U.S. FOOD & DRUG ADMINISTRATION

An Introduction to PRISM (precisionFDA Regulatory Information Service Module)

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FDA Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration.

Agenda

- Background
- Description of PRISM – Research Collaboration Agreement
- Expected Outcome
- Participants
- Discussion of the two current use cases
- Benefits to FDA and the Industry

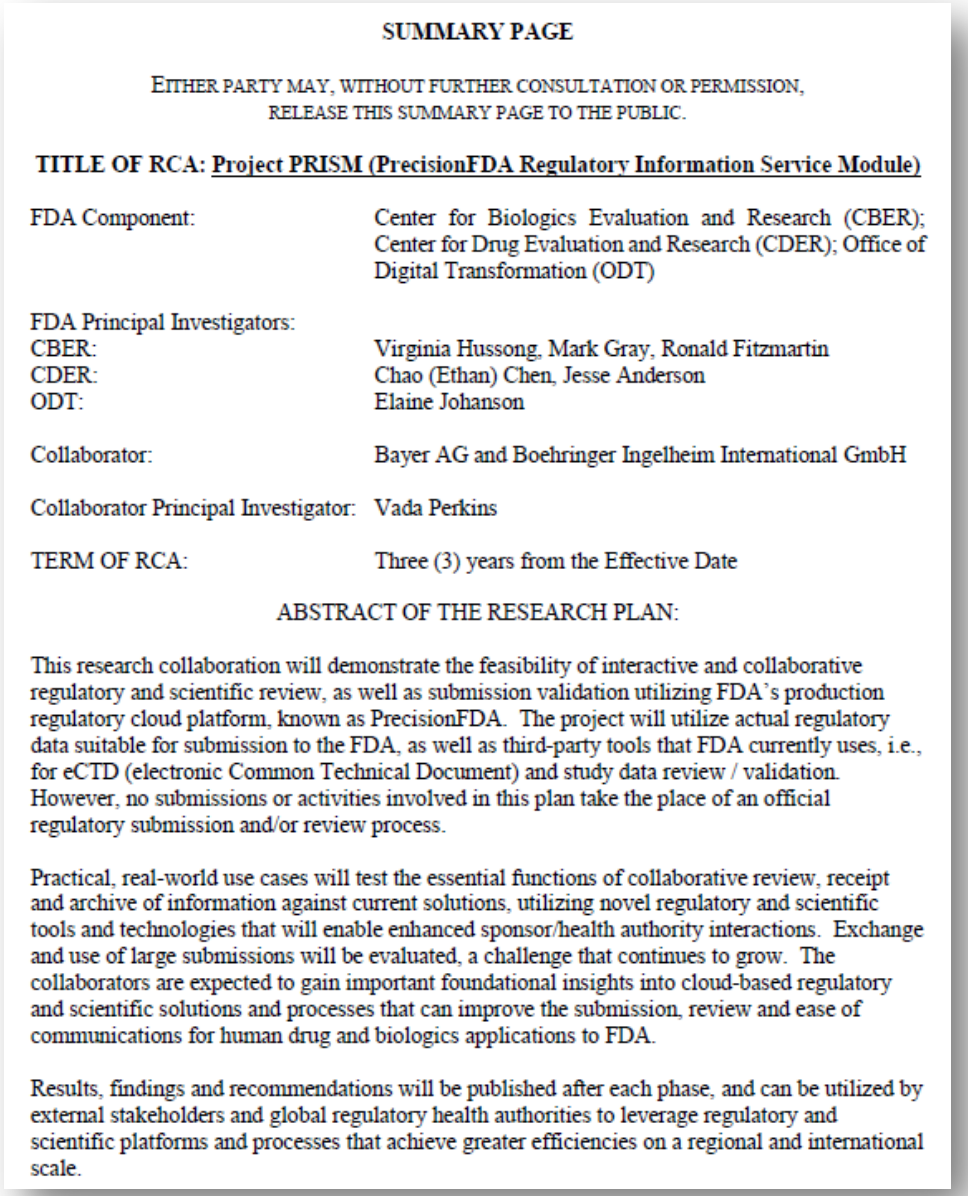
Background – PDUFA VII Commitments

- *"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."*

- *"Projects will demonstrate applications of cloud technology to applicant-regulator interactions and secure shared environments for specific regulatory activities (e.g., support labeling negotiations between FDA and applicants, develop a standard protocol template to accelerate review and provide usable archive, improve statistical analysis plan between FDA and applicants)."*

What is Project PRISM?

