



Edinburgh 2017 PhUSE Annual Conference

ADaM Programming The good, the bad and the ugly

Presenter: Pam Howard, VP Biostatistics & Programming

Agenda



- Background
- ADaM datasets: Why, Who, How many
- Process improvement
 - Define
 - Measure
 - Analyse
 - Improve
 - Control
- Key messages

Background

- Implementing CDISC standards
- FDA, PMDA, EMA & China FDA
- It is now an FDA requirement for NDAs, ANDAs, BLAs, and DMFs on studies that start after December 17, 2016. Sponsors must submit data in FDA-supported formats listed in the FDA Data Standards Catalog, which specifies the use of CDISC standards: SDTM, SEND, **ADaM**, Define-XML and Controlled Terminology.

Why ADaM datasets?

iACE (**I**CON's **ADaM** **C**entre of **E**xcellence) is ICON's umbrella strategy that focuses on ADaM delivery

CDISC End to end lifecycle

- However despite the regulatory requirement currently approx. 35% of studies are not using ADaM standards. The reasons why some studies do not require ADaM datasets are as follows:
 - Client standards
 - Legacy study
 - Partial tasks such as DMC support that uses other than ADaM datasets as its source

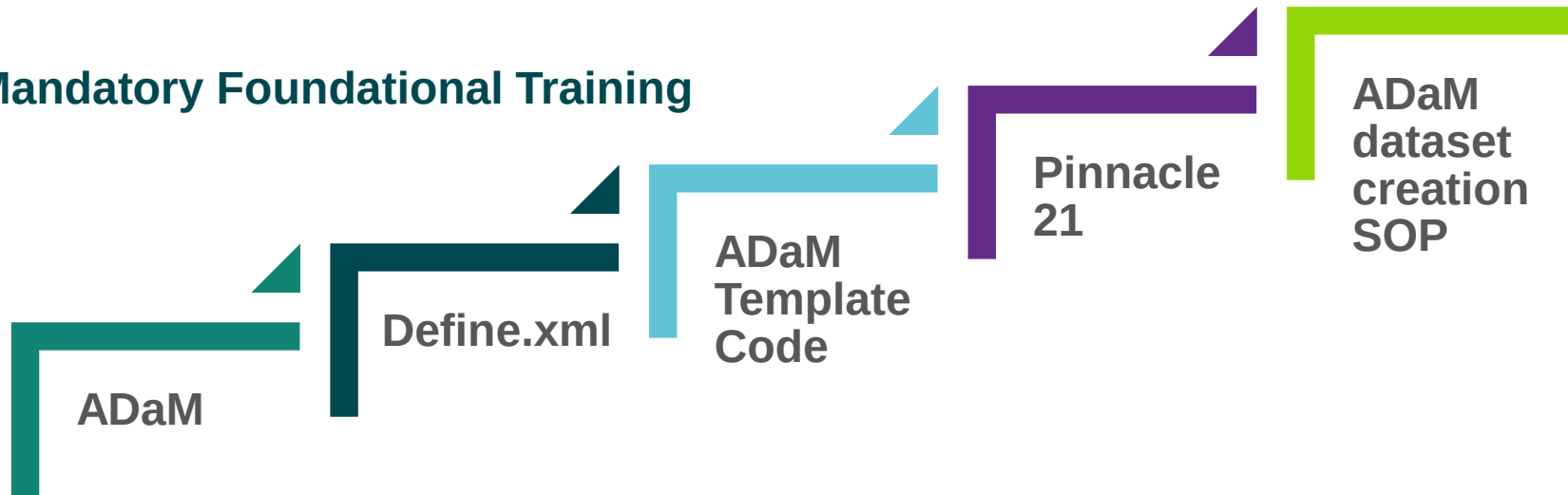
Who: Roles and Responsibilities ADaM Datasets

	Specification	Development	Validation	Review
Project Statistician				
Lead Programmer				
Programming Team				

Who generates ADaM datasets?

Since beginning of 2017, 85% of programmers have developed or validated ADaM datasets

Mandatory Foundational Training



How many ADaM datasets?

