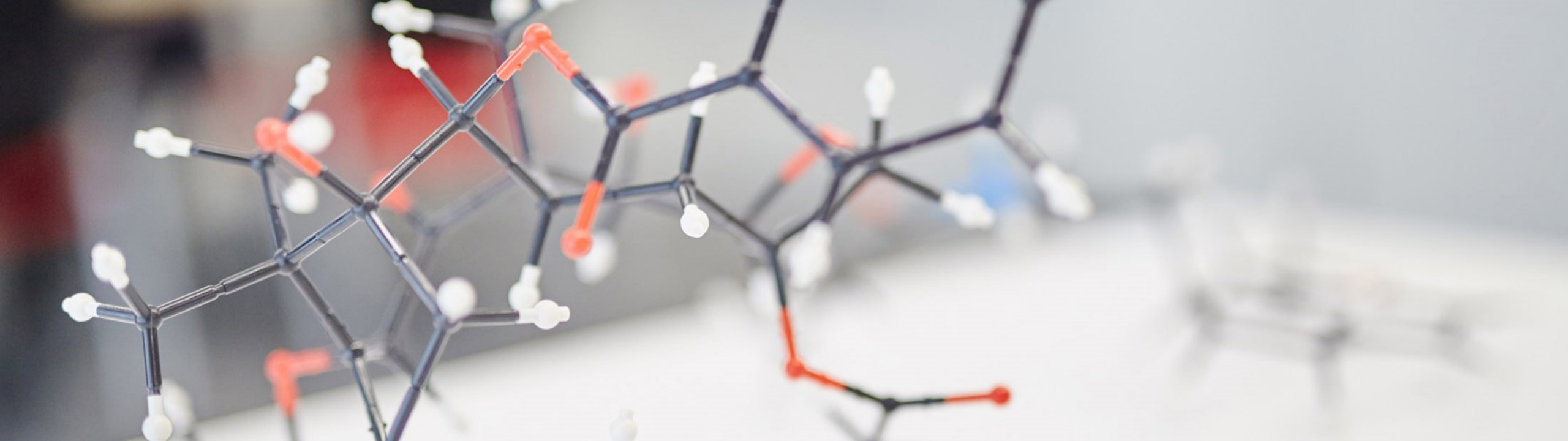




A paradigm shift to represent and manage Clinical Data Standards for creating a data driven specification

Feb, 2019

Veena Nataraj

Clinical Standards

Takeda Pharmaceutical Company Limited



Better Health, Brighter Future

Introduction

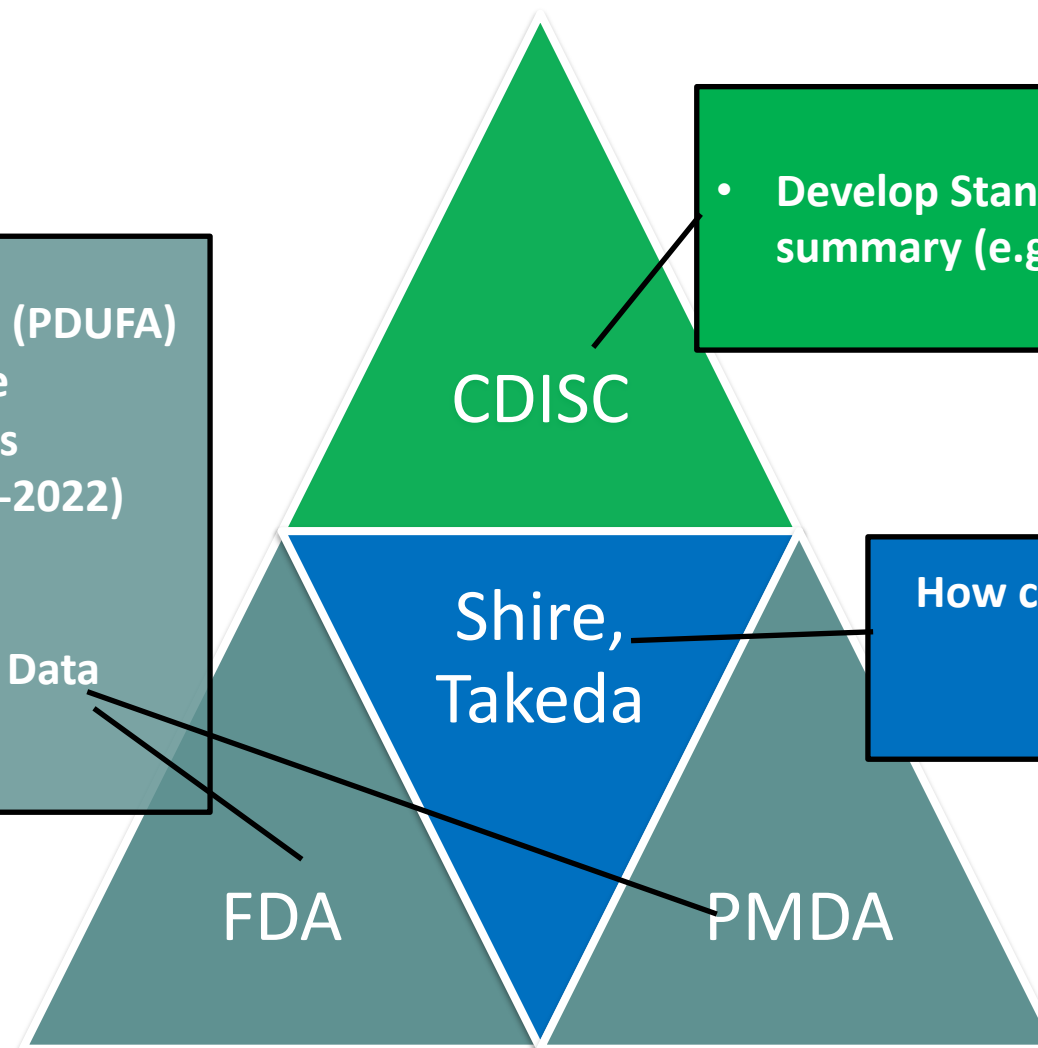
FDA:

