



Developing, Implementing and Governing End-to-End Standards at Gilead

Dhananjay Chhatre

Associate Director, Gilead Sciences

February 26th, 2019

PhUSE US Connect 2019



Agenda

1. Lessons Learned Improved Development and Implementation Strategy
2. Governance Strategy
3. Biometrics eSubmissions (eSub) Team
4. Standards Landscape – A Survey



Lessons Learned Improved Development and Implementation Strategy



Gilead has made significant progress towards leveraging standards and automation utilities for increasing end-to-end quality and transparency

Results as of today:

- ✓ **3** new tools created
- ✓ **14** new standards created
- ✓ **11** standards updates
- ✓ **11** new trainings offered
- ✓ **9** new process documents

Collection



Data Processing



Submission



Change Management



Training and Process Documents



Governance



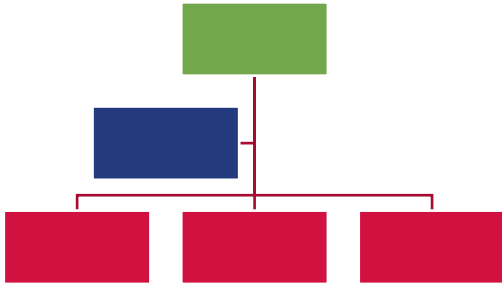
Lessons Learned

Development Processes Changed



We implemented changes to three processes which improved our standards development efficiency and overall quality of deliverables