Up to 900 datasets are built each quarter



Simple Safety

Does not fit into the complex category



Complex Safety

Datasets with either complex structure requiring significant manipulation of input data and/or with large volumes of derivations



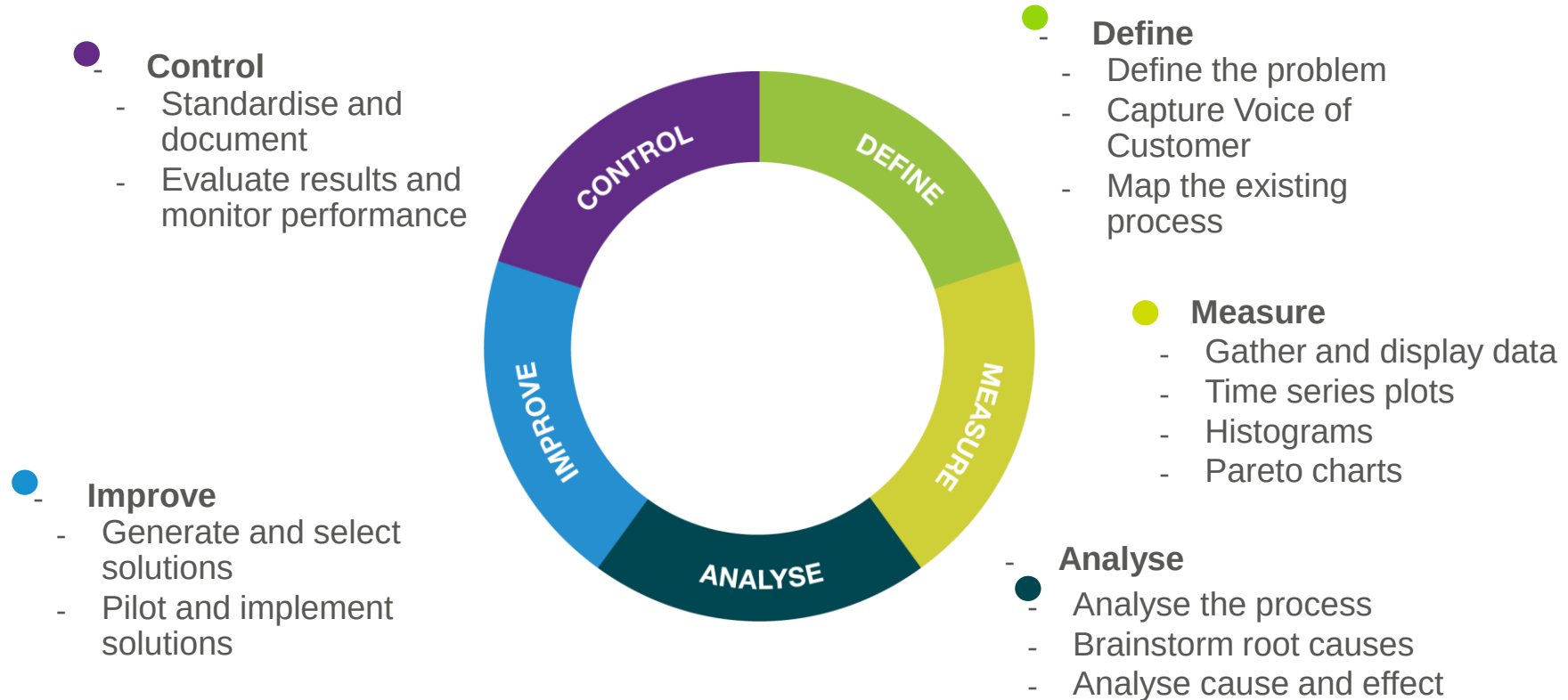
Efficacy

Datasets with efficacy parameters

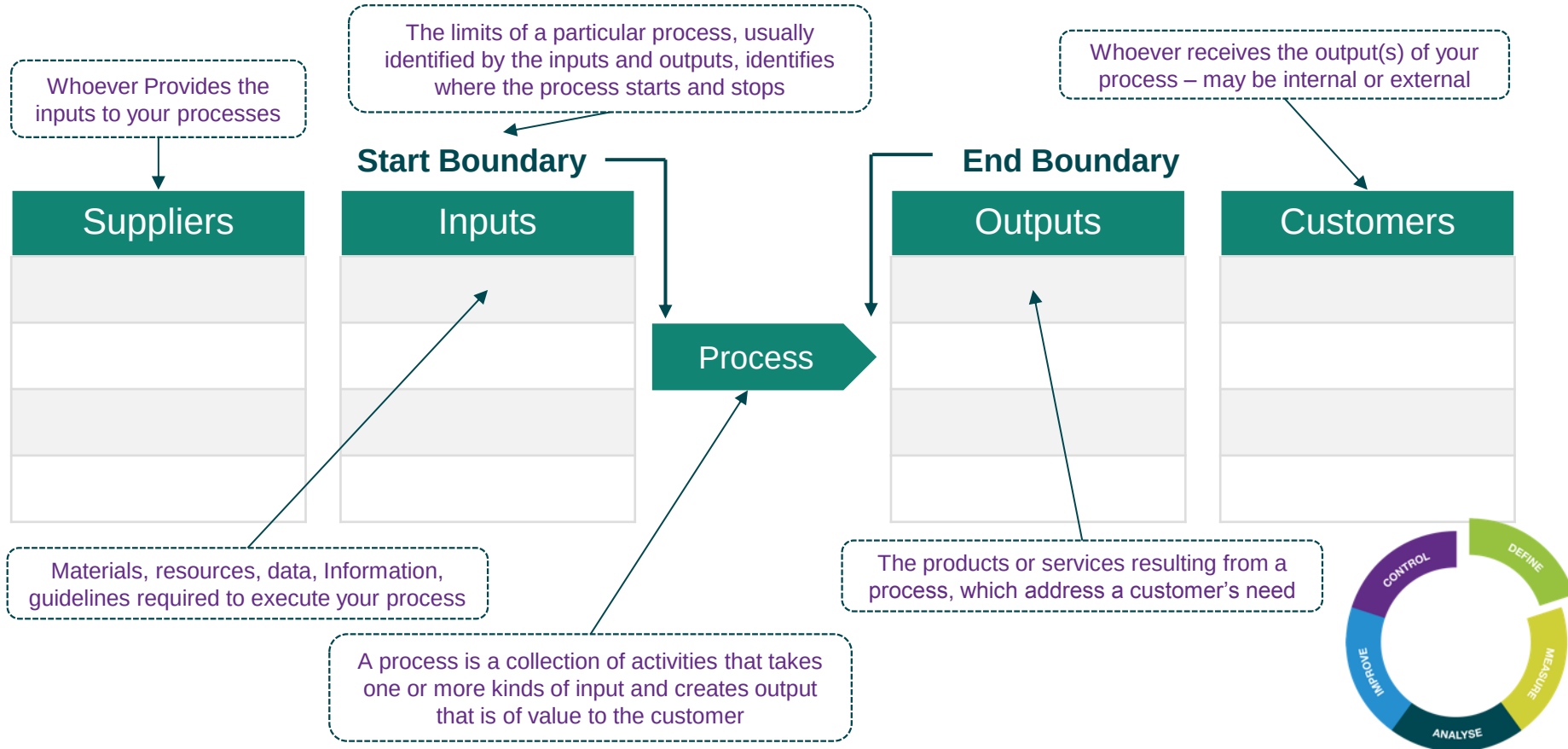
ADaM

Process Improvement

Continuous improvement - DMAIC



Define: Map the process



Define: Map the ADaM datasets process

Suppliers	Inputs	Process	Outputs	Customers
- DM - Clients - Biostatistics - Clinical - Patients	- Protocol - Data - SAP - ADaM dataset specifications - ADaM template code - Metadata - Programming rules - Training materials	- ADaM specifications - ADaM Program Development - ADaM Program validation - Various reviews	- Datasets - Programs - Logs - Documentation - Metadata - Specification changes	- Programmers - Biostatistics - Medical Writing - Clients - Regulatory authorities - Patients



Measure: Gather and display data

Output Type	Failure Reason	Reports Effected due to Errors Vs Overall Reports with Errors	Reports Effected due to Errors Vs Overall Reports
Datasets	- Data Displayed Incorrectly - Derivation Incorrect - Updated/Corrected Data Received - Cosmetic Updates - Others - Total (Reports with at least one error)		

Process Output	Measure	Defect
Datasets	# of ADaM with errors divided by # of ADaM datasets delivered	Error is defined as....