- Prescription Drug User Fee Act (PDUFA) (2018-2022) which governs the requirement for data standards
- Data Standards Strategy (2018-2022)

PMDA & FDA:

- Technical Conformance Guide, Data Standards Catalog

- Develop Standards to support data analysis and summary (e.g., pattern analysis and data mining)



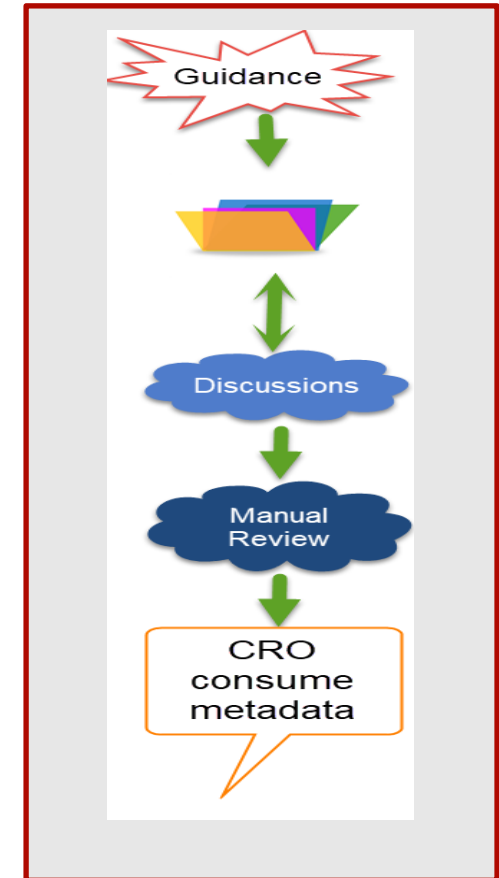
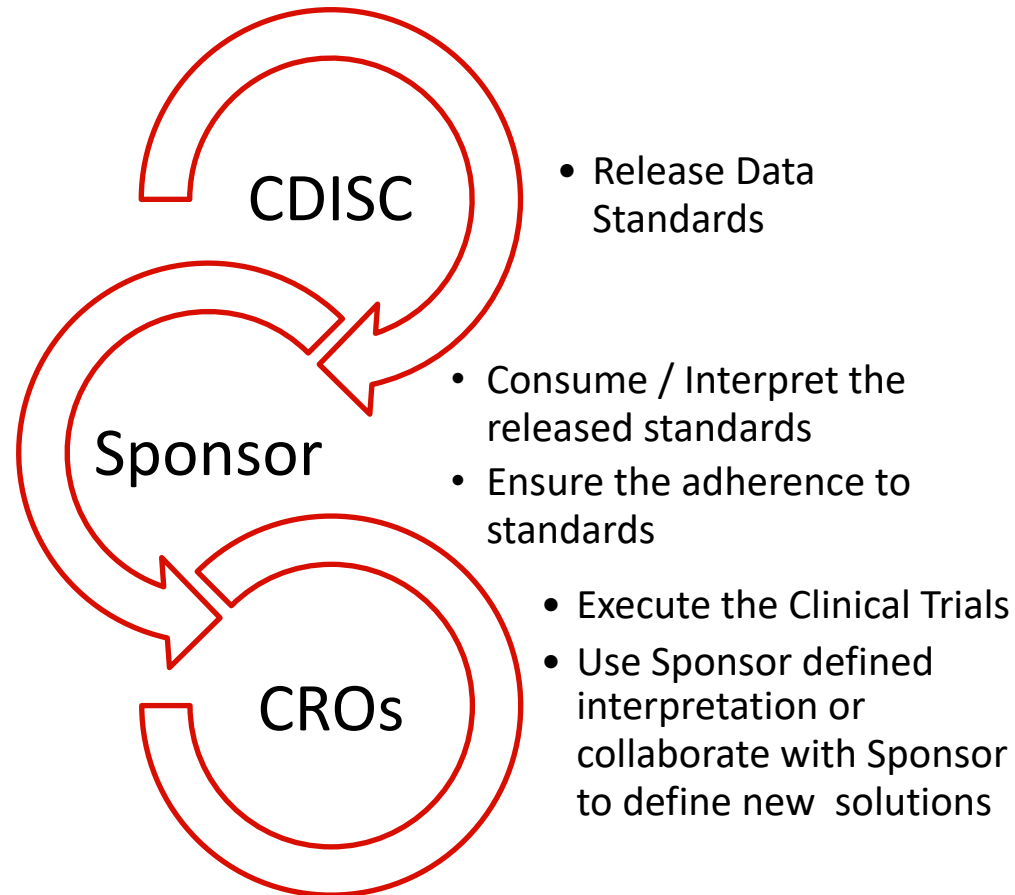
Paradigm Shift:

