

Incremental Automation

Lessons from a Pragmatic and Agile Journey of Improvement

Agenda

- Background
 - Automation Scope
 - Why Automate?
 - Why Automate *Incrementally*?
- Getting Started
- Overview of Automation Sub-Projects
- Lessons Learned
 - What has worked well?
 - What can be improved?
 - Key Takeaways
- Next Steps

Disparate Solutions with Manual Connections

Lack of Process & Consistency Across Compounds

Why Automate?



Siloed Activities = Duplicative Work

Repetitive Tasks Drain Time & Resource

Incorporate Existing Tools

Learnings from Previous Automation Efforts

Manageable Scope

Why Automate *Incrementally*?

Short Term Value; Long Term Impact

Bring People Along

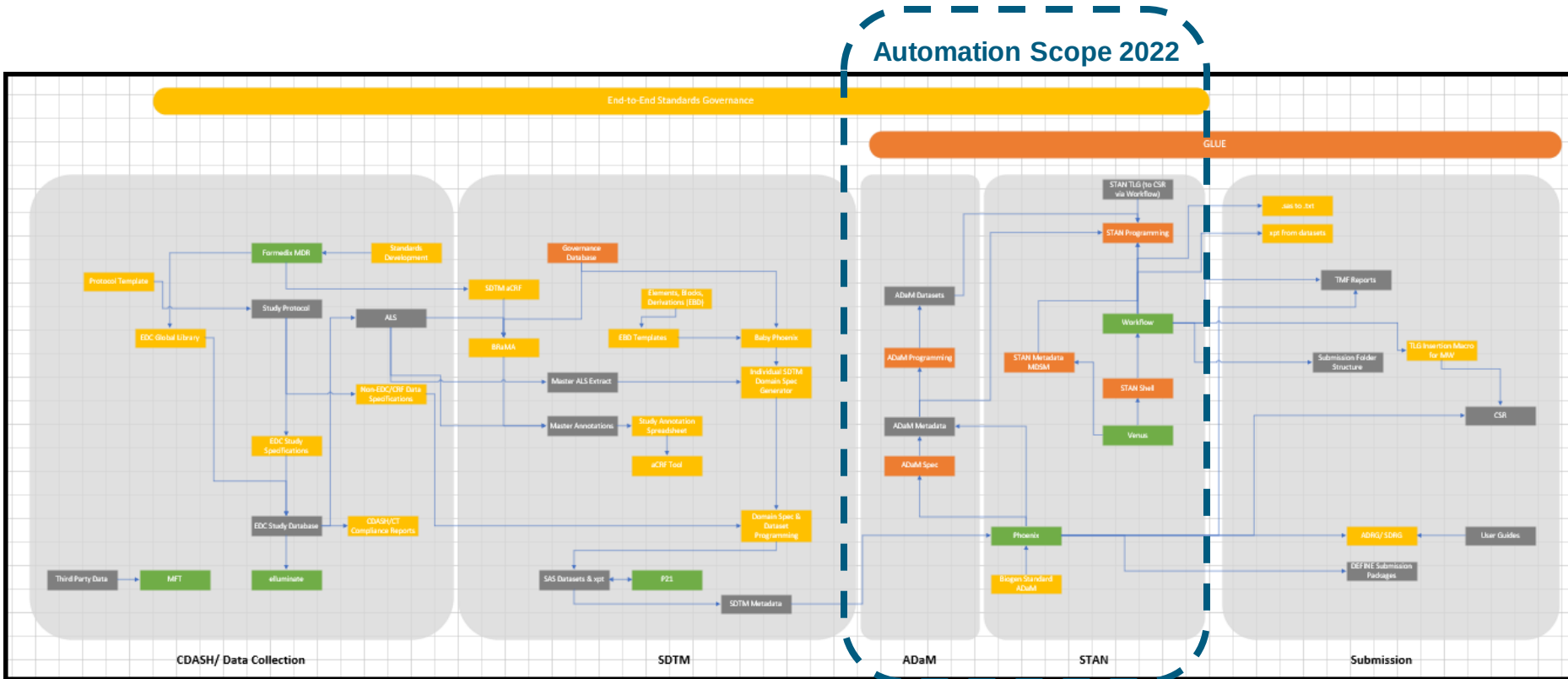
Automation Strategy

Automation is viewed as a **multi-year initiative** with a strategy geared toward the identification and **prioritization of sub-projects** that will optimize/automate a process or deliverable and add significant value in the short term.

This modular approach ensures we gain efficiencies in the short term by creating **incremental improvements to existing processes and tools** while contributing to the **longer-term vision of end-to-end automation.**

Getting Started

End-to-End Study Data, Metadata and Artifact Generation Process Flow



2022 Sub-Projects (Overview)

Automation Sub-Projects (2022)

1. Auto-ADaM: A turn-key solution to produce an immediately executable ADaM program that creates select ADaM baseline and safety datasets with seamless compatibility with MDSM

Impact: Truly standardize the execution of ADaMs to significantly reduce creation and QC time & resources

2. MDSM (Metadata Driven STandard ANalyses Macros): A programming process that will generate specified displays by calling a suite of STAN macros based on input metadata

