PROJECT PRISM UPDATE:
USE CASES AND PILOTS
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PRISM Background

- *"FDA will leverage cloud technology to progress regulatory digital transformation, including demonstration projects to explore application of cloud-based technologies to streamline, improve and enable a variety of applicant-regulator interactions."* --PDUFA VII Commitment Letter Section IV

- FDA and Industry signed a Research Collaboration Agreement (RCA) for PRISM (PrecisionFDA Regulatory Information Service Module) – October 2023

- PrecisionFDA is an FDA-owned information platform in existence since 2015
  - Fully secure: FedRAMP Moderate – FISMA Moderate
  - FDA Center for Veterinary Medicine currently uses the platform for regulatory review
  - precisionFDA - Overview

PRISM RCA and Relevant Parties

SUMMARY PAGE

EITHER PARTY MAY, WITHOUT FURTHER CONSULTATION OR PERMISSION, RELEASE THIS SUMMARY PAGE TO THE PUBLIC.

TITLE OF RCA: Project PRISM (PrecisionFDA Regulatory Information Service Module)

FDA Component:	Center for Biologics Evaluation and Research (CBER); Center for Drug Evaluation and Research (CDER); Office of Digital Transformation (ODT)
FDA Principal Investigators:	
CBER:	Virginia Hussong, Mark Gray, Ronald Fitzmartin
CDER:	Chao (Ethan) Chen, Jesse Anderson
ODT:	Elaine Johanson
Collaborator:	Bayer AG and Boehringer Ingelheim International GmbH
Collaborator Principal Investigator:	Vada Perkins
TERM OF RCA:	Three (3) years from the Effective Date

ABSTRACT OF THE RESEARCH PLAN:

This research collaboration will demonstrate the feasibility of interactive and collaborative regulatory and scientific review, as well as submission validation utilizing FDA's production regulatory cloud platform, known as PrecisionFDA. The project will utilize actual regulatory data suitable for submission to the FDA, as well as third-party tools that FDA currently uses, i.e., for eCTD (electronic Common Technical Document) and study data review / validation. However, no submissions or activities involved in this plan take the place of an official regulatory submission and/or review process.

Practical, real-world use cases will test the essential functions of collaborative review, receipt and archive of information against current solutions, utilizing novel regulatory and scientific tools and technologies that will enable enhanced sponsor/health authority interactions. Exchange and use of large submissions will be evaluated, a challenge that continues to grow. The collaborators are expected to gain important foundational insights into cloud-based regulatory and scientific solutions and processes that can improve the submission, review and ease of communications for human drug and biologics applications to FDA.

Results, findings and recommendations will be published after each phase, and can be utilized by external stakeholders and global regulatory health authorities to leverage regulatory and scientific platforms and processes that achieve greater efficiencies on a regional and international scale.

FDA Principal Investigators:

- Center for Biologics Evaluation and Review
- Center for Drug Evaluation and Review
- Office of Digital Technology

Industry Participants:

- Bayer
- Boehringer-Ingelheim
- Bristol Myers Squibb
- EMD Serono
- Takeda
- Gilead
- Biogen

FDA software & service providers

Other entities such as CDISC, Transcelerate, etc.

How the collaboration works

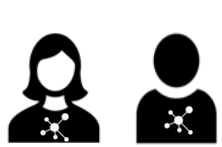
- Specific Use Cases evaluate essential functions of interactive communication and collaboration using the private and shared spaces within PRISM
- Actual regulatory data (BLA/NDA), or data suitable for submission to the FDA will be used, including large submissions
- Third party tools currently used by FDA for validation and review (e.g., eCTD, statistical analysis tools) will be used
- Results, findings and recommendations will be published after each phase

PrecisionFDA Interactive Review Spaces

Building blocks to enable sponsor/regulator interaction while maintaining a secure separation

