Delivering a Data-Driven Clinical Protocol - ICH M11

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ICH M11 Rapporteur

FDA Disclaimer

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Topics

- What's PRISM?
- Brief Update on ICH M11
- M11 as a Use Case in PRISM
- Imagine a Future State

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

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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.

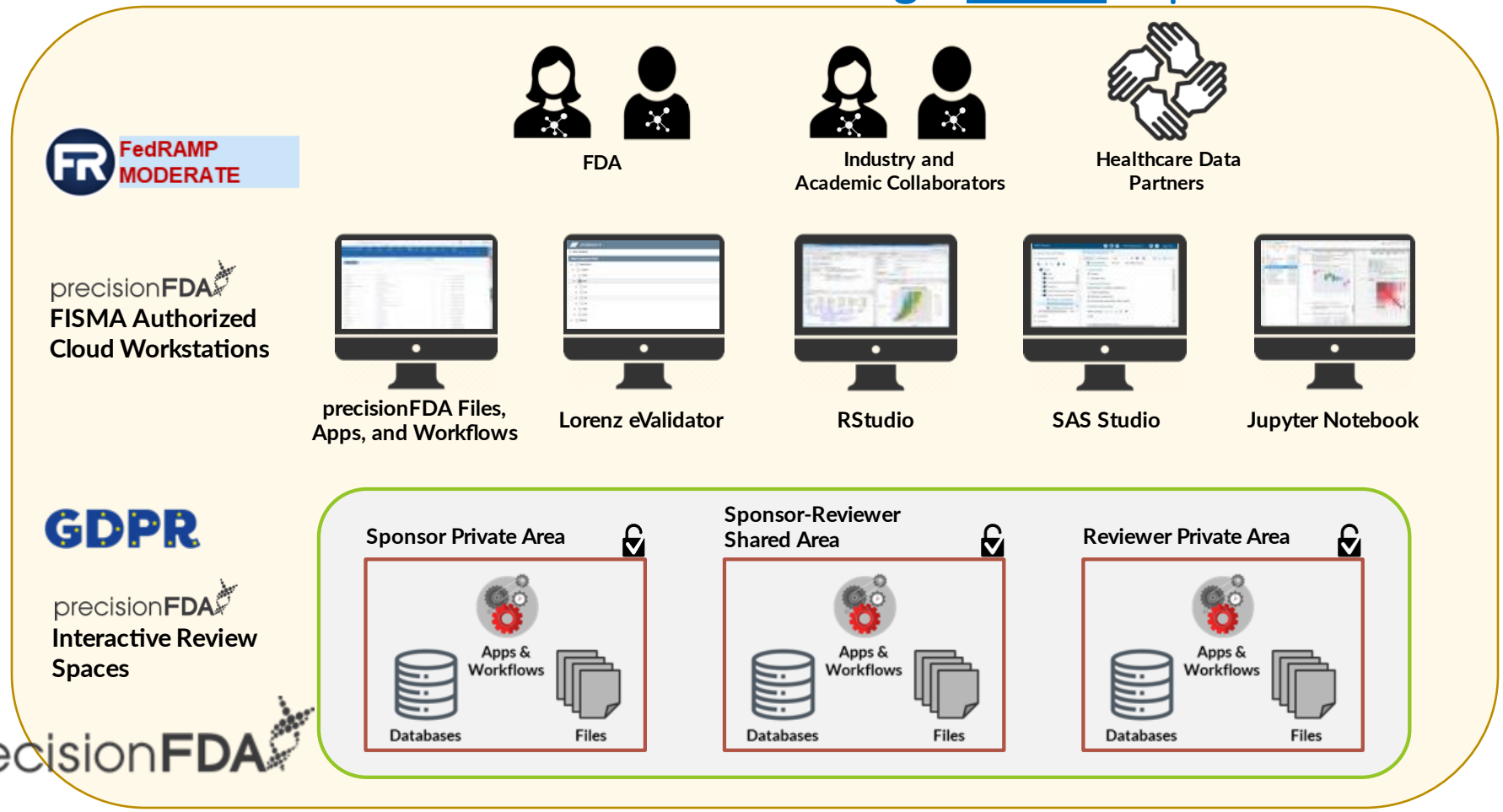
Practical, real-world use cases will test the essential functions of collaborative review, receipt and archive of information against current solutions, utilizing novel regulatory and scientific tools and technologies that will enable enhanced sponsor/health authority interactions. Exchange and use of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