A fundamental change in the basic concepts and experimental practices of a scientific discipline
- Thomas Kuhn

Historic Process

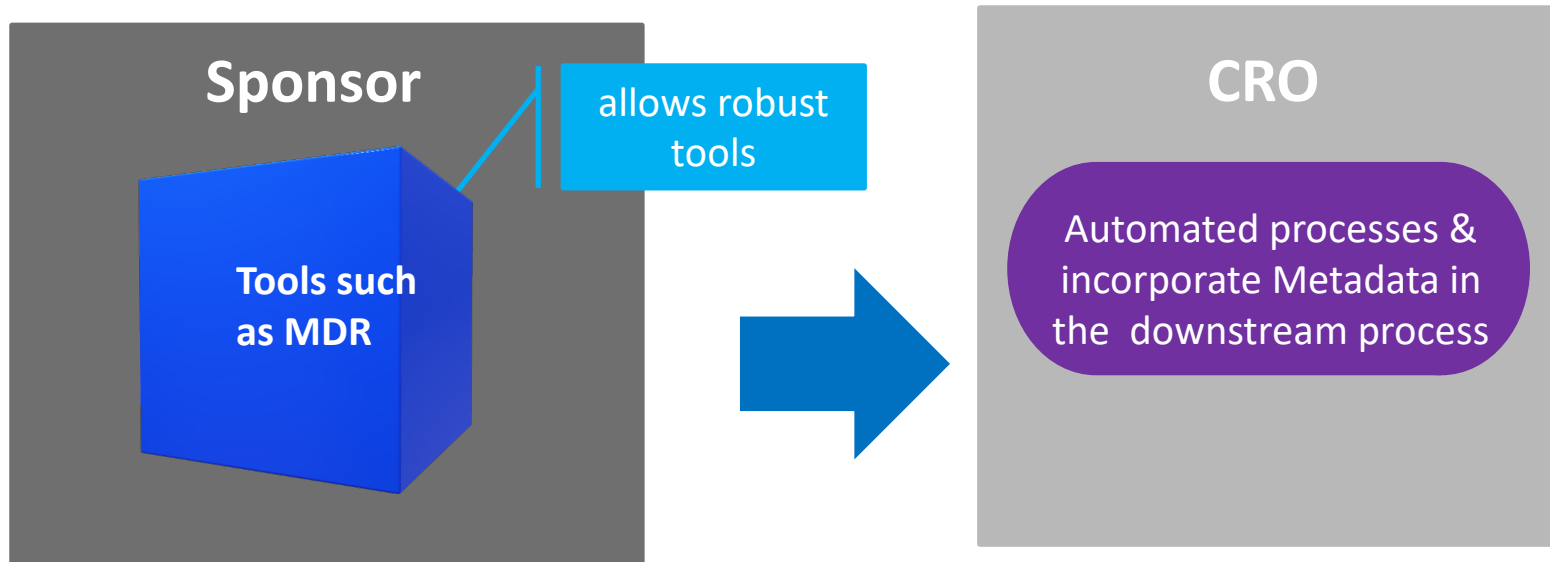


Limited
by CRO
processes
and tools

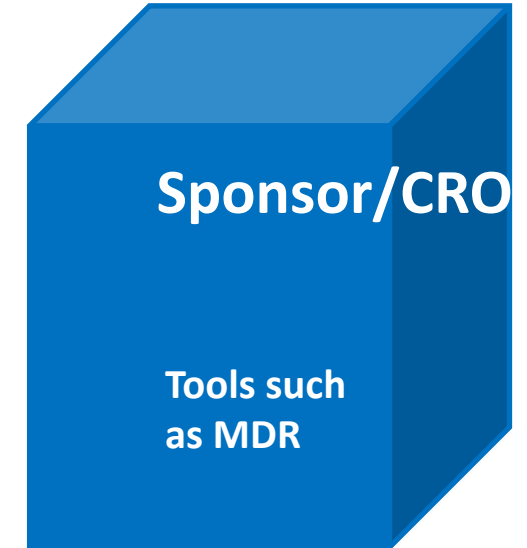


Paradigm Shift:

Now



Future