FDA owned and authorized information system

FDA



Industry and Academic Collaborators

Healthcare Data Partners

precisionFDA FISMA Authorized Cloud Workstations

precisionFDA Files, Apps, and Workflows

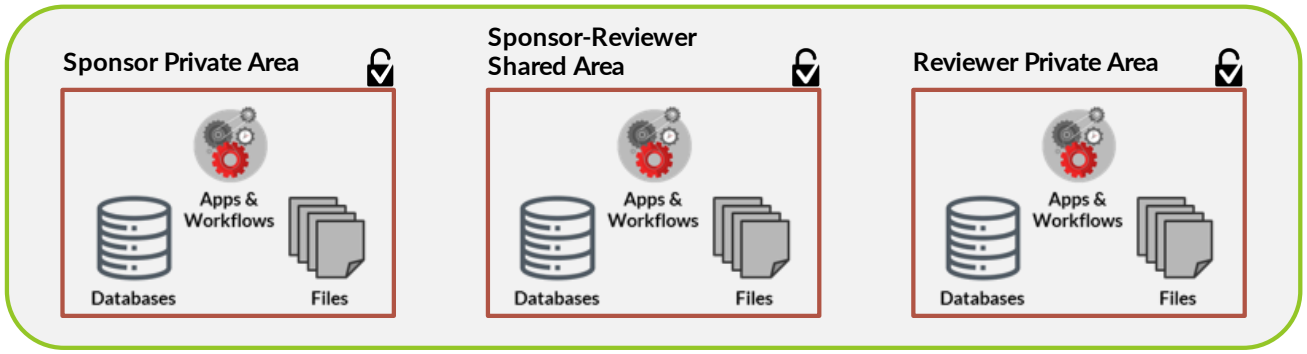
Lorenz eValidator

RStudio

SAS Studio

Jupyter Notebook

precisionFDA Interactive Review Spaces



precisionFDA

- Users can easily move files between ***spaces*** that are available to them.
- Users can not see or move files into or out of someone else's private ***space***
- Users can access shared tools to facilitate interaction