- A research collaboration and proof of concept project utilizing FDA's production regulatory cloud platform, precisionFDA
- Proposed to FDA by industry companies
- Demonstrate the feasibility of collaborative regulatory submission validation and scientific review
- RCA principal investigators include CBER, CDER and ODT



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.

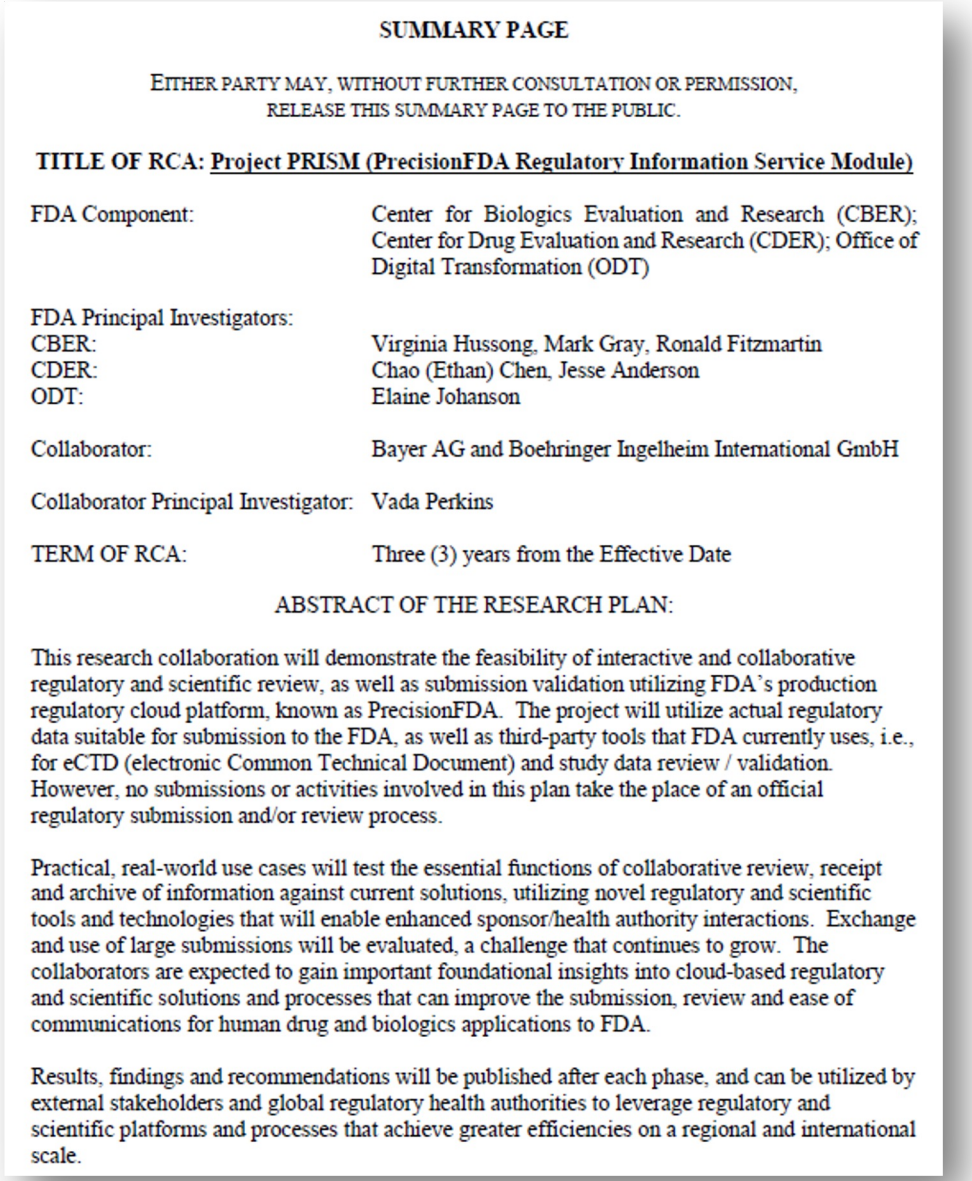
Practical, real-world use cases will test the essential functions of collaborative review, receipt and archive of information against current solutions, utilizing novel regulatory and scientific tools and technologies that will enable enhanced sponsor/health authority interactions. Exchange and use of 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.

