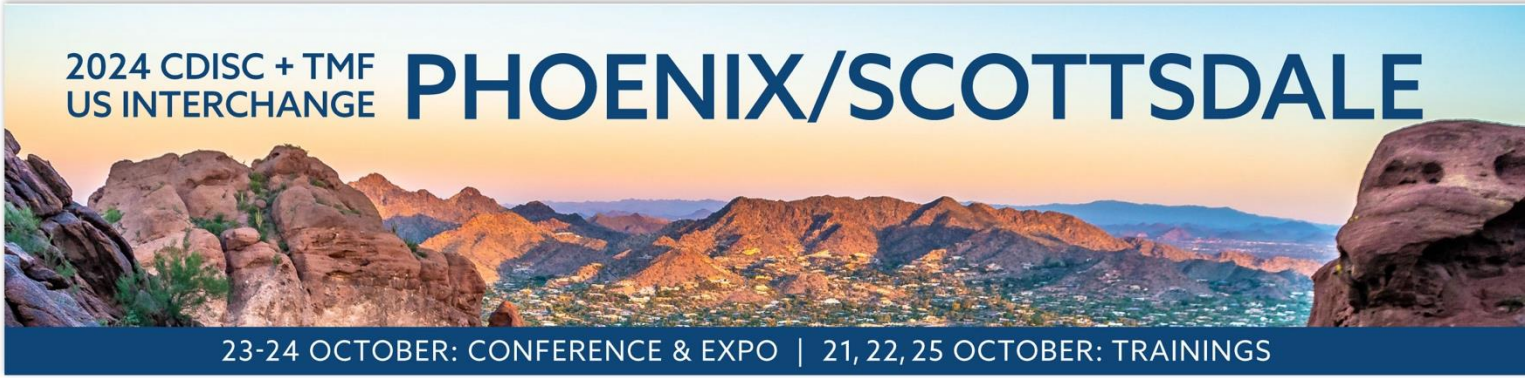

Advancing Clinical Data Integrity: Moderna's Integrative Approach to Metadata Compliance and Governance

Presented by Fred Bermont, Director, Clinical Data Standards & Integrations, Moderna, and Erica Gonzales, Sr Manager, Clinical Data Standards, Moderna

Meet the Speakers

Fred Bermont

Title: Director, Clinical Data Standards & Integrations

Organization: Moderna

Fred Bermont is a seasoned leader in clinical data standards and technology implementation, serving as the Director of Clinical Data Standards & Integration at Moderna Inc., based in Cambridge, MA since May of 2020

Erica Gonzales

Title: Sr. Manager Clinical Data Standards

Organization: Moderna

Erica Gonzales has been a part of the Clinical Data Standards team at Moderna for over two years. Throughout her career, she has served various roles, including database design and programming, data management, and clinical data standards. She has also been a volunteer with the CDISC CDASHIG team for over 6 years and was a co-lead for Phase 2 of the CDASH eCRF Portal team.