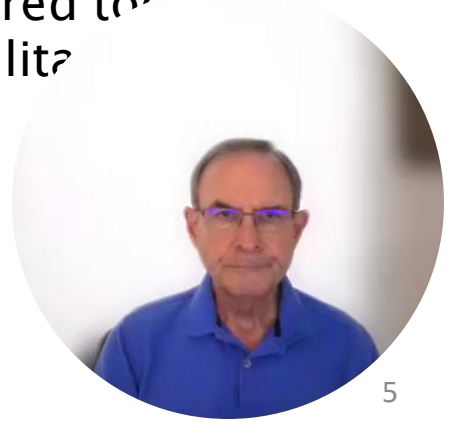
Research Collaboration Agreement (RCA)

PrecisionFDA Interactive Review Spaces

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



- 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 tool facilita



FDA owns precisionFDA
It is an FDA authorized information system

How will the PRISM 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
- Actual regulatory BLA and NDA data, suitable for submission to the FDA (including large submissions).
  - *NOTE: No submissions or activities involved in this plan take the place of an official regulatory submission and/or review process*
- Actual 3rd party tools that FDA currently uses for validation and review (e.g., eCTD, statistical analysis tools)
- Results, findings and recommendations will be published after each phas

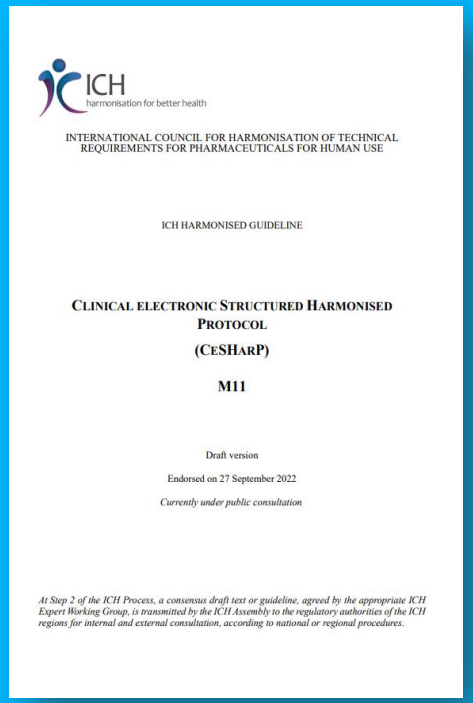
Benefits to FDA & Industry

- **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
  - Provides **insight** into how collaborative regulatory review could impact current processes, procedures and tools
- **PrecisionFDA provides**
  - Immediate availability, at no cost to Industry
  - FedRAMP security rated for cloud service providers / FISMA rated for computer systems.
  - Compliance with EU General Data Protection Regulation on privacy

ICH M11

Clinical electronic Structured Harmonised Protocol

Guideline



ICH harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11

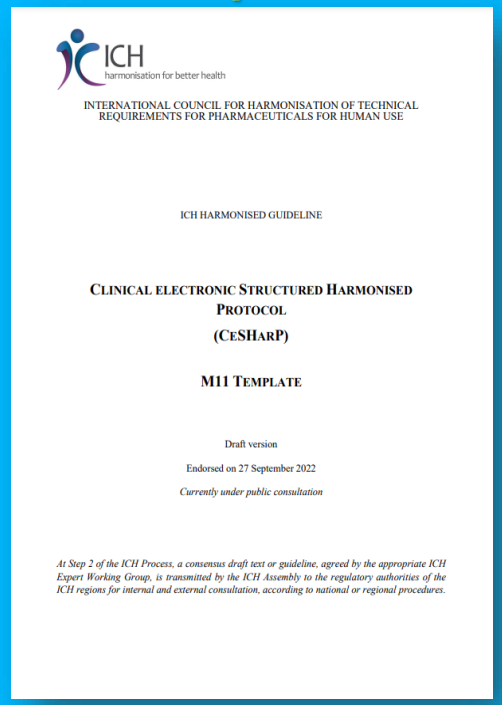
Draft version

Endorsed on 27 September 2022

Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

Template



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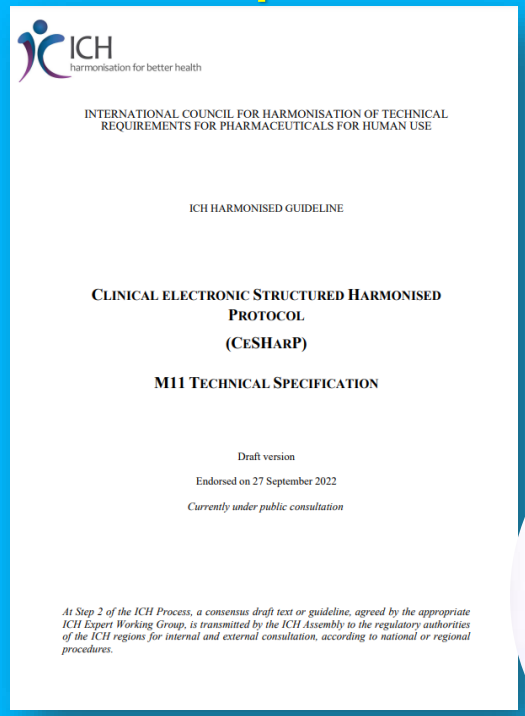
Technical Specification