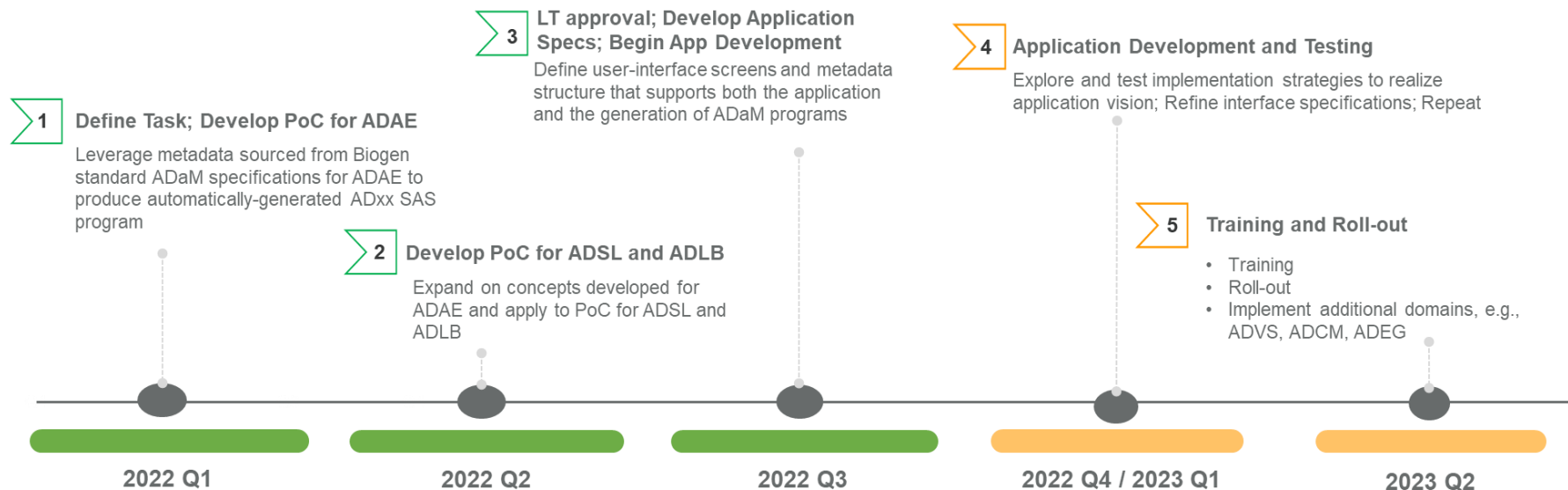
Impact: Reduce standard table production time and parallel programming to free up resources for value-forward work

3. Workflow Dashboard / Automation Hub (“GLUE”): A user-focused dashboard that pulls useful information from various tools to help users execute their daily work activities from a fully informed perspective

Impact: User-friendly, agile interface, that builds a connection between all custom-built applications within the automation initiative

1. Auto-ADaM Overview

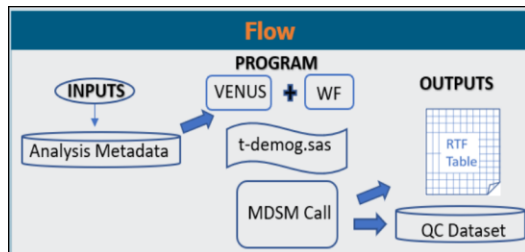
- Leverage Biogen standard analysis dataset metadata to automatically generate ADxx.SAS programs for Baseline and Safety
- Employ modular approach for data manipulations and derivations ensuring standardization consistency and governance compliance across domains, studies, and compounds thus improving quality and efficiency
- Provide interactive GUI user-interface enabling programmer to visualize and modify program code details and process flow



2. MDSM (Metadata Driven Standard Analyses Macros) Overview

- Metadata Driven Standard Analyses Macros (MDSM) is a programming process that will generate specified displays by calling a suite of standard macros based on input metadata. MDSM reduces standard table generation time from hours to minutes.
- MDSM can be applied to any table output that meets the following conditions:
 - Display standard columns** (i.e., Each data column defines a subset of the analysis population: treatment groups, cohorts, subgroups, etc. with or without one-level column span)
- Summarizes categorical and defined continuous statistics**
- Version 1.0 (production live Q2 2022)

Placebo (N=xx)	Treatment A (N=xx)	Placebo		Treatment A	
		Japan (N=xx)	Ex Japan (N=xx)	Japan (N=xx)	Ex Japan (N=xx)



eMock Shells Selected study: testproduct/mdsm/test_unit

Study Settings Workflow Export to PDF file Shell Versioning STAM Documents User Guide

Population Set Metadata

Add Row

Pop_Set_ID	Population Set	Population Set Definition	Population Set Dataset	ACTION
ENBL	enrolled subjects	ENBLFL="Y"	ordcr.adcd	DELETE
PAS	full analysis set	PASFL="Y"	ordcr.adcd	DELETE
SAF	safety analysis set	SAFFL="Y"	ordcr.adcd	DELETE
RAND	all randomized subjects	RANDFL="Y"	ordcr.adcd	DELETE