Analysis - 6 months

Percentage

Number of ADS with errors	9%
Number of first time right ADS	91%

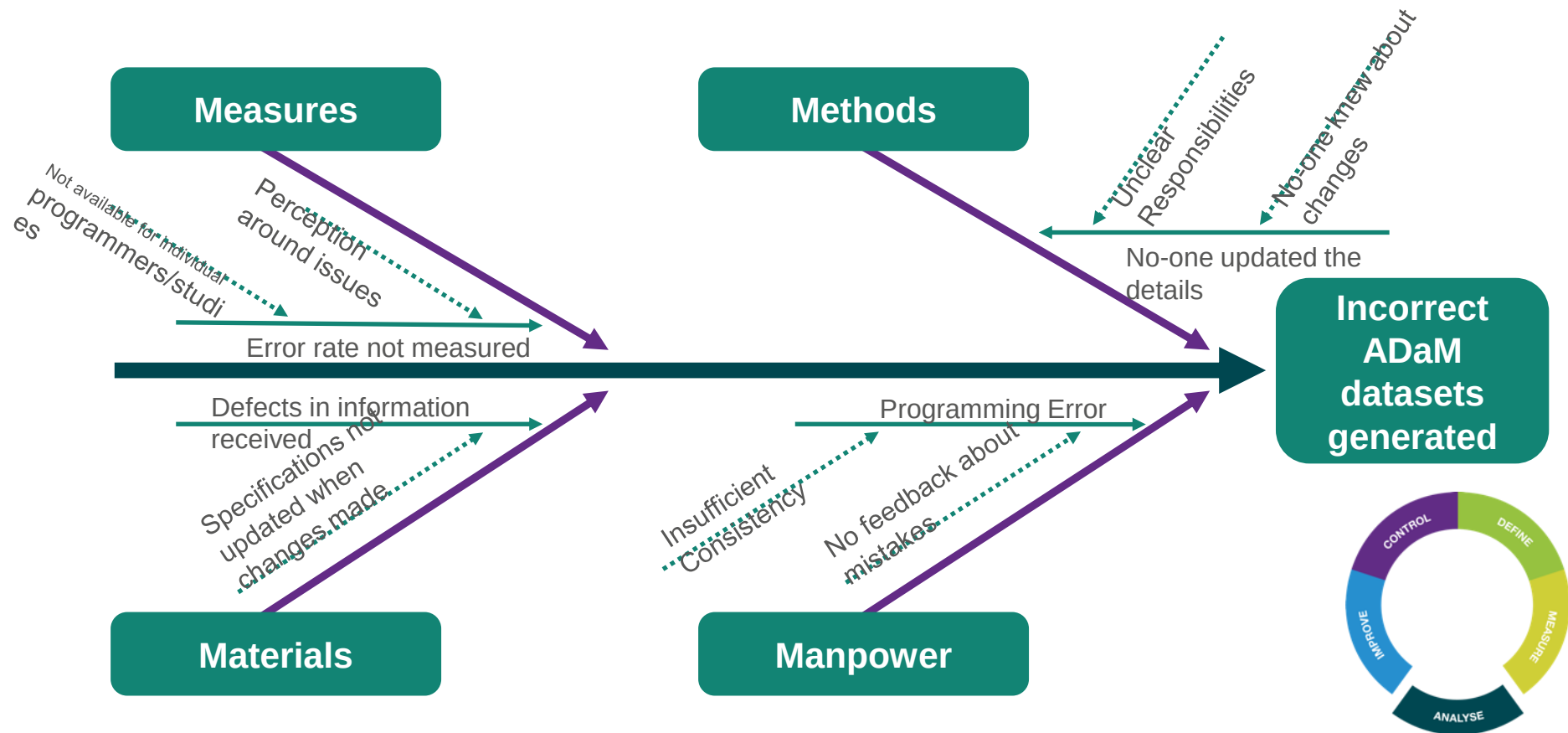


Analyse: Common root cause categories

6 M's	Related Categories	Illustrative Questions
Manpower	People, Staffing, Organisation, Skills, Management	- Are people trained with right skills? - Is there person to person variation? - Are people over-worked?
Mother Nature	Environment, Work Environment, Market Conditions, Regulatory Environment	- Is the workplace safe and comfortable? - Are outside regulations impacting the business? - Does the company culture aid the process?
Materials	Parts, Supplies, Forms, Information, Inputs	- Are parts, forms or supplies obsolete? - Are there defects in the inputs/specifications? - Is information stable throughout process?
Methods	Procedures, Policies, Documentation, Management Systems	- How is the work performed? - Are procedures correct? - Are procedures enforced?
Machines	Tools, Software, Technology, Equipment, Facilities	- Is equipment reliable? Properly maintained? - Is there sufficient capacity? - Are software platforms compatible?
Measures	Judgment, Evaluation, Measurement Units/Methods/Devices	- Is data good enough? Is data readily available? - Is data open to interpretation or bias? - Do different people judge inputs and outputs the same way?