Standards Organizational Structure



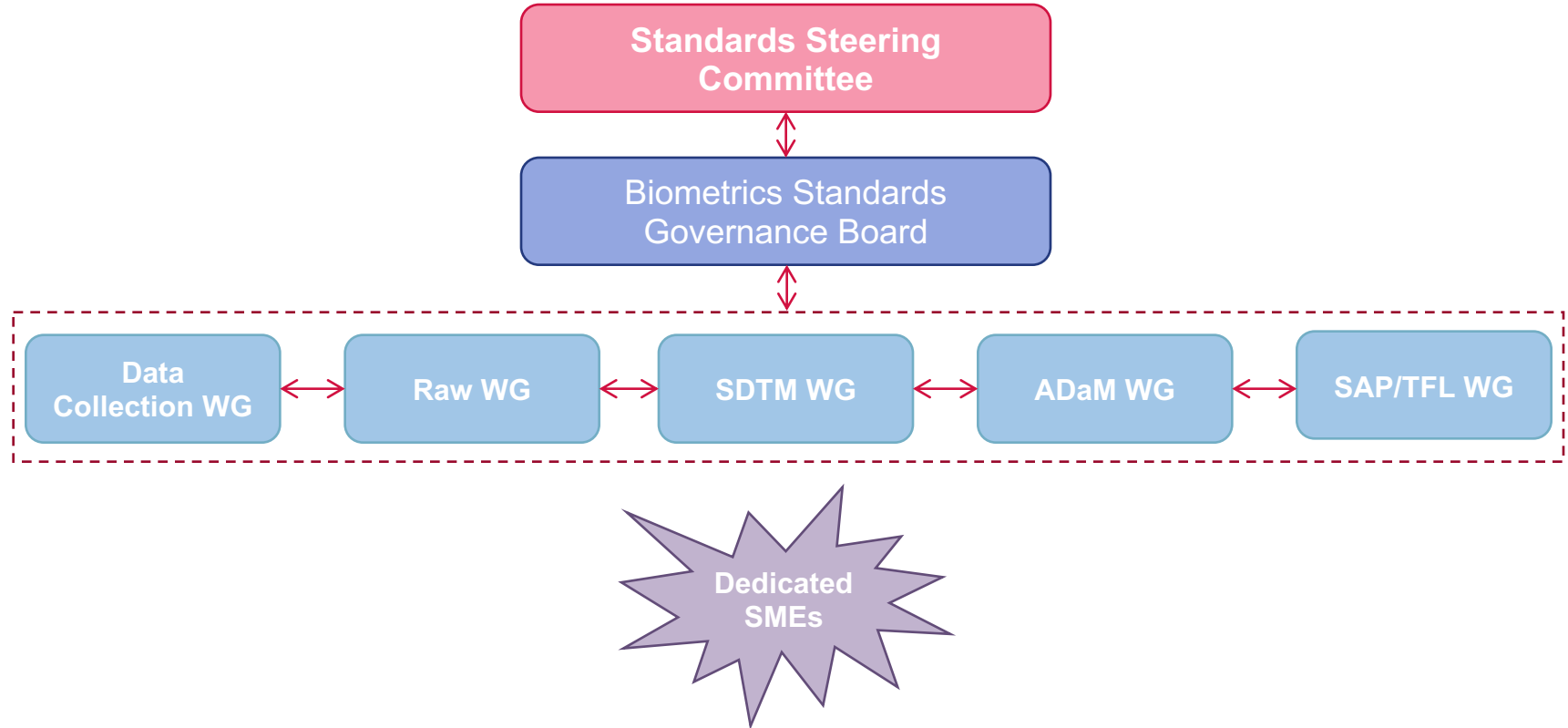
Tools to Assess Consistency



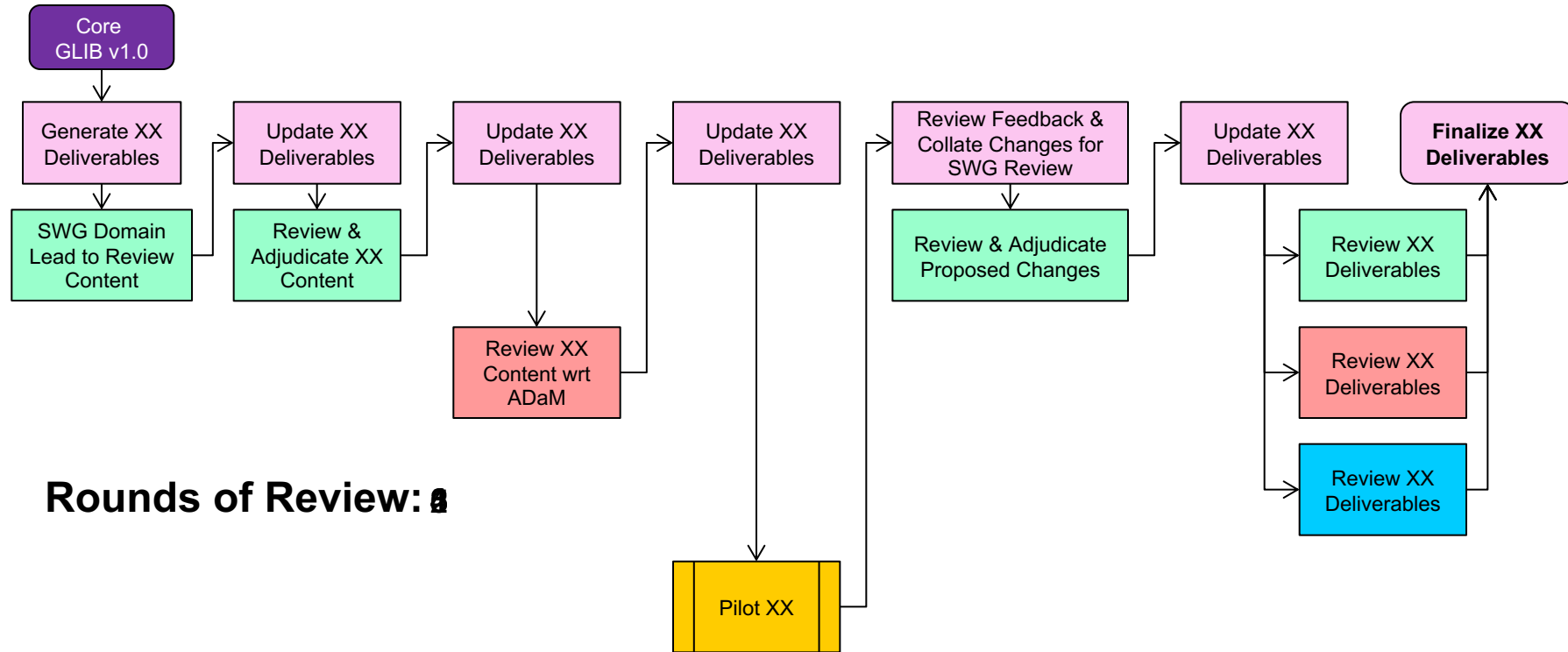
Dedicated SME Support



1. Defined more formal standards organizational structure, promoting cross-working group (WG) collaboration and an issue escalation process

