t1.lst	tpopu_t1.lst	tpopu.log
pgm/ctr/ct/demo.sas	demo.sas	T1	lst/demo_t1.lst	demo_t1.lst	demo.log
pgm/ctr/ct/demo.sas	demo.sas	T2	lst/demo_t2.lst	demo_t2.lst	demo.log
pgm/ctr/condiag.sas	condiag.sas	T1	lst/condiag_t1.lst	condiag_t1.lst	condiag.log

shell name	Parameter 1	Parameter 2
sh_popu1	pop=%STR(RANFL='Y')	
sh_dem1	pop=%STR(TRTFL='Y')	vars=AGE #SEX #RACE HT WT
sh_dem1	pop=%STR(FASFL='Y')	vars=AGE #SEX #RACE HT WT
sh_cd1	pop=%STR(TRTFL='Y')	

Store all the meta-data into a system

Study Name: study_001 

Select Data Currency:

Select Section: Total Number of Outputs: 9

■ No Program 0 ■ In Development 7 ■ To Be Validated 0 ■ Validated 2
● No Output 1 ● Old Output 4 ● Current Output 4

Expand All

Expand Sections

Auto Generate
Programs

Collapse All

Collapse Sections

Active Data Currency : Base

1 CTR 2

1.1 Disposition of patients

- Table 1.1.1 - Disposition of patients - SCR1
- Table 1.1.2 - Disposition of patients in relation to the timing of the implementation
- Table 1.1.3 - Primary reason for not randomising screened patients - SCR
- Table 1.1.4 - Number of screened, randomised and treated patients by region and country - SCR
- Table 1.1.5 - Number of treated patients in study part A by country and centre - TS
- Table 1.1.6 - Number of treated patients in study part B by country and centre - TS2

1.2 Important protocol violations

- Table 1.2.1 - Number of patients with important protocol violations in study part A - TS

1.3 Definition of analysis set

- Table 1.3.1 - Patient analysis sets and reasons for exclusion - TS

1.4 Figure

- Figure 1.4.1 - Adjusted HbA1c mean change from baseline over time during study part A using mixed model repeated measures analysis - FAS OC

Auto-generated programs – follow GPP

```
/*=====
*
* STUDY          : Study          CREATION DATE: 12JUL2016
*
* PROGRAM        : demo.sas
*
* PROGRAMMER     : John Smith
*
* DESCRIPTION     : Create following outputs:
*                  - T1 Demographic data - TS
*                  - T2 Demographic data - FAS
*
* USER REQUIREMENTS : SAP
*
* SAS VERSION    : SASV9.4
*
* COMMENTS       :
*
*-----
*|
* REVISION HISTORY
*
* DATE          :
* PROGRAMMER    :
* REASON FOR CHANGE :
*
*=====*/

*****;
***
*** Output No. T1
*** Title: 1.2.1.1 Demographic data - TS
***
*****;

%sh_dem1 ( outno = T1
           ,pop=%STR(TRTFL='Y')
           ,vars=AGE #SEX #RACE HT WT
           );

*****;
***
*** Output No. T2
*** Title: 1.2.1.2 Demographic data - FAS
***
*****;

%sh_dem1 ( outno = T2
           ,pop=%STR(FASFL='Y')
           ,vars=AGE #SEX #RACE HT WT
           );

*****;
***
*** End of Program
***
*****;
```

Search meta-data for historical tables

Advanced Search Across Studies

Select Category:

Criteria - Phase: ☒ Phase 1 ☐ Phase 3 ☐ Phase 2

Criteria - Population Type:

Search Result

5 studies found for: phase = 1 | population = TS |

Show entries

#	Access	Study	Table Number And Output Name
1		study_001	Table 1.1.5 Number of treated patients in study part B by country and centre - TS2
2		study_001	Table 1.2.3 Number of patients with important protocol violations in study part A - TS
3		Study_004	Table 1.1.5 Number of treated patients in study part B by country and centre - TS2
4		Study_004	Table 1.2.3 Number of patients with important protocol violations in study part A - TS