Research Collaboration Agreement (RCA)

What is the expected outcome?

"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"



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Research Collaboration Agreement (RCA)

Who is involved?

	Industry	U.S. FDA
Executive Sponsors	Dr. Max Wegner *SVP/Head of Regulatory Affairs* Bayer Dr. Thomas Seck *SVP/Head of Global Regulatory Affairs* Boehringer-Ingelheim	Vid Desai, FDA *Chief Information Officer/Office of Digital Transformation* Ram Iyer, FDA *Chief Data Officer/Office of Digital Transformation* Dr. Christopher Joneckis, FDA/CBER *Director, Office of Regulatory Operations*
Program Committee	Rene Kluensch Bayer Joerg Stueben Pam Cafiero * Vada A. Perkins Boehringer-Ingelheim	* Elaine Johanson, ODT/FDA *Program Manager, PrecisionFDA* Omar Serang *FDA Contractor-Technical (DNAnexus)* * Virginia Hussong, FDA/CBER Ethan Chen, FDA/CDER

Newest collaborators:
EMD Serono
Bristol Myers Squibb
Takeda

**PRISM Program Committee Co-Chairs*

FDA Principal Investigators: CBER: Mark Gray, Ron Fitzmartin CDER: Ethan Chen, Jesse Anderson

How will the collaboration work?

- Utilize precisionFDA, FDA's production cloud platform originally built for multi-omics and real-world data regulatory science and review
- Evaluate essential functions of technical validation, interactive communication and collaboration using PRISM's cloud capabilities against the current state using specific use cases
- Use of actual regulatory data (BLA/NDA), suitable for submission to the FDA, including large submissions
- Use of actual 3rd party tools currently used by FDA for validation and review (e.g., eCTD, statistical analysis tools)
- Results, findings and recommendations will be published after each phase