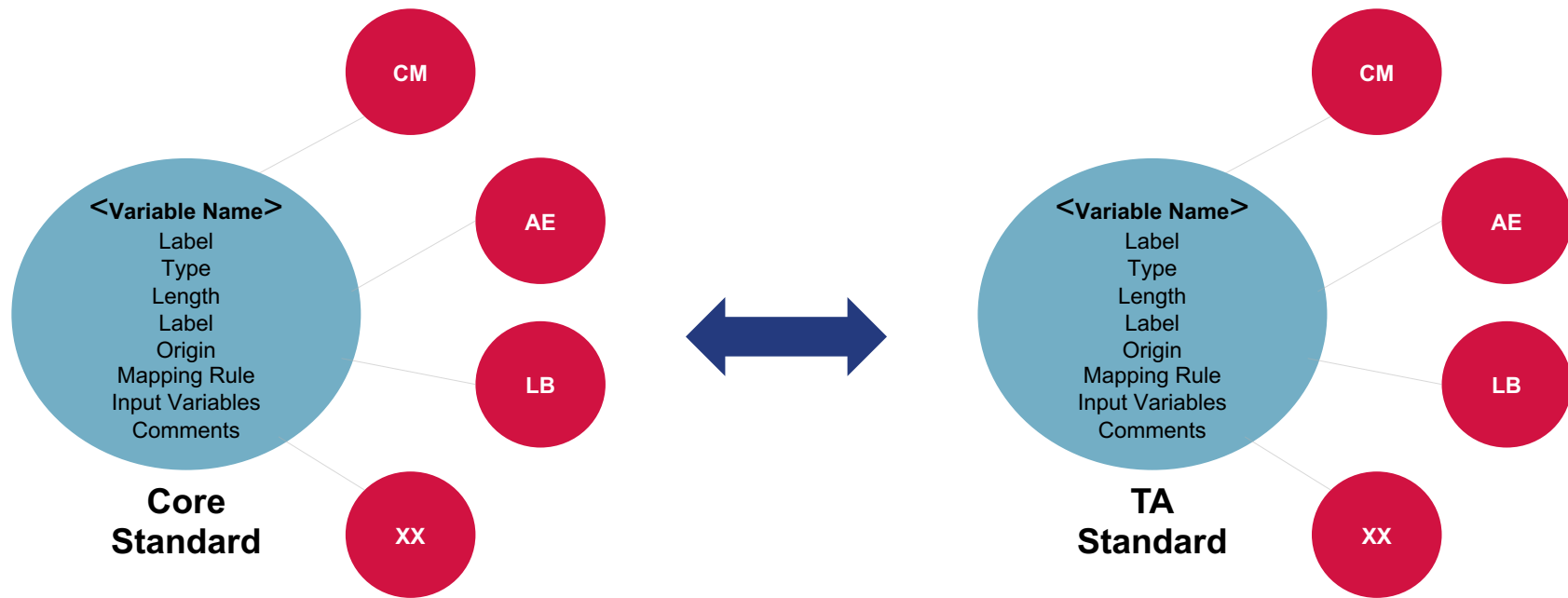


2. Improved Efficiency of standards WG by supporting study team members with dedicated SMEs for heavy lifting and research



e.g. SDTM WG

3. Leveraged programs to check consistency of variables mapped across domains, TAs, and between standards versions



Since multiple SMEs work on different domains, checking consistency across domains was critical



3. Leveraged programs to check consistency of variables mapped across domains, TAs, and between standards versions

Example of Comparison Result across domain – Different SMEs worked on CM and EX

Domain	Variable Name	Label	Length	Mapping Rule
SUPPCM	CMRTOTH	Other Route of Administration	200	Populate in Upper Case
SUPPEX	EXRTOTH	Route, Other Specify	100	Map Original Value in Upper case
SUPPCM	CMDSFROT	Other Dosing Frequency	200	Populate in Upper Case
SUPPEX	EXDSFROT	Frequency, Other Specify	100	Map Original Value in Upper case