Reset to default

Column Layout Metadata

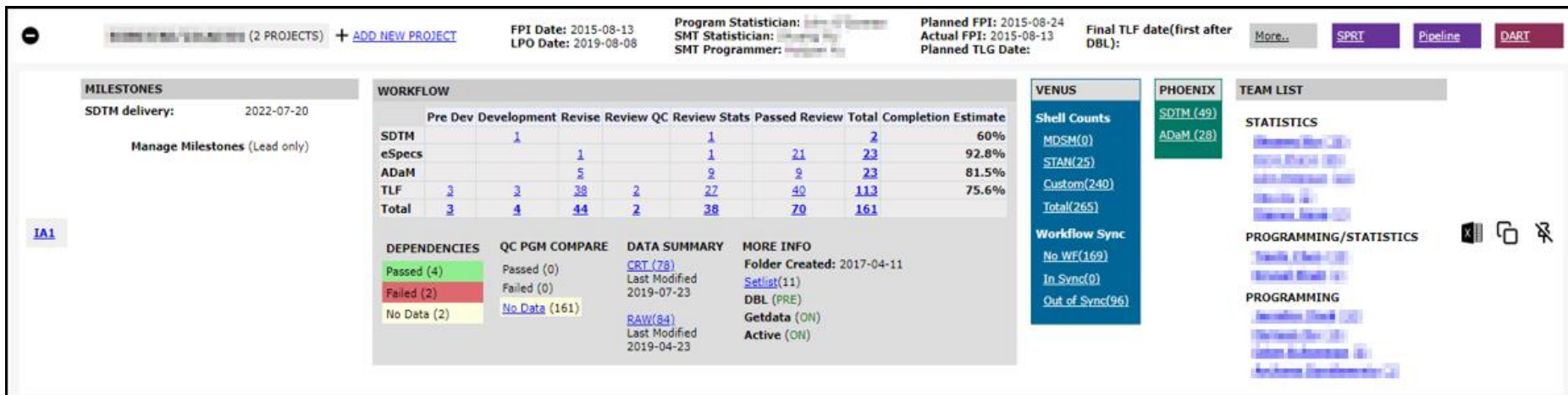
Add Row

Col_Layout_ID	Column Display Definition	Column Display Order	Column Display Label	Span Label (if any)	Column Width (in.)	Orientation	ACTION
TA	TST01AB in (0)	1	Placebo		3.3	Landscape	DELETE
TA	TST01AB in (2)	2	Treatment B		3.3	Landscape	DELETE
TA	TST01AB in (1)	3	Treatment A		3.3	Landscape	DELETE
TA	TST01AB in (1,2)	4	Total (A+B)		3.3	Landscape	DELETE
TP	TST01PN in (0)	1	Placebo		3.1	Landscape	DELETE
TP	TST01PN in (1)	2	Treatment A	Active	3.1	Landscape	DELETE
TP	TST01PN in (2)	3	Treatment B	Active	3.1	Landscape	DELETE
TP	TST01PN in (3)	4	Treatment C	Active	3.1	Landscape	DELETE
TP	TST01PN in (0,1,2,3)	5	Total		3.1	Landscape	DELETE

Reset to default

3. Workflow Dashboard / Automation Hub (“GLUE”) Overview

- Connects (i.e., “glues”) core internal tools to underpin automation efforts
- Version 1.0 (production live Q3 2022) of the Workflow Dashboard provides users with a holistic view of a project/study and their corresponding deliverable. Users can track, manage deliverable activities, timelines, & resources
- The dashboard also enables users to manage milestones, view a project’s status, copy a deliverable, and access other applications to more effectively coordinate work from an informed perspective
- Version 1.1 to include functionality to launch automation tools (e.g., Auto-ADaM, MDSM) and serve as the Automation Hub



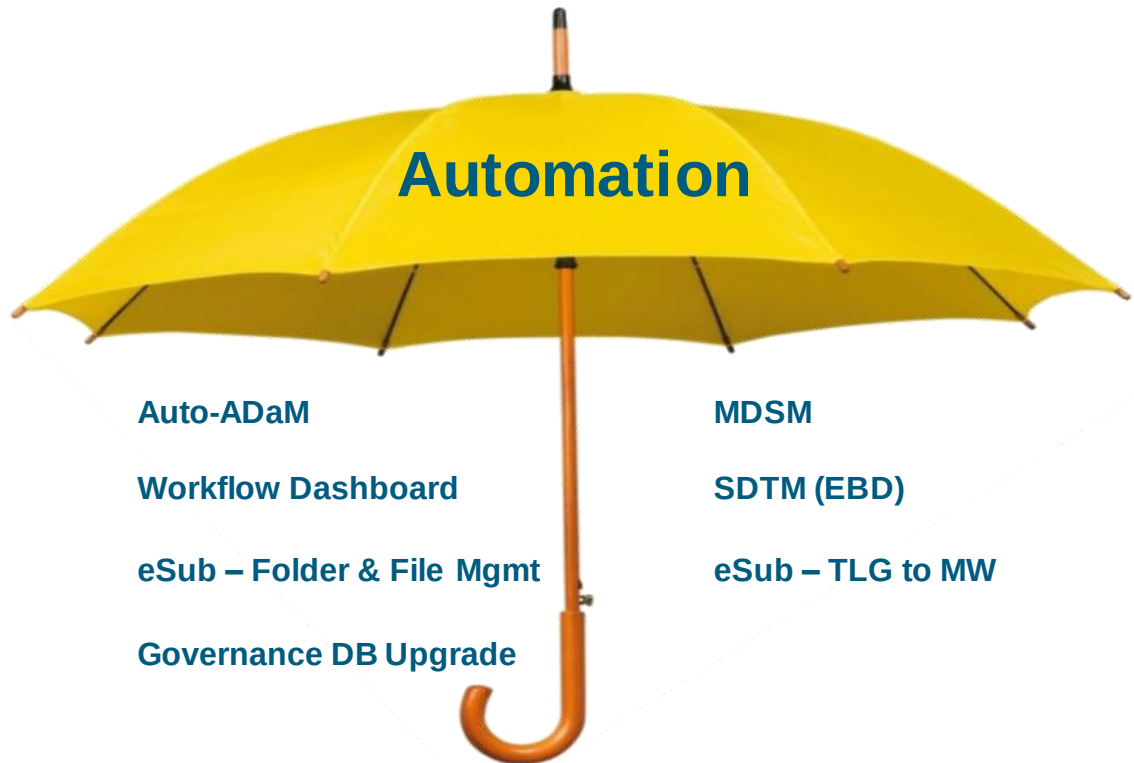
Lessons Learned

Lessons Learned

Lesson 1: Leverage an overarching/umbrella initiative (“Automation”)