Current Phase 1 Use Cases

Technical validation of eCTD and Study Data

- Currently underway, finished validation, evaluating feedback

ICH M11 Clinical Electronic Structured Harmonized Protocol

- Currently underway

Real World Data

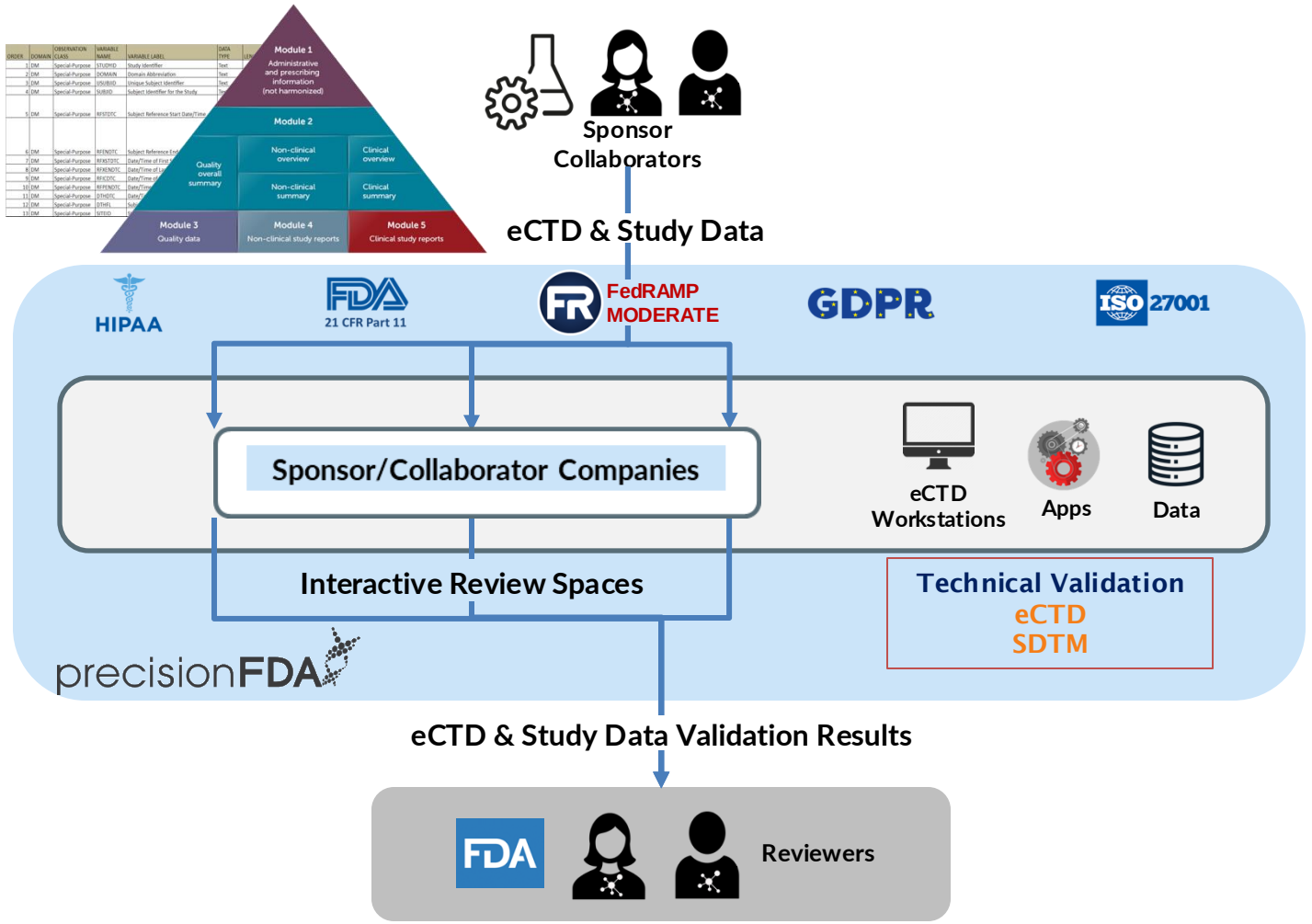
- In development

Labeling

- In development

Phase 1

eCTD & Study Data Technical Validation



GOAL: Evaluate greater efficiencies in submission receipt and processing; perform eCTD and Study Data Validation prior to Gateway submission and eliminate technical rejection.

Sponsors upload a large eCTD (BLA/NDA) with study data to their **PRISM Private Interactive Review Space**.

Using 21 CFR Part 11-compliant precisionFDA Workstations, Sponsors validate their eCTD and study data using FDA-managed applications.

Potential for Sponsors to select from multiple validation profiles to validate against multiple regulators requirement.

Sponsors share the eCTD and study data validation results with FDA using **Shared Interactive Review Spaces**.

Collaborator Validation Use Case Submissions

EMD Serono Application type	Submission type	Modules	Study data	Seq Size
CDER NDA	Original	1, 2 (ex 2.3), 4, 5	SDTM, ADaM, SEND	8.33 GB
	Amendment to original	1	N/A	4 MB
	Amendment to original	1	N/A	4 MB

Boehringer Application type	Submission type	Modules	Study data	Seq Size
CDER BLA	Original	1, 2 (ex 2.3), 4, 5	SDTM	1.64 GB
	Amendment to original	1, 5	N/A	8 MB
	Amendment to original	1, 5	N/A	3 MB
	Amendment to original	1	N/A	4 MB
	Amendment to original	1	N/A	2.75 MB
	Amendment to original	1, 5	N/A	180 MB

Bayer Application type	Submission type	Modules	Study data	Seq Size
CBER BLA	Original	1, 2 (ex 2.3), 4, 5	SDTM, SEND, ADaM, Legacy - 3.69 GB	5.85 GB
CDER NDA	Original – Rolling Submission Original – Rolling Submission	1, 2 (ex 2.3), 4, 5 1, 2, 5	SDTM, SEND - 448 MB SDTM, SEND, ADaM, BIMO, Legacy - 8 GB	983 MB 18 GB
	Efficacy Supplement (RTOR) Efficacy Supplement (RTOR)	1, 5 1, 5	SDTM, ADaM, BIMO, Legacy - 8 GB N/A	9 GB 5 GB
	Efficacy Supplement (sNDA) – Project Orbis	1, 2, 4, 5	SDTM, ADaM - 792 MB	1.4 GB
CDER NDA	Original	1, 2 (ex 2.3), 4, 5	SDTM, SEND, ADaM, BIMO, Legacy - 93 GB	99.5 GB
	Efficacy Supplement (sNDA)	1, 2, 5	SDTM, ADaM, BIMO, Legacy - 121 GB	125 GB