Lessons Learned

Automation Tools to Support Implementation



Implementation of developed standards aided by strict regulatory requirement effective dates and automation tools improving efficiencies



Regulatory requirements
(SDTMIGV3.2,
define.xml v2.0)



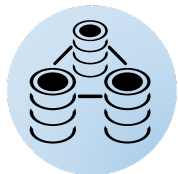
Automation of
dataset and
define.xml v2.0
generation



Gilead-
Customized
define.xml v2.0
stylesheet



Automation of
Analysis Results
Metadata (ARM)
in define.xml v2.0



**Metadata-driven
(safety) TFL
generator**



Data Transfer
Specifications
development and
QC tool checks

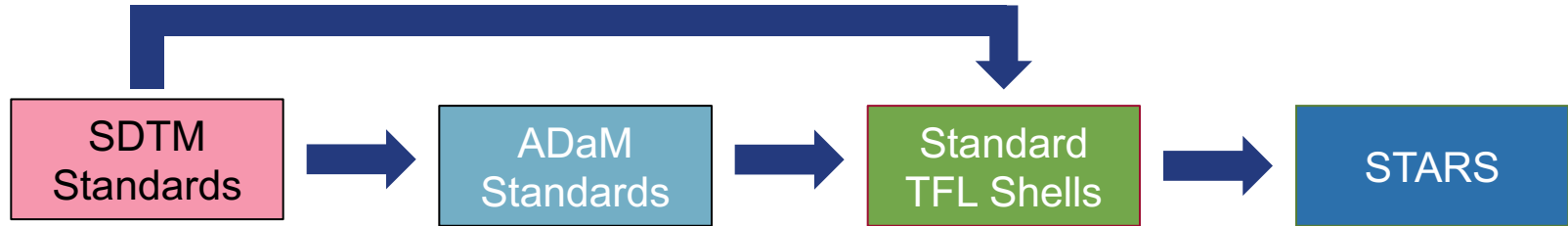


Utilizing P21 API



And MORE!

Case Study: Standard TFL Analysis Reporting System (STARS)



- Metadata-driven tool used to create a set of standard SAS programs and standard safety TFLs by leveraging SDTM, ADaM and TFL standards
- Qualified system allows for unique TFL validation methodology (i.e. not IP)
- STARS to be published in batches with multiple rounds of testing & review
- Initial testing metrics have shown reductions of ~70% in time/per TFL

Governance Strategy



Following standards development and implementation, we are establishing a formal governance structure to improve operational efficiency



Standards governance must evolve to oversight and enforcement by addressing adherence issues in real-time