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

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Agenda

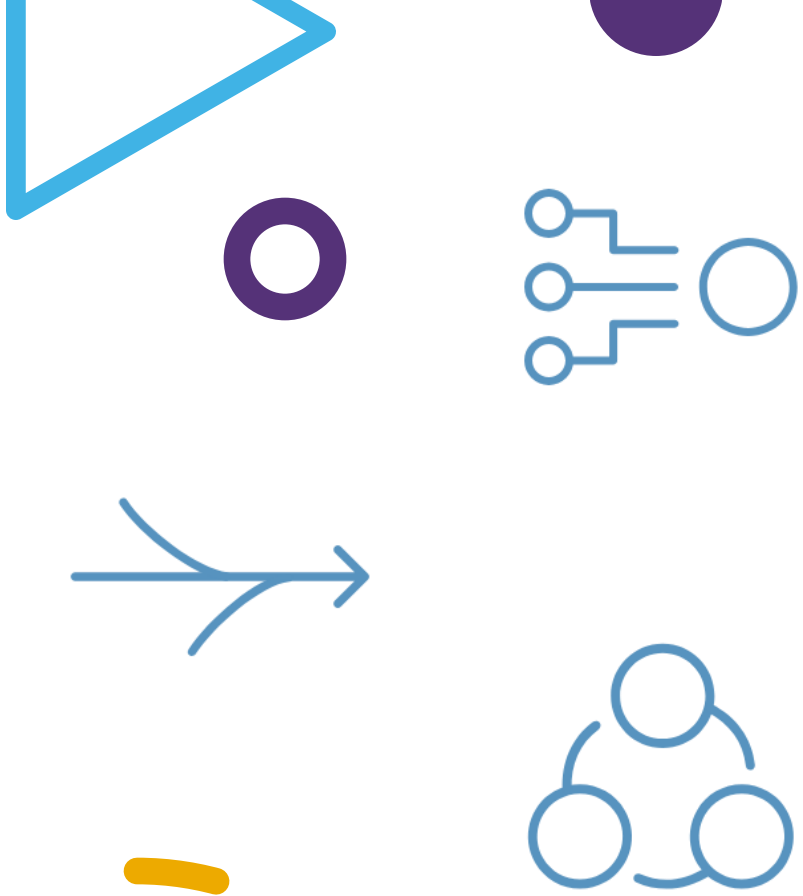
1. Overview / Introduction
2. MDR and CDW
   - Standards Compliance
   - 3rd Party Lab Integration
   - Use Cases
3. Looking to the Future
4. Conclusions

Overview: Advancing Clinical Data Integrity at Moderna

- **Moderna's Data Integrity Philosophy**: How Moderna's core principles guide the digitization and governance of clinical data.
- **MDR and CDW Implementation**: An overview of the Metadata Repository and Clinical Data Warehouse, their roles, and how they contribute to data standardization and compliance.
- **Compliance and Data Cleaning**: The strategies employed for ensuring data compliance and integrity, including the use of passive data cleaning methods.
- **Innovations with AI and LLMs**: Introduction to "mCHAT" and other AI tools being piloted to further enhance metadata management and standardization.

Introduction

- Moderna mindsets:
- We **digitize** everywhere possible, using the power of code to maximize our impact on patients.
- We remove **viscosity** to encourage collective action.
- We behave like **owners**. The solutions we're building go beyond any job description.