An Umbrella Initiative:

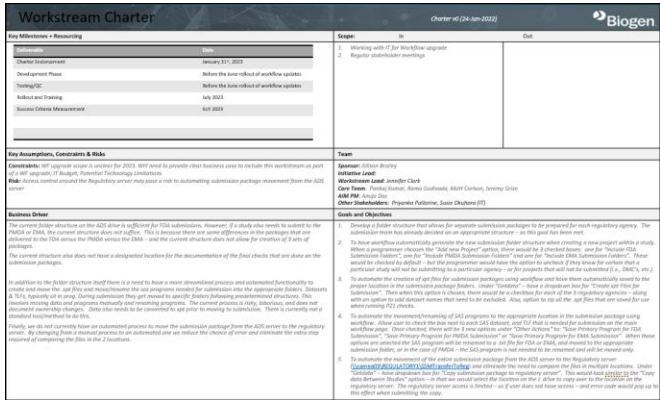
- Harnesses Sr. Management Support for Sub-Projects
 - Assists with Prioritization
 - Resourcing
 - Funding
- Engages End-Users
 - Assists with recruiting sub-project team members
 - Ignites creativity / new ideas



Lessons Learned

Lesson 2: Dedicated project management support is critical to success

- Charter (or equivalent): Up-front, detailed documentation framing goals, business drivers, team members and stakeholders, approval status, resources, success criteria, and milestone/timeline info etc.
- Importance of identifying achievable milestones for each effort to allow for frequent examination of progress, timeline, resources, roadblocks, etc.
 - for a single task, but
 - also, if dependencies between tasks – e.g., falling behind on one task could impact another task or project



Workstream Charter

Charter v2 (14 Jan 2022)

Key Objectives & Resources

Key Objectives	Resources
Regulatory	
Regulatory	January 2022
Development Phase	Before the start of workflow updates
Testing/QC	Before the start of workflow updates
Submission & Review	July 2022
Submission & Review	July 2022

Key Assumptions, Constraints & Risks

Assumptions: All regulatory review is done by 2022. All need to provide other business case to include this workstream as part of all regulatory, IT, Biogen, Biogen Technology resources.

Risks: Focus control around the Regulatory review may pose a risk to automating submission package preparation from the ADS server.

Business Driver

The current regulatory structure as the ADS does is efficient for ADS submissions. However, it is likely also needs to be updated to the ADS or ADS, the current structure does not reflect. This is because there are some differences in the packages that are submitted to the ADS versus the ADS server (the ADS) – and the current structure does not allow for review of 2 sets of packages.

The current structure also does not have a designated location for the documentation of the first checks that are done on the submission packages.

In addition to the ADS structure itself there is a need to have a more streamlined process and automated functionality to create and review the ADS and the submission package. The current structure is not efficient for the ADS and the ADS, the current structure does not reflect. This is because there are some differences in the packages that are submitted to the ADS versus the ADS server (the ADS) – and the current structure does not allow for review of 2 sets of packages.

The current structure also does not have a designated location for the documentation of the first checks that are done on the submission packages.

Finally, we do not currently have an automated process to move the submission package from the ADS server to the Regulatory server. By changing this current process to an automated one we reduce the chance of error and streamline the entire cycle required of comparing the files in the 2 locations.

Team

Sponsor: Oliver Bickley
Initiative Lead:
Workstream Lead: Jennifer Clark
Core Team: Patrick Kester, Anna Goffredo, Albert Carlson, Jeremy Grier
ADP Lead: Patrick Grier
Other Stakeholders: Proprietary, David Chikara (IT)

Goals and Objectives

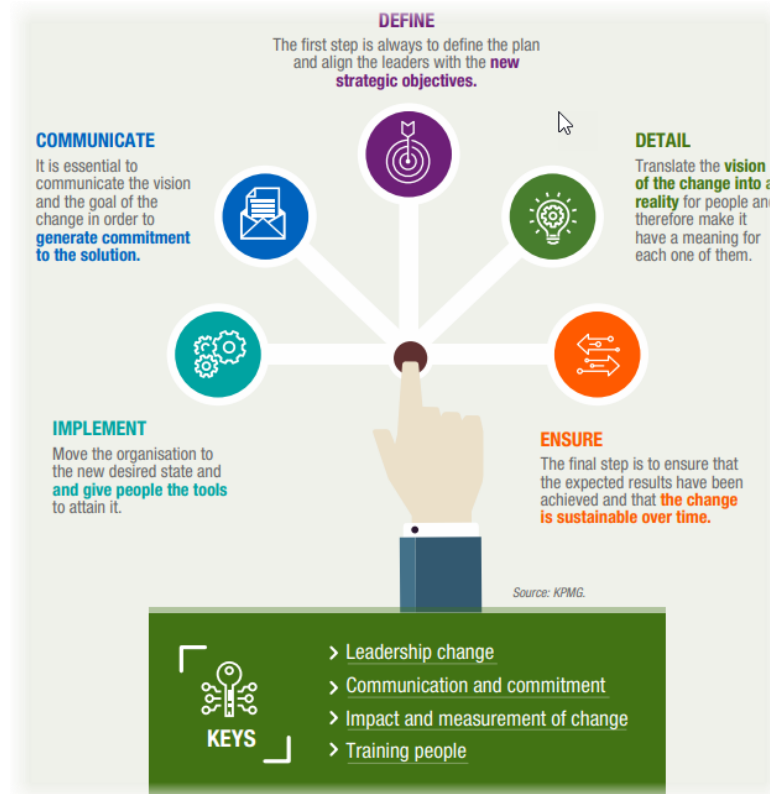
1. Develop a clear structure that allows for separate submission packages to be prepared for each regulatory agency. This submission has already been done for an appropriate structure – in this part has been met.
2. To have workflow automatically generate the new submission folder structure when creating a new project within a study, where a program manager creates the "New Project" option, there would be a dedicated folder, one for "Regulatory (ADS)" and one for "Regulatory (ADS)" and one for "Regulatory (ADS)". These would be created by default – but the program manager would have the option to select if they know for certain that a particular study will not be submitted to a particular agency – or the projects that will not be submitted (e.g., ADS, ADS, and ADS).
3. To automate the creation of all files for submission packages using workflow and have them automatically saved to the appropriate location in the submission package folder. Under "Workflow", there is a dropdown for "Create and Files for Submission". When this option is chosen, there would be a checkbox for each of the 3 regulatory agencies – using which option to select submit review that need to be included. Also, option to select if the ADS files that are used for ADS when creating ADS files.
4. To automate the submission/transfer of ADS packages to the appropriate location in the submission package using workflow. Allow user to check the box next to each ADS location, and "I" that is needed for submission on the ADS workflow page. Once checked, there will be a new option under "Other Actions" for "New Package (Regulatory for ADS Submission)". This option will be for ADS submission. "New Package (Regulatory for ADS Submission)" – when these options are selected for ADS program and be required to a sub file for ADS or ADS, and would be the appropriate submission folder, or the ADS or ADS – the ADS program will not need to be reviewed and will be reviewed only.
5. To automate the movement of the entire submission package from the ADS server to the Regulatory server. This would be done by a "New Package (Regulatory for ADS Submission)" and "New Package (Regulatory for ADS Submission)" – when these options are selected for ADS program and be required to a sub file for ADS or ADS, and would be the appropriate submission folder, or the ADS or ADS – the ADS program will not need to be reviewed and will be reviewed only.