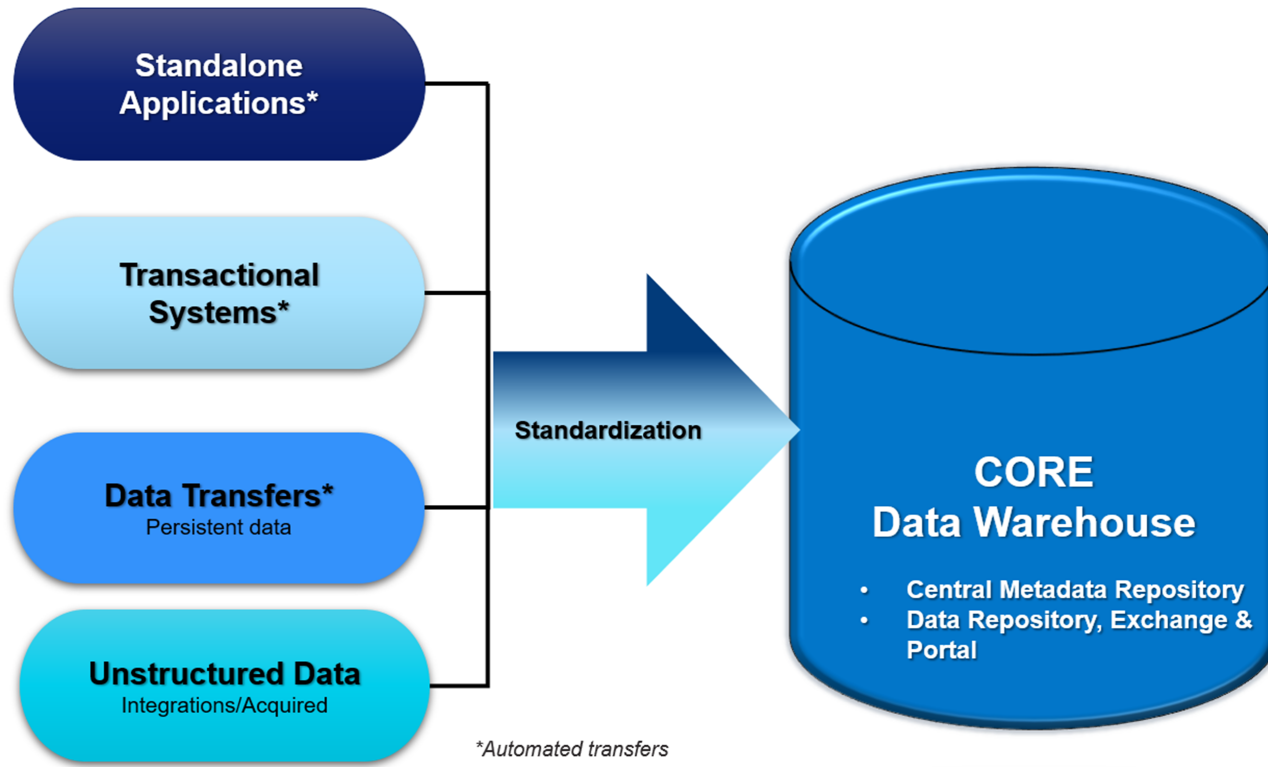


End Goal- not yet a reality:

- Transform these complex interactions
Specifications and Requirements = Resource-heavy programming tasks
INTO
Streamlined mapping activity largely based on configuration rather than original programming

What is Metadata Repository (MDR)?