Analyse: Root cause analysis



ADaM strategy and strategies implemented

Measure

- Systemic method of collecting data on ADaM datasets
- Analysis done on sources of programming errors
- Also collecting cycle times and other metrics

Methods

- ADaM template code
- Standard macros

Materials

- More reviews of specifications
- Only work from stable specifications
- Work with supply chain in terms of inputs

Manpower

- Governance of standards
- Training
- Measuring individual performance



Improve: Pilot and implement solutions

Governance

Standards Group

Compliance

- Standard ADaM template code
- Standard ADaM specifications linked to standard TFLs
- Patient walk through
- Additional checks



ADaM template code



Consistent

- Consistent source of ADaM code
- Increase effectiveness
- Defensive programming
- Process around exceptions



Adaptive

- Based on the latest ADaM guidance
- Includes many standard safety datasets & more planned
- User feedback encouraged and incorporated



Robust

- Governance process and steering committee
- Commitment to continue to develop and improve
- Follows SDLC and documented processes



Patient walk through



- Documented check of the traceability of raw/SDTM data to ADaM derived variables
- Done a defined # of patients / different types of patients
- Scope of review is pre-specified in QC Plan
- Effective in increasing specificity and understanding
- Biostatistics activity



Tools and Utilities



Compliance checks



Utility that converts the study ADaM specification to shell datasets, that are then checked by P21 and the ICON customised utilities.



Additional ADaM checks added



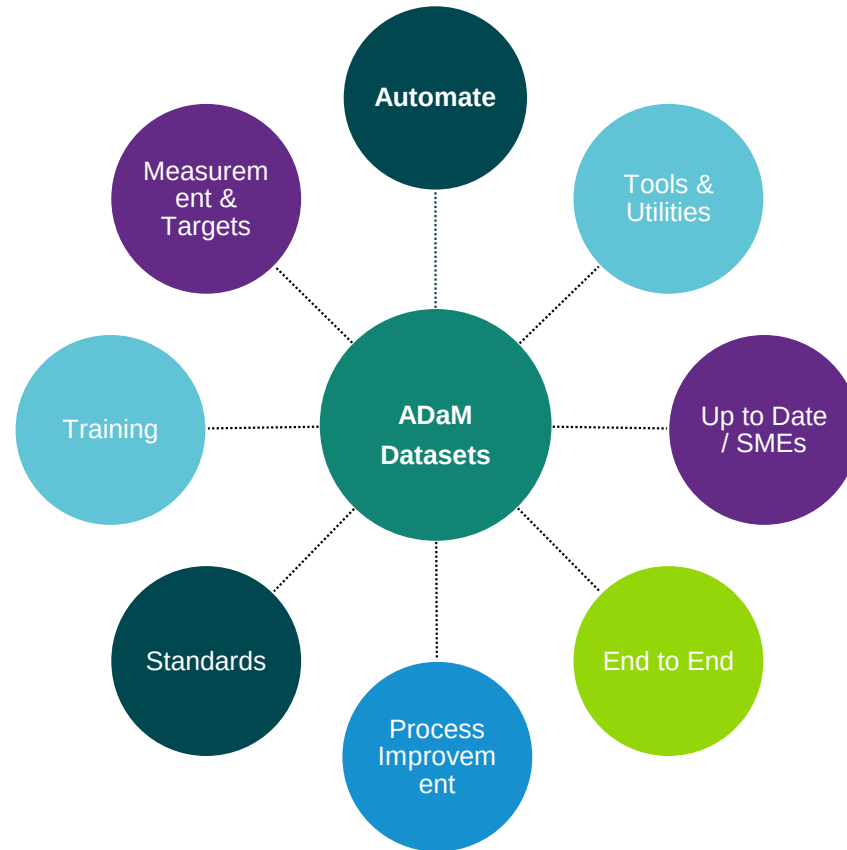
Sponsor specific checks



TA specific checks



Control: Evaluate results and monitor performance



ADaM Datasets – Key Messages



ADaM datasets key deliverables



Leveraging standards and processes



Continuous Process Improvement needed



Therapeutic area & client focus



Time, quality & cost

Thank you

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