Charter for each sub-project critical to ensure alignment between team members and Sr. Leadership

Lessons Learned

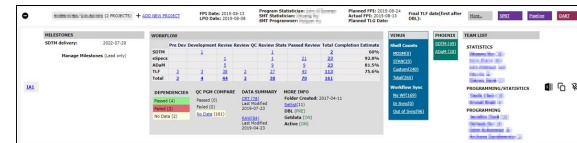
Lesson 3: If you build it, they may not come

- Don't assume incremental improvements will lead to greater adoption
- Change Management is critical!



Lessons Learned

Lesson 3: If you build it, they may not come (continued)



Example

Following the release of v1.0 of the Workflow Dashboard / Automation Hub (“GLUE”), several trainings, communications, etc. was provided to end users and the automation team expected rapid adoption of the new tool

- Automation team quickly worked to identify a long list of improvements/new functionality to incorporate into v2.0

However, based on usage metrics, there was a low adoption/utilization of the Dashboard

- Automation team interviewed key stakeholders to learn why

Results/Actions Planned:

- Even after trainings/communications awareness of new tool still low
 - ACTION: Early adopters to promote benefits at the study team level
- Key functionality for core group of potential users was not accessible via the Dashboard
 - ACTION: Next version targeted as v1.1 – scope reduced to focus on key functionality and widespread tool adoption



Lessons Learned

Lesson 4: Ensure success can be measured

Example

- Per initial PoCs, MDSM was projected to reduce standard table production time from hours to minutes
 - Post-production automated tracking proved it



- Utilization also tracked automatically to confirm adoption

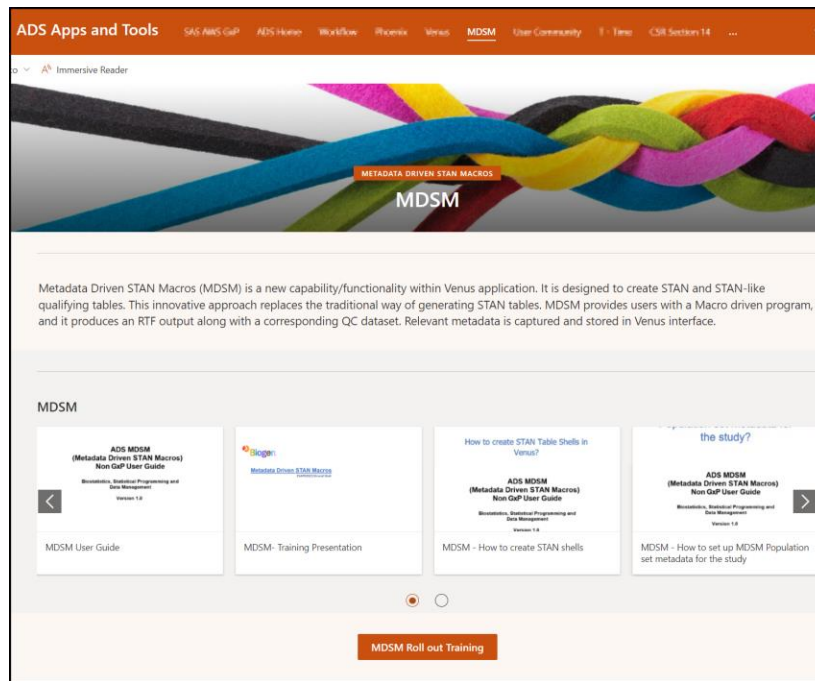
Study/Deliverable	Overall Table Counts	# of STAN Tables	# of MDSM Compliant STAN Tables	# of STAN Tables completed using MDSM	% Adoption
bib037ac0271nv104/1car	38	28	27	27	100%
aw0004402020ns402interim.tbl-2020	46	24	21	21	100%
bg12ns1104ns004interim.tbl	41	29	28	28	100%
Mechanisms0000ns001/1car	29	17	16	15	94.11%
bib050230ns003handbook	45	45	42	32	71.11%

- Success metrics has led to widespread adoption and mandated use of MDSM by Sr. Leadership**

Lessons Learned

Lesson 5: Importance of training / support resources

- End user engagement, education and support critical to success
- On-demand is key



Lessons Learned

Other Key Lessons/Takeaways

- Involve IT partners during sub-project planning to ensure alignment and available resources for any upgrade/validation activities, as applicable
- Importance of a strong standards culture and tight governance (develop, educate, govern, maintain) to underpin automation efforts
- Conduct After-Action Reviews (AARs) or Equivalent
- Celebrate Success!