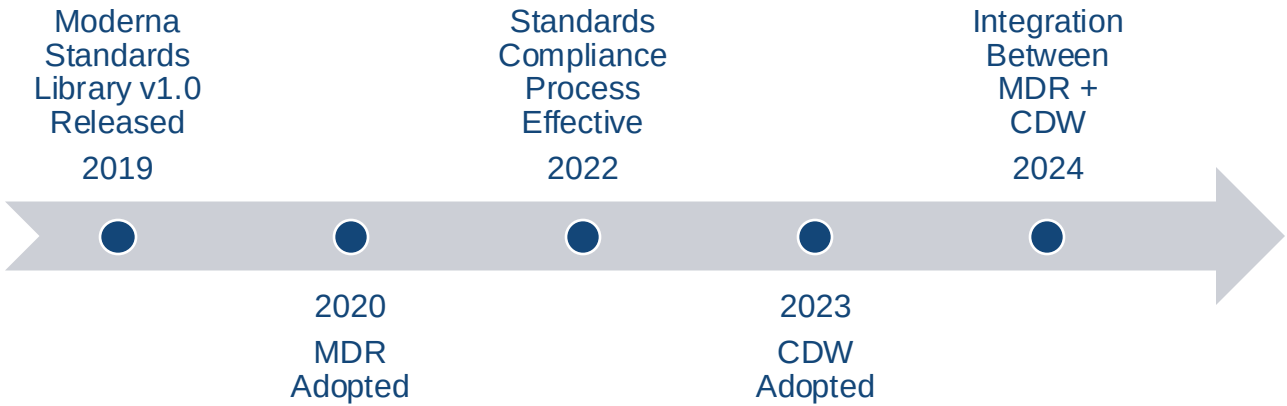


MDR / CDW

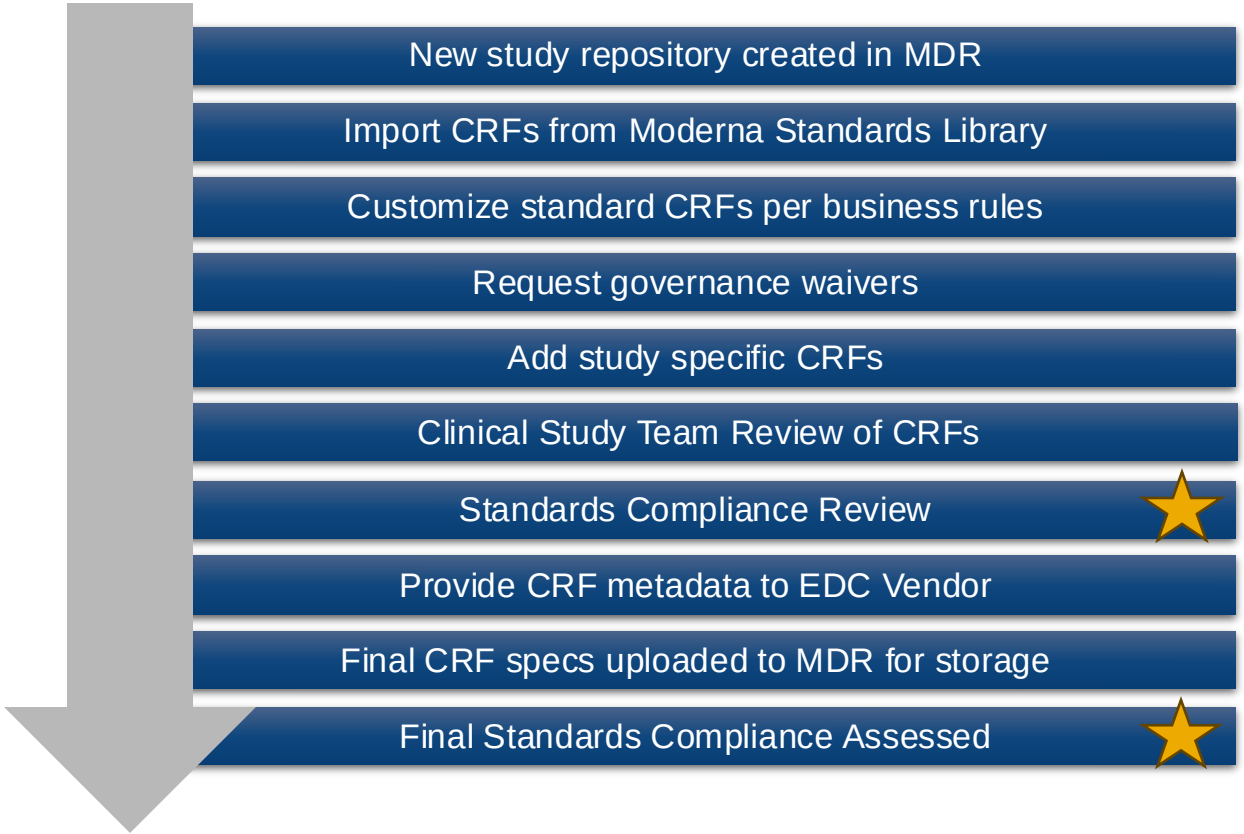
- MDR = Metadata Repository
  - Used for the development and storage of all our standard metadata for data acquisition (i.e., CRFs)
  - Used for initial study database build and storage of all production database releases
    - Allows us to constantly vet the standards for adjustments and to assess compliance with our standards
  - Stores custom datasets for major 3rd party Labs (currently building up use cases)
- CDW = Clinical Data Warehouse
  - Stores our Clinical Trial Data in an active Data Repository/Warehouse

MDR + CDW

- Utilizing our mindsets, Moderna has quickly developed our MDR + CDW
- Limited Historical Data
- Focusing on Active Clinical Trials, Database Development, and Data Cleaning (Data Management Processes)