Development

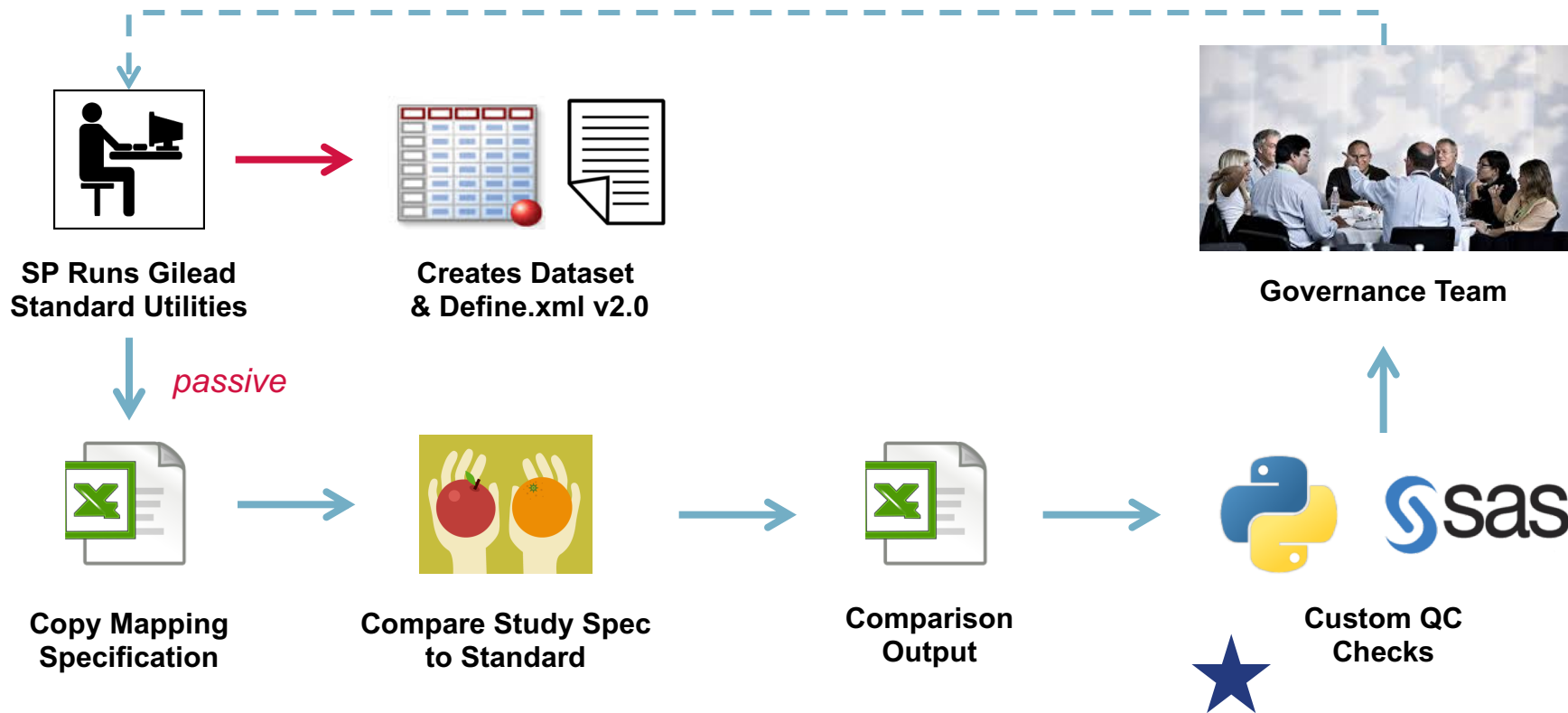


Implementation

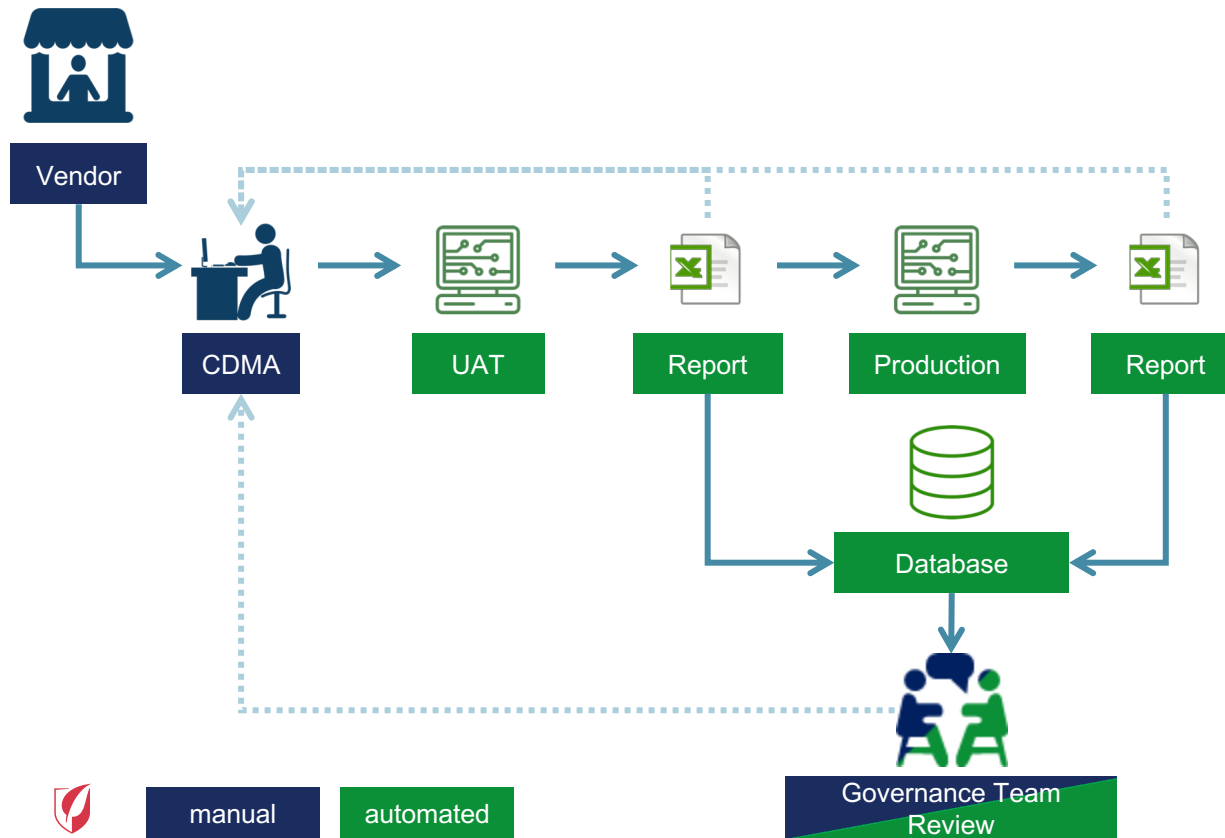


**Governance
Oversight
Enforcement**

Developed mapping spec governance model leveraging study-to-standard comparison and QC checks, applicable from data collection to TFLs



Case Study: eDTS utility leverages Excel specifications to identify issues between data and Gilead's expectations, enabling governance



- ❖ *CDMAs and CPs following processes?*
- ❖ *Real-time identification of transfers with repeating issues*
- ❖ *Risk-based assessments on vendors to better understand how to work with them*

Biometrics eSubmissions (eSub) Team (the 2nd end)



Dedicated liaison team between Biometrics and Regulatory Affairs to avoid rejections, stay abreast of regulatory changes, and reduce audit risk

1 >

Submission Rejection

Submission acceptance and technical rejection criteria change over time and vary amongst agencies

2 >

Regulatory Changes

Stay abreast of changes to regulations throughout the world and prepare Gilead to address them, as needed

3 >

Regulatory Audits

Improve traceability between submission content and our working area, including documentation for changes made/approved



eSub Team will focus on review and assessment, not creation, of dataset package contents across TAs

1	Work closely with Regulatory Affairs to understand planned submissions (US and Rest of World)
2	Work with study SP (and Biostatistician as needed) about regulatory requirements
3	Assist teams with creating separate folders for non-FDA submission packages
4	Leverage automation & utilities to QC datasets and submission documents in real time, working with study team to edit/fix critical items
5	Serve as submission SMEs internally, as well as externally with regulatory agencies during EOP2, Type B or pre-NDA meetings