A **metadata repository** is a database created to store **metadata**. **Metadata** is information about the structures that contain the actual data.



In 2018, Shire decided to invest in a Operational Data warehouse

- Operational data warehouse (CORE) is a solution that enables CDO decision-makers
 - with easy access to the portfolio
 - Provide reliable data to analyze, share and report;
 - decreasing extensive manual efforts.
- Metadata Repository is one of the component within CORE

Implementation Considerations

- **Representing and Organizing Metadata**

- **CDISC Metadata Standards**

- Read only
 - Industry Standard

- **Organizational Standards**

- Global Standards interpretation
 - End users can clearly differentiate

- **Study Standards**

- Therapeutic Area Standards

- **Templates and Formats**

- Any standard represented, should have a format represented. This format structure is the template

e.g. Controlled Terminology

Without MDR, information typically exists as spreadsheets and may be centrally controlled (e.g. Share Point)

Advantages:

- Structural changes are easily identified
 - no structural creep
 - Consistent representation of organization specific terms of synonyms

Implementation Considerations (contd.)

- **Comparison and Business Compliance**

Select Source : CDISC Standards >> Co SDTM Terminol Select Target : CDISC Standards >> Co SDTM Terminol Compare Export ☒ Show only differences

	Code	Codelist...	Codelist Extens...	Codelist Name	CDISC Submis...	CDISC Synony...	CDISC Definition	NCI Preferred T...
4...								
4...								
4...								
4...								
4...	C63321	C65047		Laboratory Tes...	NEUT	ANC; Neutrop...	A measurement of the neutrophils in a biologica...	Absolute Neut...
4...								
4...								
4...	C64810	C65047		Laboratory Tes...	NITRITE	Nitrite	A measurement of the nitrite in a urine specimen.	Nitrite Measur...

	Code	Codelist Code	Codeli...	Codelist Name	CDISC Submissi...	CDISC Synony...	CDISC Definition	NCI Preferred T...
	C154742	C65047		Laboratory Tes...	MANNITOL	Mannitol	A measurement of the mannitol in a biological speci...	Mannitol Meas...
	C154757	C65047		Laboratory Tes...	MNC	Mononuclear ...	A measurement of the mononuclear cells in a biologi...	Mononuclear ...
	C154744	C65047		Laboratory Tes...	NCCPTN	Nociceptin; Or...	A measurement of the nociceptin in a biological spec...	Nociceptin Me...
	C63321	C65047		Laboratory Tes...	NEUT	Neutrophils	A measurement of the neutrophils in a biological spe...	Absolute Neut...
	C154756	C65047		Laboratory Tes...	NEUTSGBP	Neutrophils, S...	A measurement of the segmented and band form ne...	Segmented, B...
	C154755	C65047		Laboratory Tes...	NEUTSGB	Neutrophils, S...	A measurement of the segmented and band form ne...	Segmented an...
	C64810	C65047		Laboratory Tes...	NITRITE	Nitrite	A measurement of the nitrite in a biological specimen.	Nitrite Measur...
	C154733	C65047		Laboratory Tes...	PLATBIZ	Bizarre Platelets	A measurement of the bizarre platelets (large with a...	Bizarre Platele...