Preview Window

Table 4.1: 1 Demographic data - TS

	Red\Blue	Blue\Blue	Green\Green	Brown\Brown
Number of patients	135 (100.0)	135 (100.0)	134 (100.0)	134 (100.0)
Gender [N (%)]				
Male	77 (57.0)	70 (51.9)	66 (49.3)	84 (62.7)
Female	58 (43.0)	65 (48.1)	68 (50.7)	50 (37.3)
Race [N (%)]				
Amer.Ind./Alaska Nat	0 (0.0)	2 (1.5)	1 (0.7)	2 (1.5)
Asian	1 (0.7)	3 (2.2)	3 (2.2)	4 (3.0)
Black/African Amer.	14 (10.4)	18 (13.3)	16 (11.9)	21 (15.7)
Hawaiian/Pacif. Isle	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
White	120 (88.9)	111 (82.2)	114 (85.1)	107 (79.9)

How automation can add benefit

- The system is designed to enforce standards:
 - Standard TLF shells
 - Standard macros
 - SAS programs follow Good Programming Practices
 - SAS programs are easy to read for FDA reviewers
- Automation will give programmers time to do more interesting programming and check to raise quality
- Automation is NOT there to reduce the role of programmers or to reduce the size of programming groups

Summary

Excel Metadata for TLFs and shells

Type	tlfnum	Title
Table	1.1.1	Patient analysis sets and reasons for exclusion - RS
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Table	1.2.1.3	Concomitant diagnoses by MedDRA SOC and preferred term - TS

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pgm/ctr/ct/demo.sas	demo.sas	T1	lst/demo_t1.lst	demo_t1.lst	demo.log
pgm/ctr/ct/demo.sas	demo.sas	T2	lst/demo_t2.lst	demo_t2.lst	demo.log
pgm/ctr/condiag.sas	condiag.sas	T1	lst/condiag_t1.lst	condiag_t1.lst	condiag.log

shell name	Parameter 1	Parameter 2
sh_popu1	pop=%STR(RANDFL=Y)	
sh_dem1	pop=%STR(TRTFL=Y)	vars=AGE #SEX #RACE HT WT
sh_dem1	pop=%STR(FASFL=Y)	vars=AGE #SEX #RACE HT WT
sh_cd1	pop=%STR(TRTFL=Y)	

Search historical programs & output

Search Result

5 studies found for: phase=1 (population=TS)

Study

Table Number and Output Name

Study 001

Table 1.1.1 Number of treated patients in study part B by country and centre - TS

Study 002

Table 1.2.1.1 Number of patients with important potential concomitant events - TS

Study 003

Table 1.2.1.2 Number of patients with important potential concomitant events - TS

Study 004

Table 1.2.1.3 Number of patients with important potential concomitant events in study part B - TS

Preview Window

Number of treated patients in study part B by country and centre - TS

Obs	Name	Sex	Age	Height	Weight
1	Alfred	M	14	65.0	122.5
2	Allison	F	13	56.0	94.0
3	Barbara	F	15	65.0	98.0
4	Carol	F	14	62.0	100.0

Database

Display current summary status

Total Number of Outputs: 15

No Program 15
 In Development 0
 To Be validated 0
 Validated 0
 No Output 15
 Old Output 0
 Current Output 0

Display titles in an informative format

15.1 TRIAL SUBJECTS
15.1.1 Disposition of patients
Table15.1.1.1 Disposition of patients
Table15.1.1.2 Disposition of patients
Table15.1.1.3 Primary endpoint
Table15.1.1.4 Number of patients
Table15.1.1.5 Number of patients
Table15.1.1.6 Number of patients in study part B

Use company, therapeutic area and project standards

Auto-generate and submit programs

Develop programs interactively in SAS

Set program status to validated that change automatically if code changes

Questions or Comments?



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