After-Action Review In A Nutshell

An after-action review (AAR) is a structured process of reflecting on the work of a group by identifying strengths, weaknesses, and areas for improvement. After action reviews were first utilized by the United States Army on combat missions. Since then, modern companies such as British Petroleum, Motorola, and General Electric have all become proponents. AARs are also used to identify gaps in public health emergency preparedness systems. After Hurricane Katrina in 2005, a searching review of the emergency response led to new methods of communicating during natural disasters.

1. What did we expect to happen?
2. What actually happened?
3. What went well, and why?
4. What can we improve on, and how?

Step 1 – Make it a priority

Step 2 – Involve everyone

Step 3 – Conducting the review

Step 4 – Crafting the report

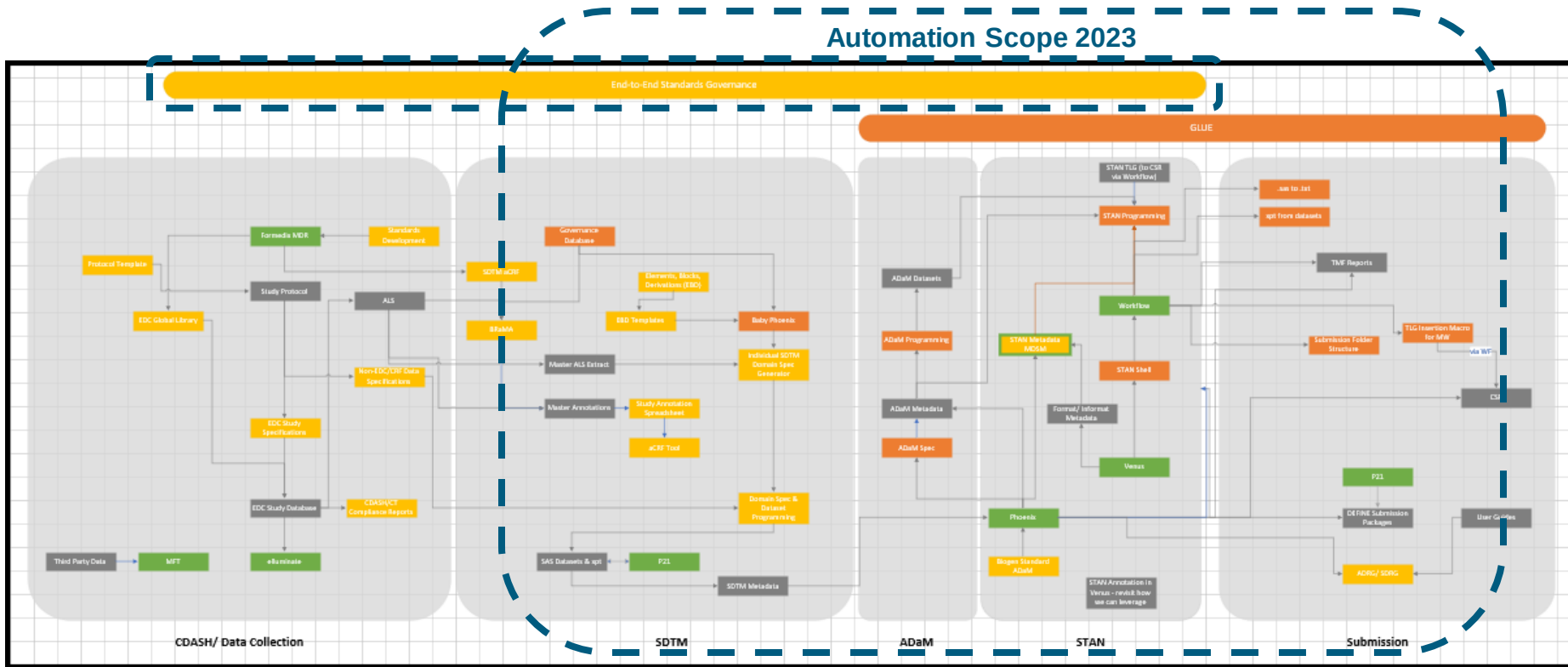
Step 5 – Implement the changes

1

1. Gennaro Cuofano | January 2023

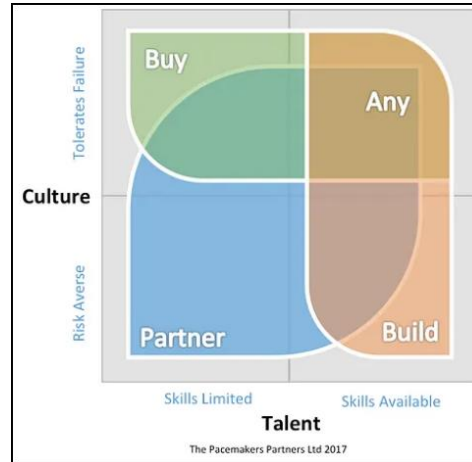
Moving Forward

End-to-End Study Data, Metadata and Artifact Generation Process Flow



Ongoing

- Continue to monitor industry advancements in supporting automation
- Continue to evaluate buy vs. build
 - Combination of tools



Thank you!