Business Rules & Standard Compliance Check :

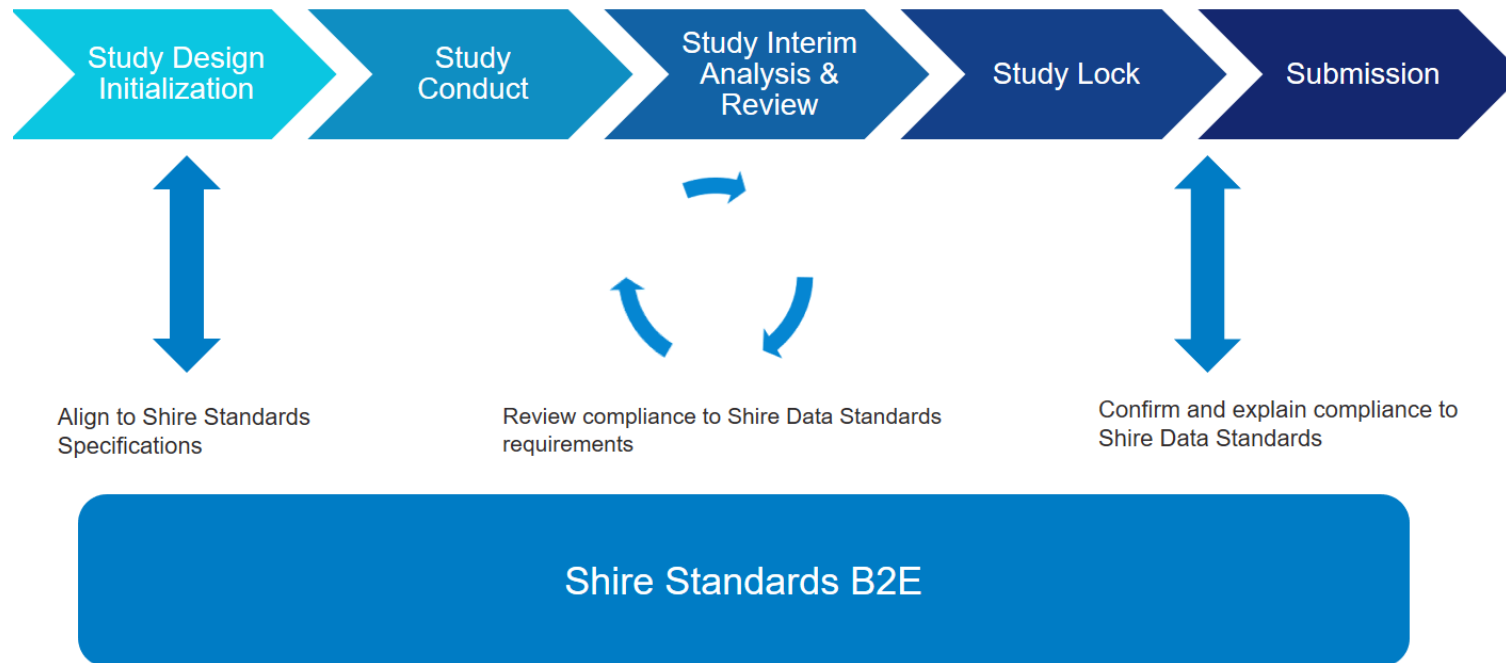
- e.g., ensure 8-character SAS variable name and 40-character for SAS variable label, P21 checks and custom checks for compliance

Advantages:

- Ensures the metadata meet the needs of down-stream processes
- Enables early detection of issues thereby streamlining the submission needs

Streamline processes and compliance/oversight

ICH E6 R2 requirements, it is important for sponsor companies to oversee the CRO on the execution and quality of deliverables.



Different CRO implementations complicate Sponsor's automation of review

Solution:

- Specify requirements - Sponsor expectations to how to receive mapped information as structured data

Advantages:

- Enables programming team to semi-automate the review
- Ensures the overall oversight of external vendors and compliance to our standards.