- These sequences have already been submitted, reviewed and approved.
- No re-review of these sequences will be performed or creating of new lifecycle sequences.

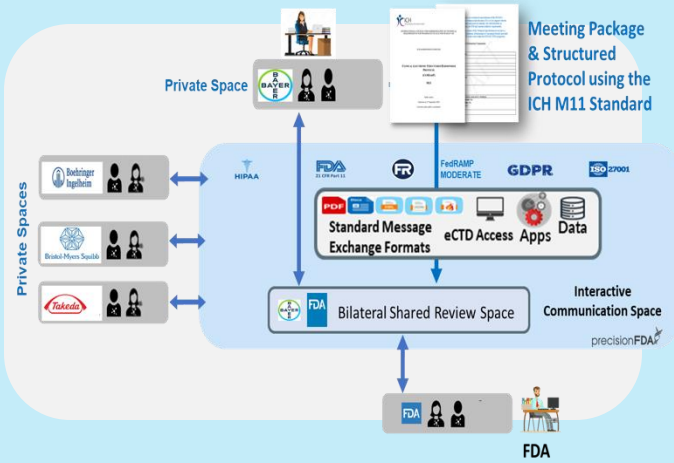
PRISM ICH M11 Demonstration Use Case

- **FDA and Sponsors**
  - Demonstrate sponsor-to-regulator electronic exchange and viewing of a M11-compliant protocol in two parts.
    - In the **first part**, sponsors will create M11 protocols in two human-readable formats, DOCX and PDF.
    - In the **second part**, sponsors will create a machine-readable FHIR exchange format of the M11 protocols expressed as JSON.
  - Results will inform the ICH M11 EWG of any content and / or technical issues that need to be addressed prior to reaching ICH Step 3 and 4.

PRISM M11
Interactive Communication on PrecisionFDA

Planned Demonstration Outcomes

- Preparation of protocols from 4 early and 4 late - stage clinical trials us M11 Template
- Preparation and exchange of protocols using both human and machine- readable formats: DOCX, PDF, JSON and FHIR.
- Gain knowledge on the ease of use of the instructional material.
- Evaluation of the FDA-EMA interactive communication and exchange of protocols using FHIR.
- Evaluation of the FDA-Sponsor interactive communication on the PrecisionFDA platform.
- Inform FDA on potential future uses of a data-driven protocol