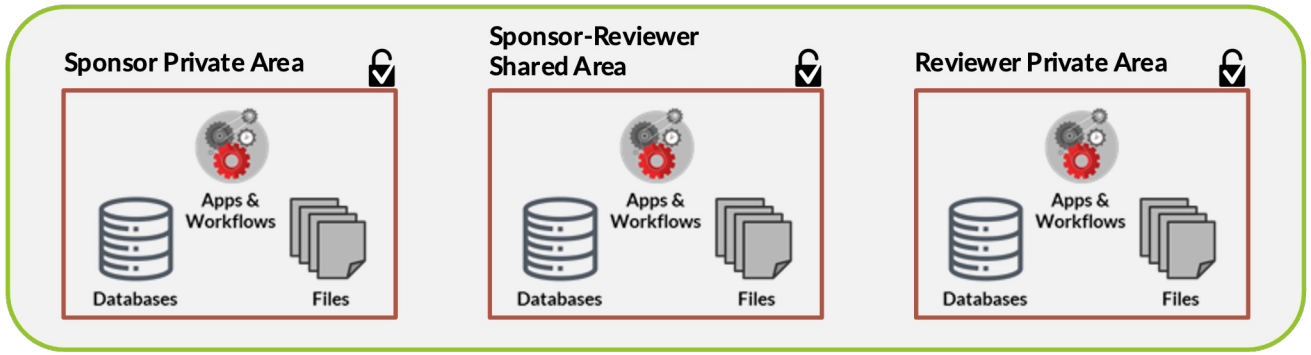
PrecisionFDA Interactive Review Spaces

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

- FDA owned
- FDA authorized information system

precisionFDA
FISMA Authorized Cloud Workstations

precisionFDA
Interactive Review Spaces

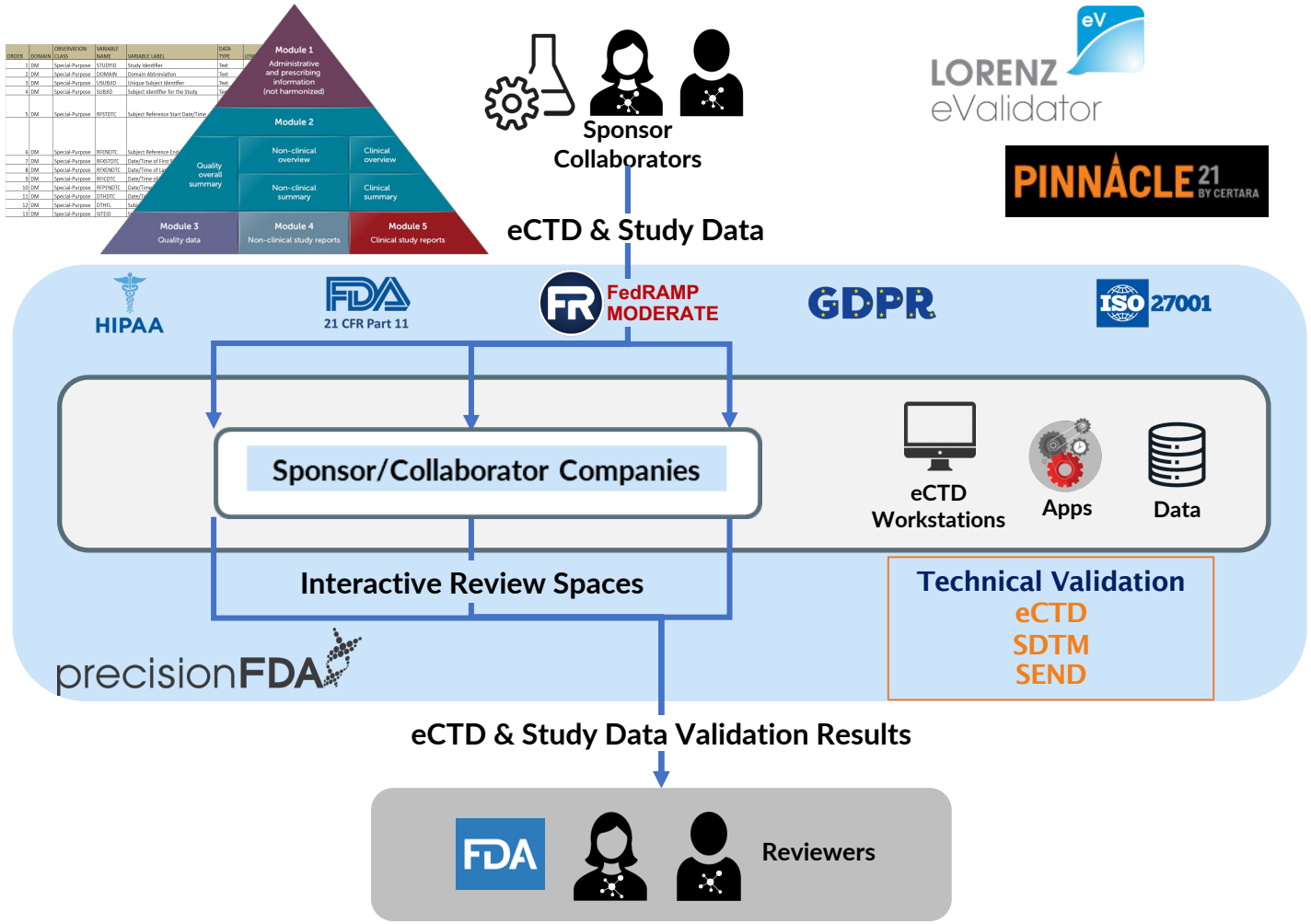


precisionFDA

- 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

Phase 1

Use Case: eCTD & Study Data Technical Validation



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

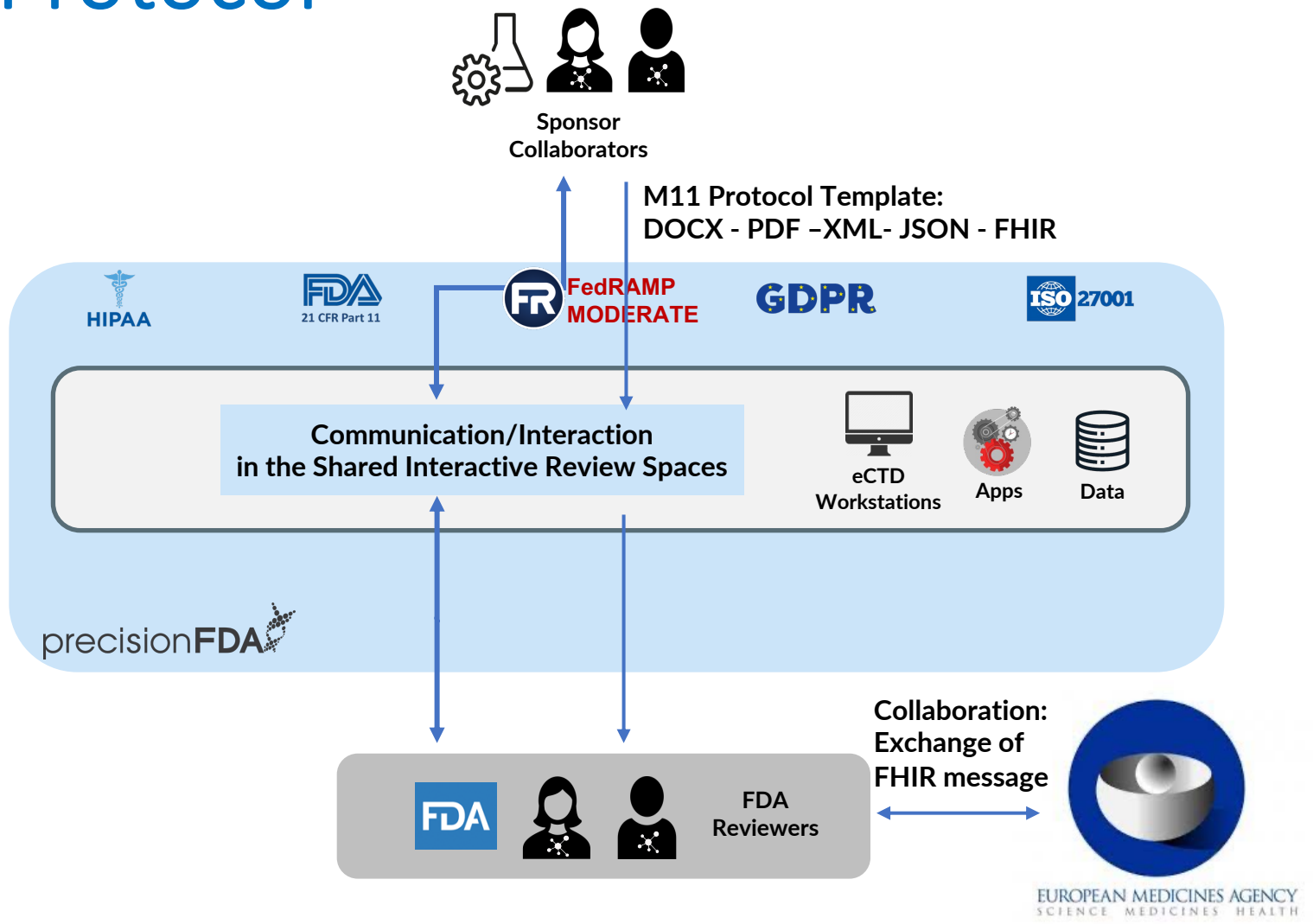
Sponsors upload a large eCTD (BLA/NDA) with study data to their **PRISM Private Interactive Review Space**.

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**.

Use Case: Interactive Communication – ICH M11 Clinical Electronic Structured Harmonized Protocol



Electronic Exchange of ICH M11 protocol to evaluate regulator-to-regulator communication.

Sponsors and Reviewers work in their **Private Spaces** and share and communicate in the **Interactive Review Spaces.**

Reviewer/Sponsor data sharing and validation activities, and inter-party communications and interactions are captured in an **Interactive Review Report**.

Collaboration will be conducted with the European Medicines Agency (EMA).

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.

Phase 2: Additional Review & Validation Scenarios

- PRISM Program Committee may add additional use case scenarios that build upon the findings and recommendations of Phase 1

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

Benefits to FDA & Industry

- **Potential efficiencies associated with regulatory review**
  - Shared applications and tools
  - Ingestion and management of large amounts of data
  - More collaborative experience for Industry and FDA
  - Insight into how collaborative regulatory review could impact current processes, procedures and tools
  - Increase confidence among both regulatory authorities and industry
- **PrecisionFDA provides**
  - Immediate availability at no additional cost to FDA or Industry
  - Secure: FedRAMP security rated for cloud service providers / FISMA rated for computer systems
  - Compliance with EU General Data Protection Regulation on privacy