Study Compliance Check

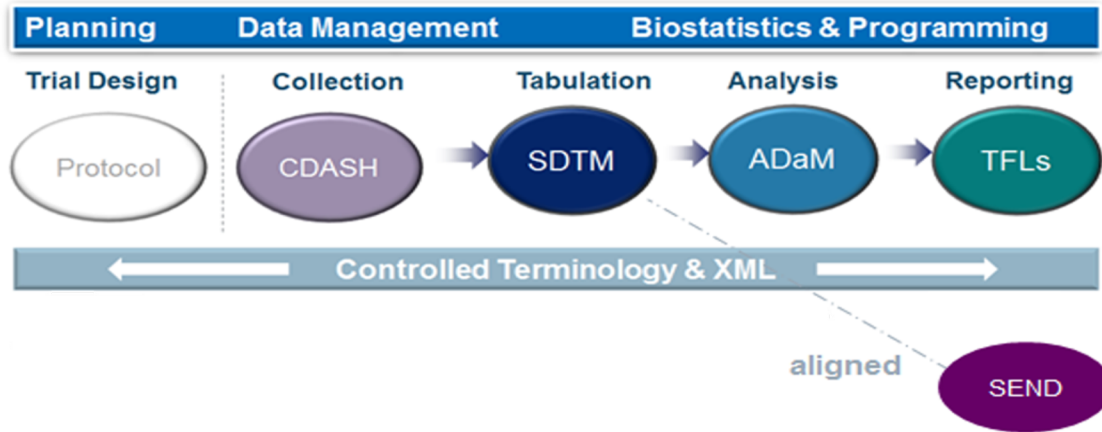
- The recent ICH E6 R2 requirements and expectations for sponsor companies to oversee the CRO on the execution
 - **Quality** is very critical to ensure the safety and efficacy of a study
 - At our company, we are ensuring this through compliance check
 - Like FDA and PMDA, Shire has identified within its metadata the *key variables* and its non-compliance classifications to be either error or violation. Such metadata was used in custom programming to evaluate pattern analysis of the study mappings to check how much of study is compliant to the standards defined
- When a study uses the global standard represented in the MDR
 - it can inherit the standards as is with little code change
 - Suppose a study needs to divert from the global or therapeutic standard, the metadata will have to be updated - may cause a divergence to the code and automation

Study Compliance Check

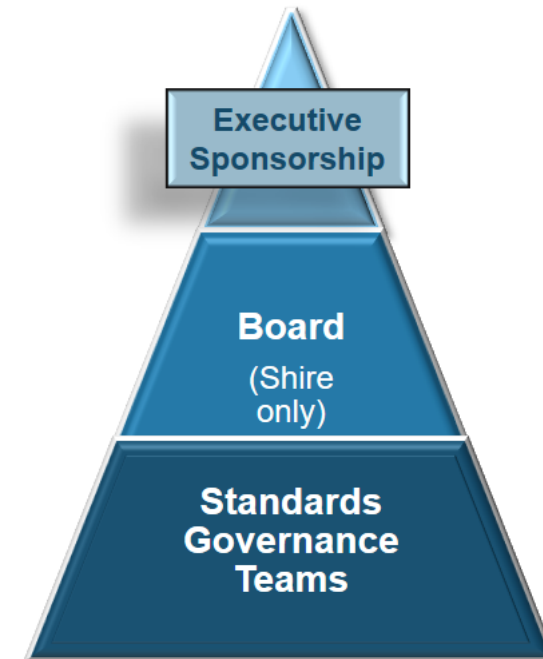
- By using the MDR, semi-automated process by using the transformation utilities within the tool supports the compliance checking of the received mapping specifications
- This provides oversight and ensure better quality for analysis of the submission deliverables which supports the reduction in time and resources and in-turn aid in reducing the costs over time