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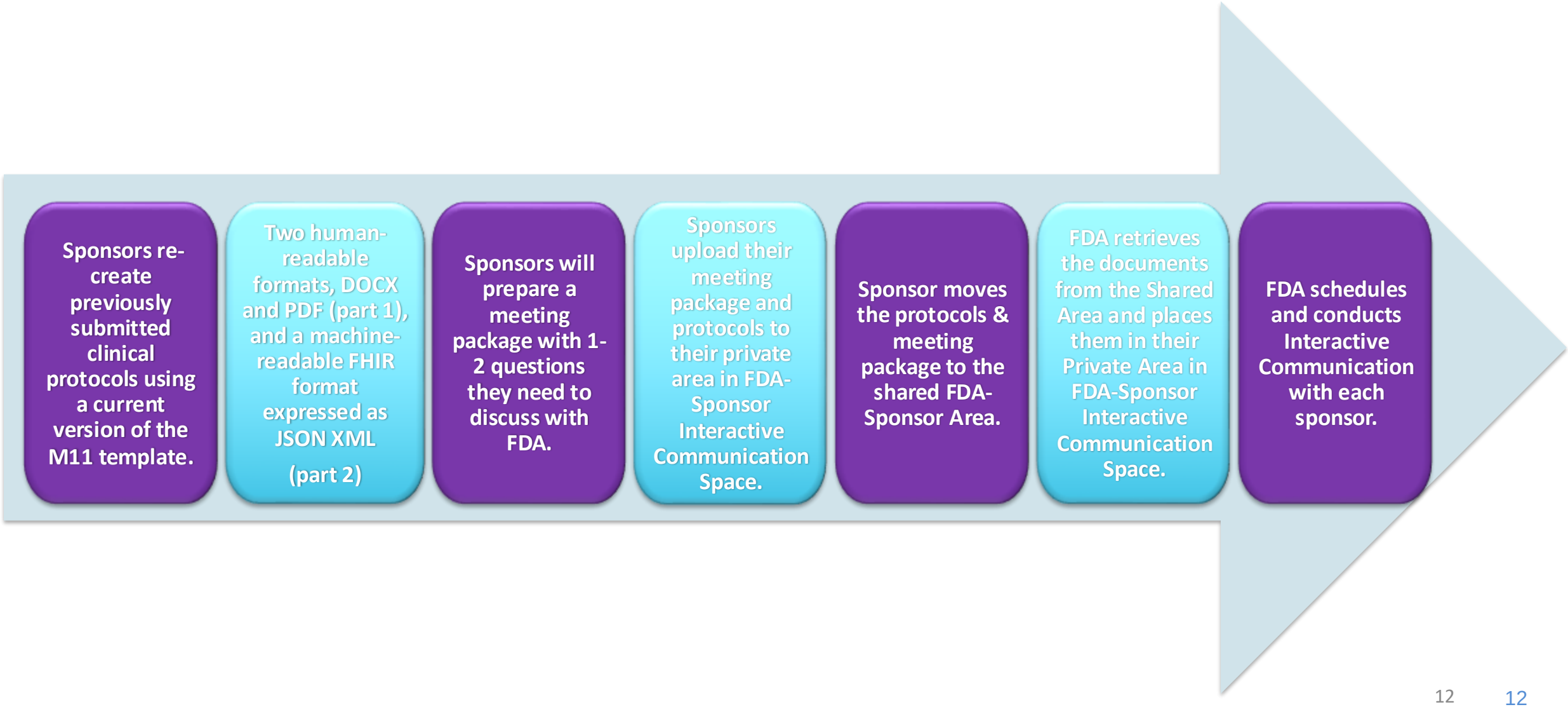
Process Steps for the PRISM M11 Interactive Communication



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Phase 2: Additional Review & Validation Scenarios

- PRISM Program Committee may add additional use case scenarios that build upon the findings and recommendations of Phase I

- PRISM may include a broader set of subject matter experts and stakeholders, depending on requirements for future scenarios, such as:
  - Additional regulators
  - Additional collaborators
  - Additional vendors and service providers

Benefits to FDA

- Provides insight into how collaborative regulatory review could impact our current processes, procedures and tools

- Utilizing precisionFDA means leveraging existing compute, storage and interactive regulatory review capabilities
  - Secure: FedRAMP security rated for cloud service providers / FISMA rated for computer systems
  - Compliance with EU General Data Protection Regulation on privacy

- Use of shared applications and tools in the review process means we can all be seeing the same thing

- Single cloud platform can consolidate numerous processes into one, reducing duplication, allowing central access control, auto-versioning of documents and archiving of communications in a single location
  - Same model can be followed for future implementations, e.g., FHIR messages, PQ-CMC and M11 protocols

- Alignment with shared strategies to modernize technology and data flows, leverage all that a secure cloud environment has to offer

Next Steps

- Complete Phase I of the Validation and M11 Use Cases
- Finalize the Phase I Real-World Data (RWD) Use Case Project Plan
- Confirm participants and Finalize Labeling Use Case Project Plan
- Exploration of additional Phase I Use Cases
- Launch public website

Thank You

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