MDR Clinical Study Database Build Process



MDR Standards Compliance Process

- Compare study CRF metadata against standard CRF metadata
- Use automated MDR report that highlights differences (new, removed, changed)

Timing	Goals

After clinical study team review and prior to EDC vendor starting build	• Ensure standard forms are used within scope of our business rules
	• Check that waivers were requested for deviations from the standard; waivers are implemented as approved
	  • Through this process we also identify where enhancements to our library are needed
	  • Inform protocol template team of adjustments needed
	• Review study specific metadata for compliance with internal metadata naming conventions and alignment with CDASH/Controlled Terminology

After Database Release to Production	• Document final study compliance • Inform downstream clients of differences compared to standard (e.g., dashboards, standard data review listings, SDTM, etc.)

MDR Standards Compliance Process – Case Studies

	Study A		Study B	
Portfolio	Infectious Disease		Therapeutics	
Timepoint	Initial	Final	Initial	Final
Overall Standards Compliance	66%	98%	59%	69%
Standard Form Compliance	69%	98%	74%	94%
Study Specific Field Compliance	80%	100%	30%	100%
# Waivers Submitted	1	5	4	11

Metric Definitions:

Overall Standards Compliance = # fields aligned with standards ÷ total # fields in study

Standard Form Compliance = # fields aligned with standards ÷ total # standard fields in study

Study Specific Field Compliance = # non-standard fields following internal conventions ÷ total # non-standard fields in study

MDR Standards Compliance Process – Benefits

>90% eCRF reuse across all trials

>98% eCRF reuse across ID trials

>90% edit check requirements met through standards library

~8 weeks from project initiation to go-live across all trials

Go-live in as little as 2 weeks for ID studies

<2 weeks UAT to go-live across all trials

Faster Study Start-Up

Cleaner Data Faster

MDR Standards Compliance Process – Challenges

Ensuring standards compliance check is not seen as a "bottleneck" for study start-up

- Being notified at the correct time
- Quick turn-around for review/feedback

Negative connotation with requesting a waiver for standards deviation

- Simply a way to formally document deviations – different levels of approval
- Used as justification for changes to standards library

Small number of deviations from standards that are not approved still making it into production

- Additional changes made after metadata sent to EDC vendor
- Changes being made during CRF amendments

MDR Standards Compliance Process – Future

Planning to add another standards compliance review during UAT

- Catch additional standards deviations made after initial review prior to go live
- Currently not required to draft CRF amendments in MDR

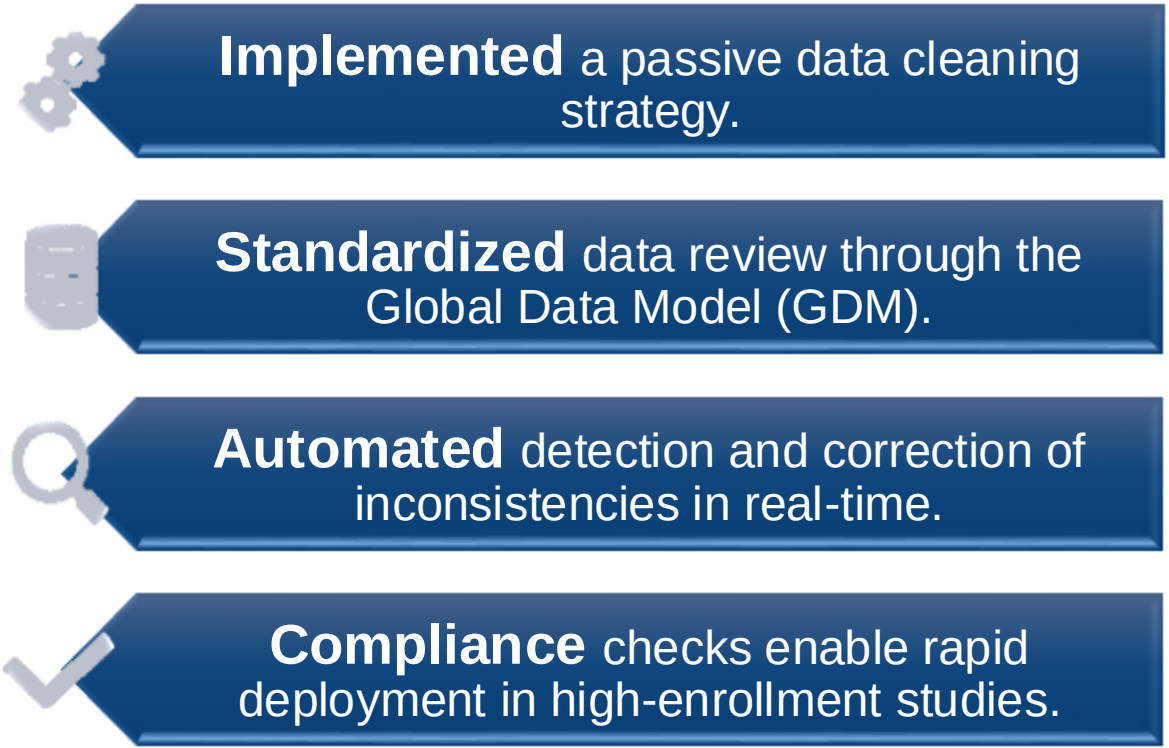
Continue to train and provide additional resources to study teams to help with standards implementation