Clinical Standards Scope

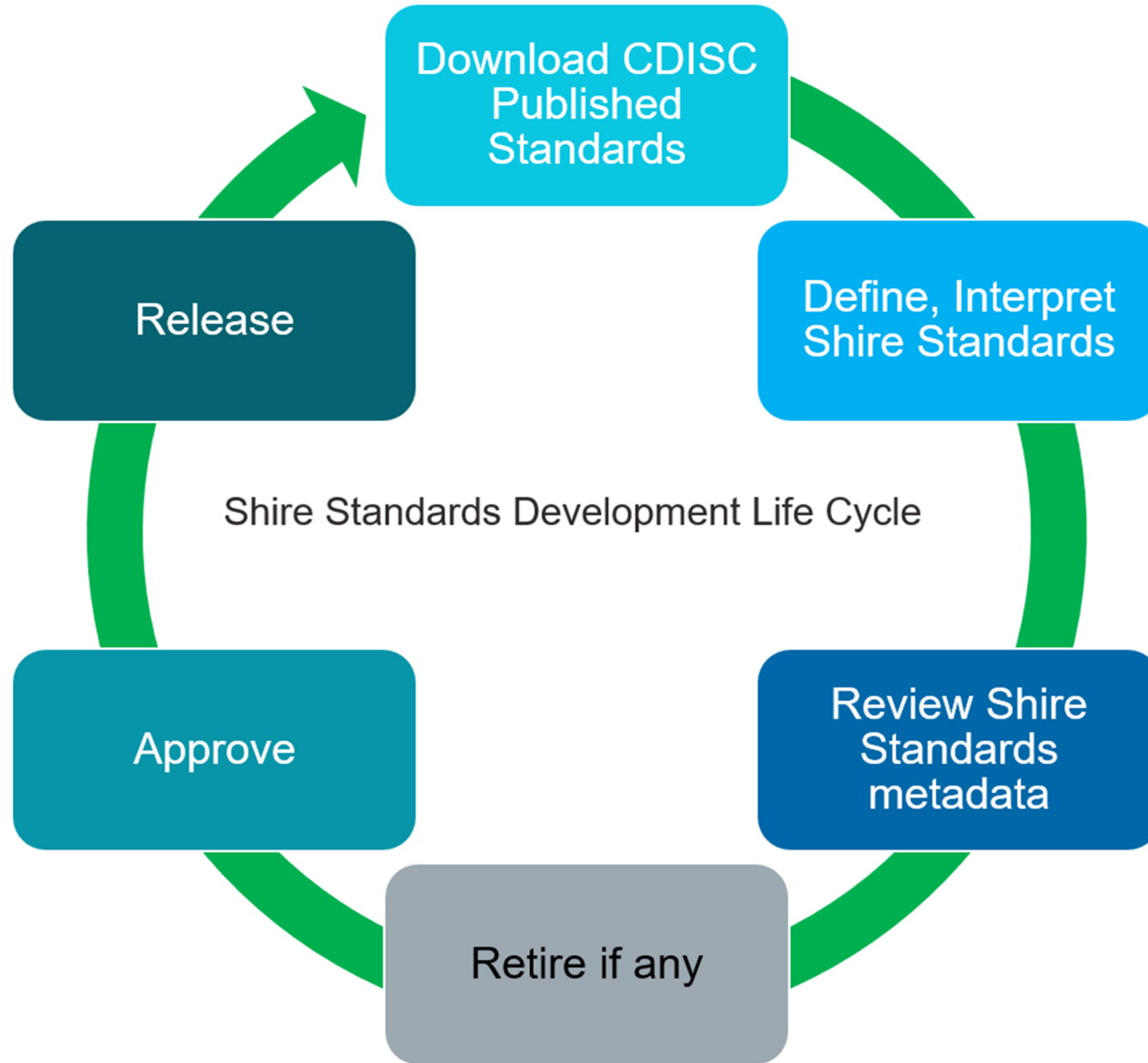
B2E standards start from protocol, collection through submission



Governance Model



MDR Workflow



MDR Workflow is used to define, approve and release metadata through the Shire Clinical Data Standards Governance Model

- ✓ Governance Teams – Define, Review
- ✓ Standards Board Members – Approve
- ✓ Governance Team Leads - Release

Process, Training and Next Steps

Process & Training

- Created new processes – Work Instructions and SOP
- Trainings and communications
 - New features which includes workflow, email notifications, comparison features

Next Steps

- As we gain more experience,
 - Integrating with external systems, where common definitions representing both clinical and operational metadata
 - Understanding if CRO systems can be integrated using APIs to transfer metadata to CROs seamlessly.
 - Defining the mappings earlier enables the CRO configuration to be applied across multiple clinical trials therefore leading to less code change

Benefits and Challenges

Benefits

- ✓ Easy management of standards
- ✓ “The ultimate source”- When information contained is maintained to be current and accurate, one stop shop
- ✓ Drives automation of business processes
- ✓ Simplify labor intensive processes
- ✓ Forces teams to think in a new way
- ✓ Change in resourcing needs (technical to understanding the standards and relationship modelling)

Challenges

- ✓ When integrating with disparate sources, understanding the common metadata and how the information will be represented
- ✓ Since the templates dictate how the information is organized within the MDR, any changes such as new column to the template, needs careful consideration
- ✓ Clear roles and responsibilities need to be identified and new processes based on the team size should be planned

Conclusion

TAKE THE FIRST
STEP

- Supports *review* and *manage* standards metadata.

Next STEP for
Paradigm Shift

- Tools such as a MDR will prompt how we manage and work with Metadata
- Processes within and across organizations can be automated and streamlined
- Changes the resourcing needs and knowledge necessary, e.g. instead of hiring programming resources, now data analyst, data analytics and overall data standards knowledge

New Tools

- New Applications - data can be analyzed and summarized
- Oversee the CROs and can satisfy ICH E6 R2 requirements

Data Traceability

- Better Quality

Automated streamlined processes

Regulatory requirements

A Foundation towards building a future paradigm shift

Important considerations when implementing a MDR:

- How to organize the information, templates to represent relationship – Helps in the comparison
- Defining compliance checks support the need for the data to be compliant with CDISC and regulatory submission needs.

Questions