Biogen Automation Core Team: Phil Brown, Matt Carlson, Pankaj Kumar, Krunal Shah, Samir Parikh, Kumar Sreeramaiah, Anuja Das

Open Discussion / Q&A

For additional questions/comments/feedback please email: todd.bazin@biogen.com, anuja.das@biogen.com

Back-Up Slides

Auto-ADaM: Dataset Content Driven by Phoenix

Current Study: biib105-dsur2022:biib105-dsur2022 - eSpec (biib105/dsur/dsur2022)

[Study](#)[Insert/Edit Data](#)[Other Resources](#)[Logout mcarlson](#)

Edit Dataset/Variable Level Metadata

Dataset ADAE

Dataset Options

Label: Adverse Events Analysis Dataset Purpose: Analysis Class: OCCURRENCE DATA

STRUCTURE

Structure: One record per subject, per AE term, per AE preferred term, per AE start date, per AE end date, per AE sequence

Keys: USUBJID, AETERM, AEDECOD, AESTDTC, AEENDTC, AESEQ

Documentation:

Notes:

Variable Level Metadata

Variable	Label	Comment or Method (for define.xml)	Mapping Spec (Comment for Programmer)	Code List	Length	Type
TRTP	Planned Treatment	TRTP is equal to ADSL.TRT01P		[Create / Edit]	20	text
TRTPN	Planned Treatment (N)	TRTPN is equal to ADSL.TRT01PN		[Create / Edit]	8	integer
TRTA	Actual Treatment	TRTA is equal to ADSL.TRT01A		[Create / Edit]	20	text
TRTAN	Actual Treatment (N)	TRTAN is equal to ADSL.TRT01AN		[Create / Edit]	8	integer
ASTDT	Analysis Start Date	numeric date version of AE.AESTDTC		[Create / Edit]	8	integer
ASTDY	Analysis Start Relative Day	AENDT - ADSL.TRTSDT + 1 for AENDT >= ADSL.TRTSDT AENDT - ADSL.TRTSDT for AENDT < ADSL.TRTSDT		[Create / Edit]	8	integer
AENDT	Analysis End Date	numeric date version of AE.AEENDTC		[Create / Edit]	8	integer
AENDY	Analysis End Relative Day	AENDT - ADSL.TRTSDT + 1 for AENDT >= ADSL.TRTSDT AENDT - ADSL.TRTSDT for AENDT < ADSL.TRTSDT		[Create / Edit]	8	integer

Auto-ADaM: Variable-Level Derivations

Auto-ADaM:: DEV ## Current Study: biib105-dsur2022:biib105-dsur2022 - eSpec (biib105/dsur/dsur2022)

[Study](#)[Insert/Edit Data](#)[Other Resources](#)[Logout mcarlson](#)

Dataset Module Details

Dataset **ADAE** ▼

Label: Adverse Events Analysis Dataset Purpose: Analysis Class: OCCURRENCE DATA

STRUCTURE

Structure: One record per subject, per AE term, per AE preferred term, per AE start date, per AE end date, per AE sequence

Keys: USUBJID, AETERM, AEDECOD, AESTDTC, AEENDTC, AESEQ

Documentation:

Notes:

Variable Level Metadata

Variable	Label	Action or Module	Module Description	History
TRTP	Planned Treatment	ADAM_ASSIGN_TO_VARVAL_V1	VAROUT = trtp VARIN = trt01p	
TRTPN	Planned Treatment (N)	ADAM_ASSIGN_TO_VARVAL_V1	VAROUT = trtpn VARIN = trt01pn	
TRTA	Actual Treatment	ADAM_ASSIGN_TO_VARVAL_V1	VAROUT = trta VARIN = trt01a	
TRTAN	Actual Treatment (N)	ADAM_ASSIGN_TO_VARVAL_V1	VAROUT = trtan VARIN = trt01an	
ASTDT	Analysis Start Date	ADAM_CHAR19DTM_TO_SASDT_V1	VAROUT = astdt VARIN = aestdte INFMT = e8601da10 IRULE = RULE1	
ASTDY	Analysis Start Relative Day	ADAM_SASDT_TO_DUR_V1	INFMT = e8601dt19 VAROUT = astdy EVTDT = astdt REFDT = trtsdt	

Auto-ADaM Interface – Program Process Flow

Create Study Process Order

Dataset ADAE

Drag and drop the items into the correct order and click the "Save" button.