- Reduce number of findings from compliance reviews

Focus on continuing to build standards library beyond ID

- Improve overall standards compliance for studies in therapeutics portfolio

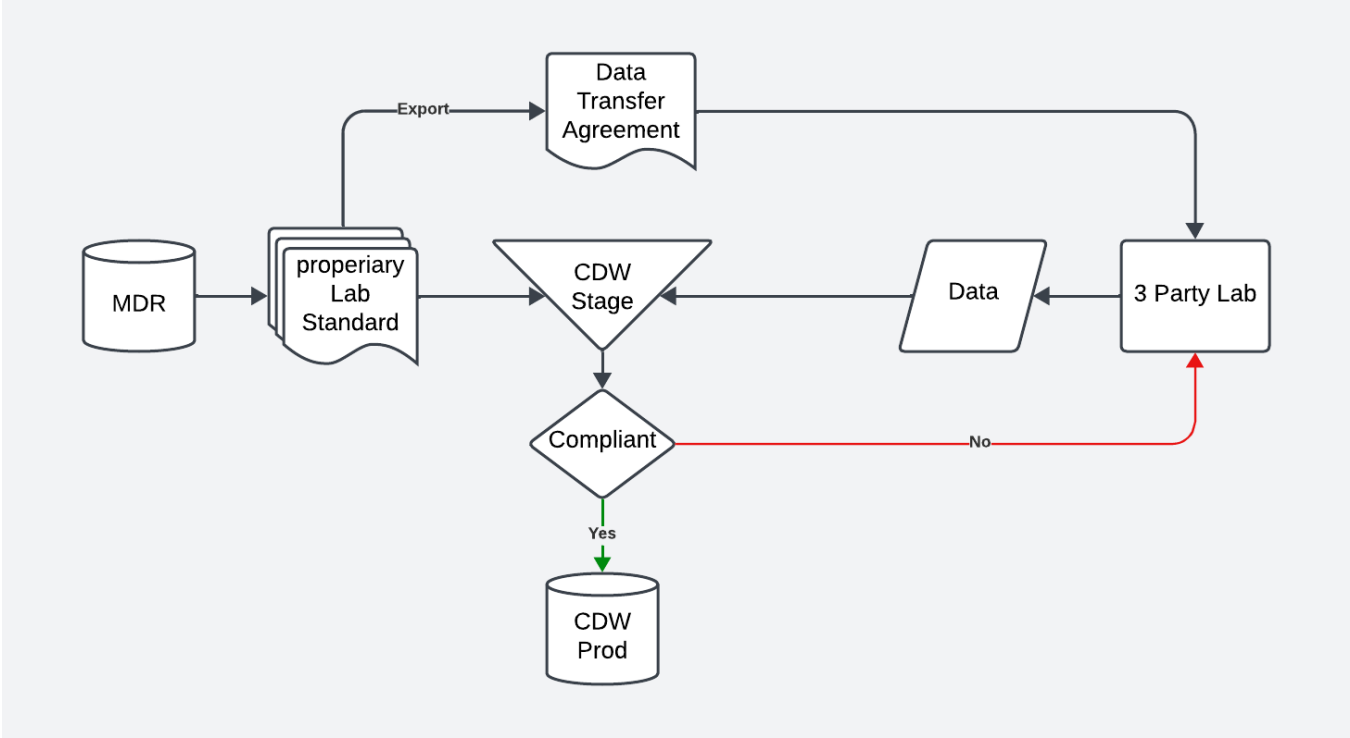
MDR and the Global Data Model: Enhancing Passive Data Cleaning