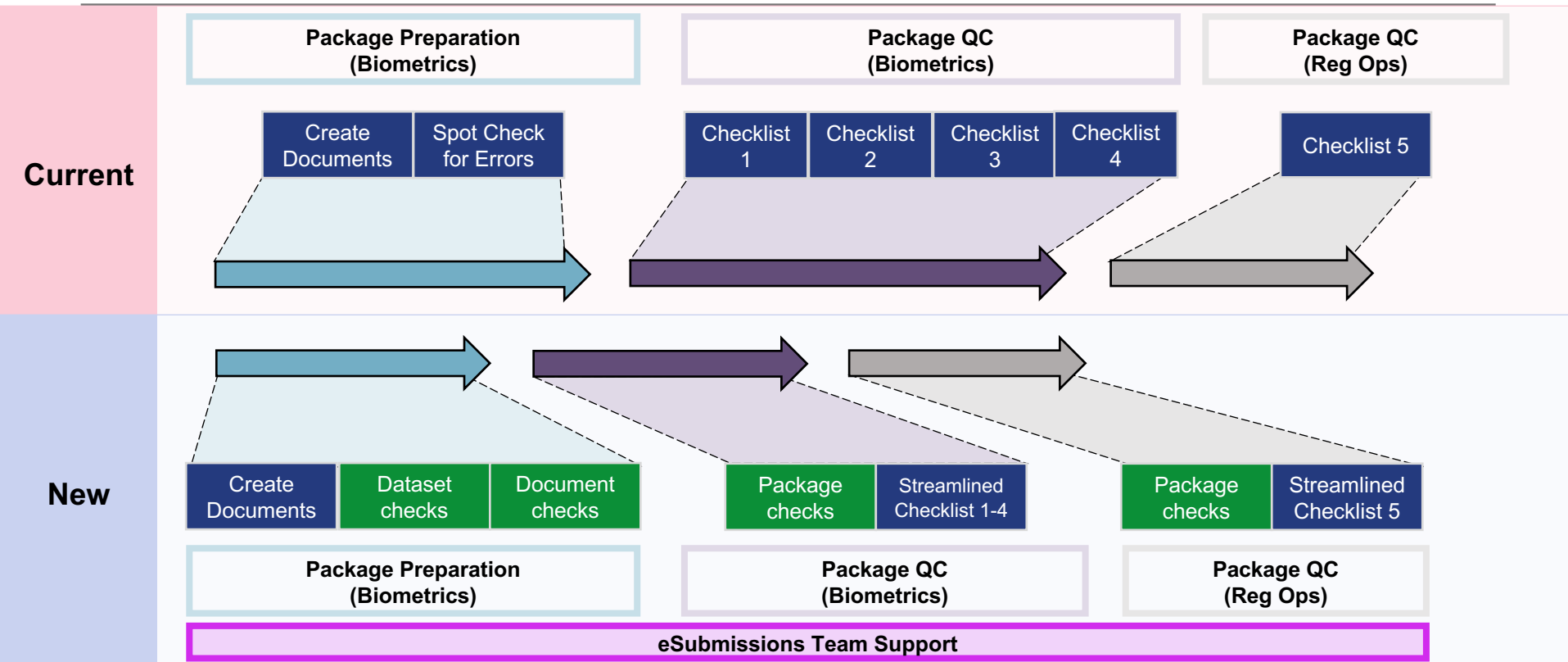


Coordinate with study SPs to spread review work across study lifecycle, identifying issues in real-time and reducing effort near time of submission

Time requirements will vary depending on the complexity of study dataset package submission



The eSub team will also be instrumental in implementing more formal, standardized processes that will leverage automation capabilities



Additional eSub initiatives will further simplify and standardize the eSubmissions process, allowing for metadata-driven governance



eSub Macros

- ❖ eSubmissions Macro
- ❖ Automated Checks
- ❖ Transfer files from task/version to /prep to /module5
- ❖ Traceability of submission content



eSubmission GUI

- ❖ Simplified User experience
- ❖ Streamlined Macro usage
- ❖ Automated email and help sessions



Standardized Structures

- ❖ eSub WRK
- ❖ Training
- ❖ Support
- ❖ Study Folder Structure

Standards Landscape – A Survey



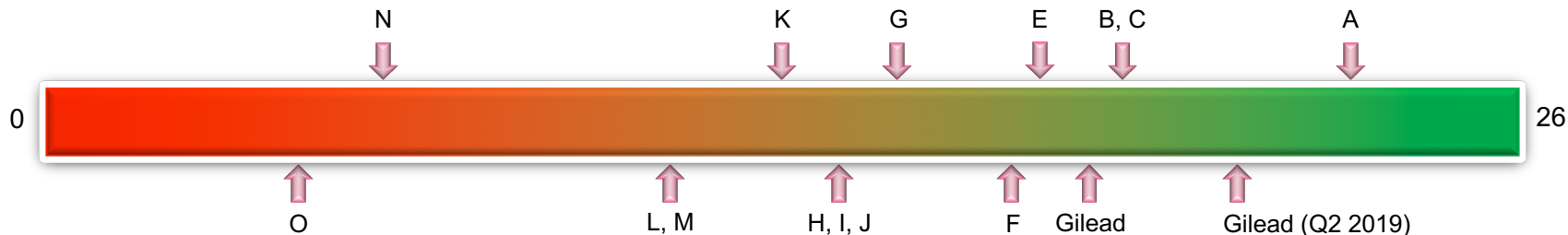
What are other companies doing, how are they doing it, and where do we stand? How can we influence senior leadership for future initiatives?