Save order Preview Initialize

Included >>> ADAE Program Flow <<<

Source	Target	Module Name	
◦ crtldr.ae	ae	ADAM_READ_DATASET_V1	[more info]
◦ crtldr.adsl	adsl	ADAM_READ_DATASET_V1	[more info]
◦ ae, adsl	ae	ADAM_MERGE_DATASET_V1	[more info]
◦ ae, adsl	ae	TRTP: ADAM_ASSIGN_TO_VARVAL_V1	[more info]
◦ ae, adsl	ae	TRTPN: ADAM_ASSIGN_TO_VARVAL_V1	[more info]
◦ ae, adsl	ae	TRTA: ADAM_ASSIGN_TO_VARVAL_V1	[more info]
◦ ae, adsl	ae	TRTAN: ADAM_ASSIGN_TO_VARVAL_V1	[more info]
◦ ae, adsl	ae	ASTDT: ADAM_CHAR19DTM_TO_SASDT_V1	[more info]
◦ ae, adsl	ae	ASTTM: ADAM_SASDTM_TO_SASTM_V1	[more info]
◦ ae, adsl	ae	ASTDTM: ADAM_CHAR19DTM_TO_SASDTM_V1	[more info]
◦ ae, adsl	ae	ASTDTF: ADAM_CHARDTM_TO_DT_IMPFL_V1	[more info]
◦ ae, adsl	ae	ASTTMF: ADAM_CHARDTM_TO_TM_IMPFL_V1	[more info]
◦ ae, adsl	ae	AENDT: ADAM_CHAR19DTM_TO_SASDT_V1	[more info]
◦ ae, adsl	ae	AENTM: ADAM_SASDTM_TO_SASTM_V1	[more info]
◦ ae, adsl	ae	AENDTM: ADAM_CHAR19DTM_TO_SASDTM_V1	[more info]
◦ ae, adsl	ae	AENDTF: ADAM_CHARDTM_TO_DT_IMPFL_V1	[more info]
◦ ae, adsl	ae	ASTDY: ADAM_SASDT_TO_DUR_V1	[more info]
◦ ae, adsl	ae	AENDY: ADAM_SASDT_TO_DUR_V1	[more info]
◦ ae, adsl	ae	ADURN: ADAM_SASDT_TO_DUR_V1	[more info]
◦ ae, adsl	ae	ADURU: ADAM_ASSIGN_TO_VALUE_V1	[more info]
◦ ae, adsl	ae	ASEVN: ADAM_ASSIGN_TO_VARFMT_V1	[more info]
◦ ae, adsl	ae	ARFI: ADAM_ASSIGN_TO_VARVAL_V1	[more info]

>>> ADAE Module/Variable "Bench" <<<

Bench

Source	Target	Module Name	
◦ ADAE	AESEQ		[more info]
◦ ADAE	ITTFI		[more info]
◦ ADAE	ITTFI		[more info]
◦ ADAE	LPREL		[more info]
◦ ADAE	SITEID		[more info]
◦ ADAE	STUDYID		[more info]
◦ ADAE	SUBJID		[more info]
◦ ADAE	USUBJID		[more info]

Undefined

- SAFFL
- TRTEMFL
- AOCCIFL
- AOCCPFL
- AOCCSIFL
- AETOXGRN
- AEDTHFL
- AEREFID
- AETERM
- AEDECOD
- AEBODSYS
- AELLT
- AEHLT
- AEHLGT

Auto-ADaM: Automatically Generated Code

```
data ae_adsl_010 (drop=&_adam_echeck_dropvars &_adam_drop_in_vars)
  adam_echeck_temp (keep=&_adam_echeck_keepvars)
;
** Note: Module [adam_datastep_init_v1] MUST appear directly after datastep DATA statement **;
%adam_datastep_init_v1;
%attrib(vars=
  TRTP TRTPN TRTA TRTAN ASTDT ASTTM ASTDTM ASTDTF ASTTMF AENDT
  AENTM AENDTM AENDTF ASTDY AENDY ADURN ADURU ASEVN AREL PREFL
  FUPFL TRTEMFL
);
merge
  ae_010      (in=in1)
  adsl_010    (in=in2)
;
by usubjid;
if in1 and in2;

*****
** ADAMID   : 3.2.1.1.1                                     **
** VAROUT   : TRTP                                          **
** ATTRIB   : $40 :: Planned Treatment                      **
** MODULE   : ADAM_ASSIGN_TO_VARVAL_V1                     **
** PURPOSE  : Assign ADxx var: to VARIN var-value          **
*****;

%adam_assign_to_varval_v1(
  varout      = trtp
  ,varin       = trt01p
  ,adamid      = %str(3.2.1.1.1)
);
```

MDSM - Overview

Programming Flow Within the MDSM Macro call

Table layout

Column layout

Placebo (N=34)	 300mg (N=32)	Total (N=66)
n (%)	n (%)	n (%)

Build Column layout + Population count Big N

```
%stan_tab_col_layout
```

Content

Age categories (years)	15 to 40	41 to 60	61 to 80
15 to 40	10 (100%)	10 (100%)	10 (100%)
41 to 60	10 (100%)	10 (100%)	10 (100%)
61 to 80	10 (100%)	10 (100%)	10 (100%)
>80	10 (100%)	10 (100%)	10 (100%)
Age (years)	48	57	65
Mean (SD)	48 (12)	57 (12)	65 (12)
Median	48	57	65
Q1, Q3	40, 56	48, 66	58, 74
Min, Max	15, 80	41, 80	61, 80
Sex			
Male	10 (100%)	10 (100%)	10 (100%)
Female	10 (100%)	10 (100%)	10 (100%)

Get the statistics for each row or category
%stan_tab_row_layout

Output

Demography - analysis set			
Page 1 of 2	Phases On-Ad n (%)	Naturalized, Missing Off-Ad n (%)	Total On-Ad+Off-Ad n (%)
Age categories (years)			
<10	10	10	20
10 to 15	10	10	20
16 to 20	10	10	20
>20	10	10	20
Age (years)			
Mean (SD)	10 (10)	10 (10)	10 (10)
Median	10	10	10
Q1, Q3	10, 10	10, 10	10, 10
Min, Max	10, 10	10, 10	10, 10
Sex			
Male	10	10	20
Female	10	10	20
Race			
American Indian or Alaska Native	10	10	20
Asian	10	10	20
Black or African American	10	10	20
Hispanic or Other Pacific Islander	10	10	20
White	10	10	20
Other	10	10	20
Not reported due to confidentiality considerations	10	10	20
	1 (1)	0	1 (1)

```
Create RTF Output
%stan_tab_rtf
```