MDR and 3rd Party Lab Integration Process

1. Run pilots to determine efficiency.
   - Evaluated systems for ongoing data transfer and processing.
2. Combine systems (MDR-CDW) for data transfer.
   - Notify lab if the file doesn't meet standards.
3. Apply active/passive cleaning checks.
   - Final data cleaning in CDW for validation.

High Level MDR / 3PL Flow in Pilot



Future @ Moderna

- **Advocating for LLM/AI/ML**: Pioneering advanced technologies.
- **mCHAT Application**: Custom ChatGPT tools for data governance.
- **Beta Projects**: mCHAT Standards, Protocol Template, CDASHIG.
- **Key Benefits**: Streamlining protocol alignment and enhancing compliance. (DDF?)
- **Next Steps**: Integrating AI into workflows for rigorous, compliant study builds.

“Standards mCHAT”

how do i submit a waiver to CDSC

To submit a waiver to the Clinical Data Standards Committee (CDSC), you should follow these steps:

1. **Identify the Need for a Waiver**: Before submitting a waiver request, ensure that your request pertains to a deviation from an established Data Handling Convention, Business Rule, or another standard that requires adherence according to the protocol. For example, waivers might be needed if you're requesting a change to standard CRFs, the inclusion of new forms or functionalities like Dynamic Search List (DSL), or deviations from Data Handling Conventions.
2. **Prepare Justification**: Clearly outline the justification for the waiver. This should include the reason why the standard cannot be adhered to and the potential impact if the waiver is not granted.
3. **Submit the Request**: You will need to submit your waiver request through the Standards Governance Request system. This is done via a Smartsheet link provided by Moderna: Submit Waiver Request.
4. **Follow Up**: After submission, the Data Governance Team (DGT) will review the request. If necessary, the issue will be escalated t[illegible]e CDSC for further review. If the request is time-sensitive, an ad-hoc meeting of the CDSC can be scheduled.

Business Rule Questions ”Standards mCHAT”

- Used file from MDR in XML format
- Had mCHAT learn the file.
- DMs can query to find specific information of standard

provide me the business rules for the Height variable

The business rules for the **Height** variable, identified by the field OID `HEIGHT_VSORRES`, are as follows:

- **Form**: Vital Signs
- **Therapeutic Area**: Global
- **Optionality**: Required
- **Business Rules**:
  - Use dynamics to hide the height field at visits where it is not necessary according to the protocol.

These rules ensure that the height is only collected when required by the study protocol, and unnecessary data collection is avoided.

If you need further details or have additional questions, feel free to ask!

Conclusions

Automated Compliance:	Leveraging the MDR enables machine-driven compliance processes.
Enhanced Standardization:	Improved compliance elevates downstream processes and data reusability.
Systematized Knowledge:	Storing study metadata in a system preserves historical knowledge beyond individual expertise.
Successful Data Ingestion:	Pilot programs for data ingestion were successful, with ongoing efforts to refine use cases and process improvements (acknowledging the current manual aspects).
Cautious Use of LLMs:	While promising, LLMs need refinement and should be used with disclaimers due to their current limitations in providing consistently accurate information.

Key takeaway: AI and automation are critical but require careful implementation.

Thank You!