Code	Standards Deliverables
1	Global CRF (following CDASH)
2	TA CRF (following CDASH)
3	Data Transfer Specifications
4	Global SDTM
5	TA SDTM
6	Global ADaM
7	TA ADaM
8	Global Analysis Results Metadata (ARM) for Study
9	Global TFL
10	TA TFL
11	Company SDSP Template
12	Company cSDRG Template
13	Company ADRG Template

Code	Technology/Automation Deliverables
14	Data Transfers QC Utility
15	Dataset Generation Utility
16	Dataset Generation Utility QC Checks
17	Define.xml Generation Utility
18	Define.xml Generation Utility QC Checks
19	TFL Utility
20	TFL Utility QC Checks
21	ARM Metadata from TFL Program
22	ARM Database
23	Module 5 Dataset Package QC Checks
24	MDR (pilot)
25	MDR (production)
26	Study-to-Standard Governance



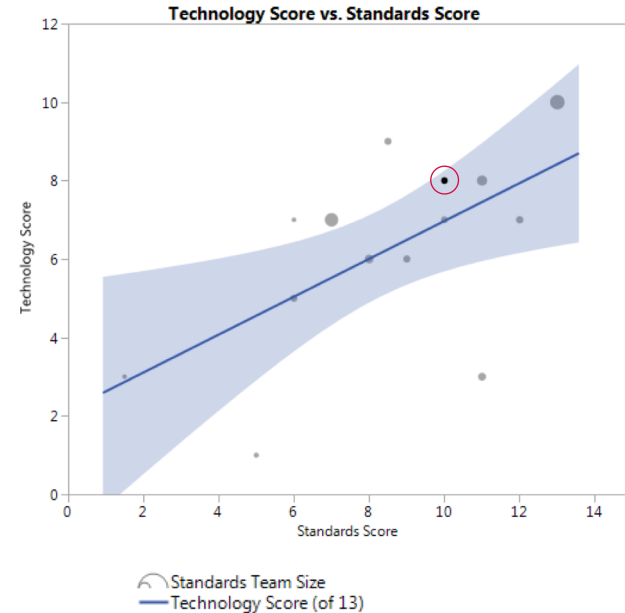
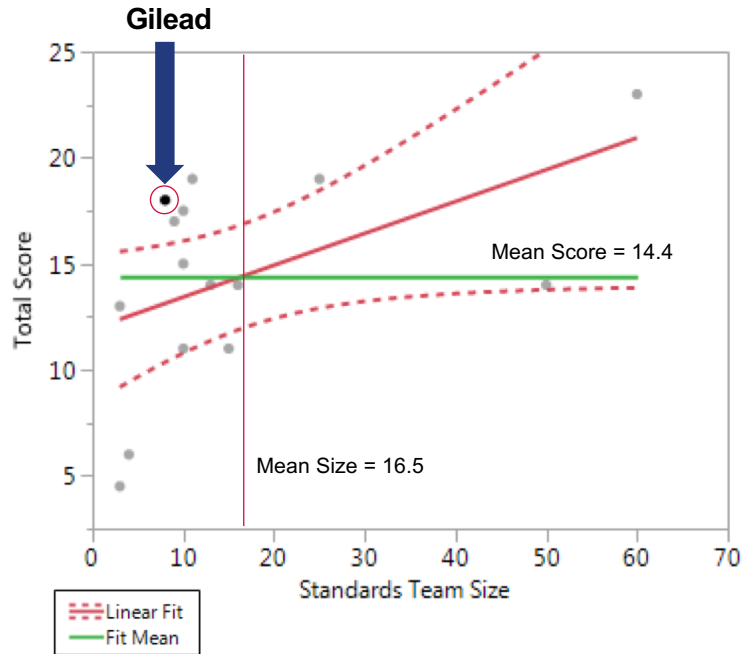
Survey results of 15 pharma companies help describe current state of standards development, as well as use of automation and technology



	Standards Score													Technology Score												Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
A																										23
B																										19
C																										19
Gilead																										18.5
E																										17.5
F																										17
G																										15
H																										14
I																										14
J																										14
K																										13
L																										11
M																										11
N																										6
O																										4.5



Analyzing the data allows us to understand how we fit in with others, where we are ahead and behind, and ideas for future initiatives



Interested? Reach out to me to take part in the survey and access de-anonymized data





Questions ?

Dhananjay.Chhatre@Gilead.com