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ICH M11

Clinical electronic Structured Harmonised Protocol

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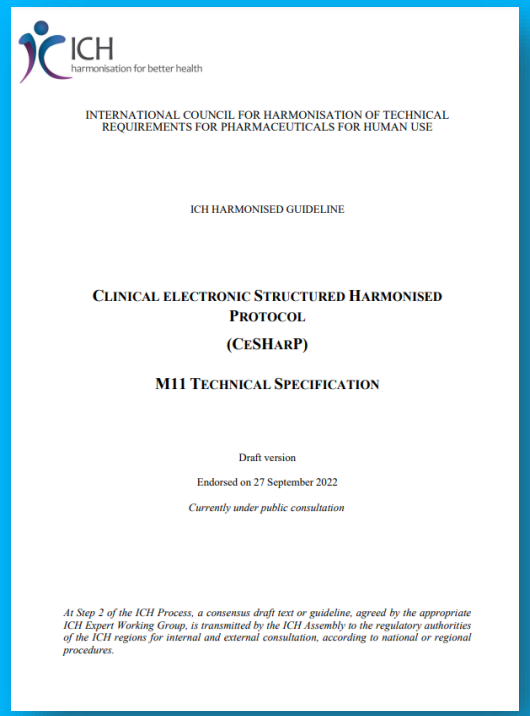

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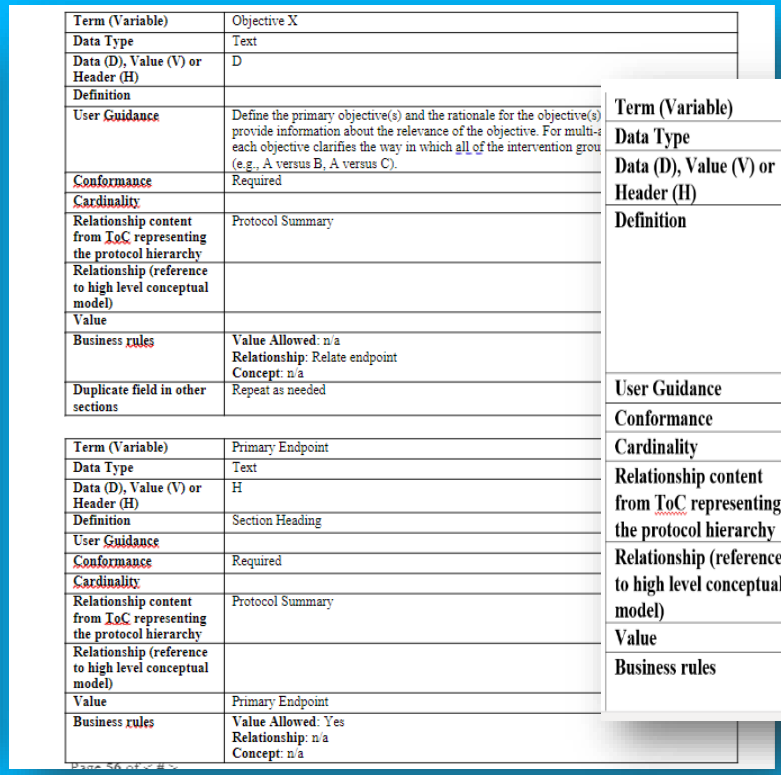

Term (Variable)	Objective X
Data Type	Text
Data (D), Value (V) or Header (H)	D
Definition	
User Guidance	Define the primary objective(s) and the rationale for the objective(s) provide information about the relevance of the objective. For multi-a each objective clarifies the way in which all of the intervention grou (e.g., A versus B, A versus C).
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed**: n/a **Relationship**: Relate endpoint **Concept**: n/a
Duplicate field in other sections	Repeat as needed

Term (Variable)	Primary Endpoint
Data Type	Text
Data (D), Value (V) or Header (H)	H
Definition	Section Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	Primary Endpoint
Business rules	**Value Allowed**: Yes **Relationship**: n/a **Concept**: n/a

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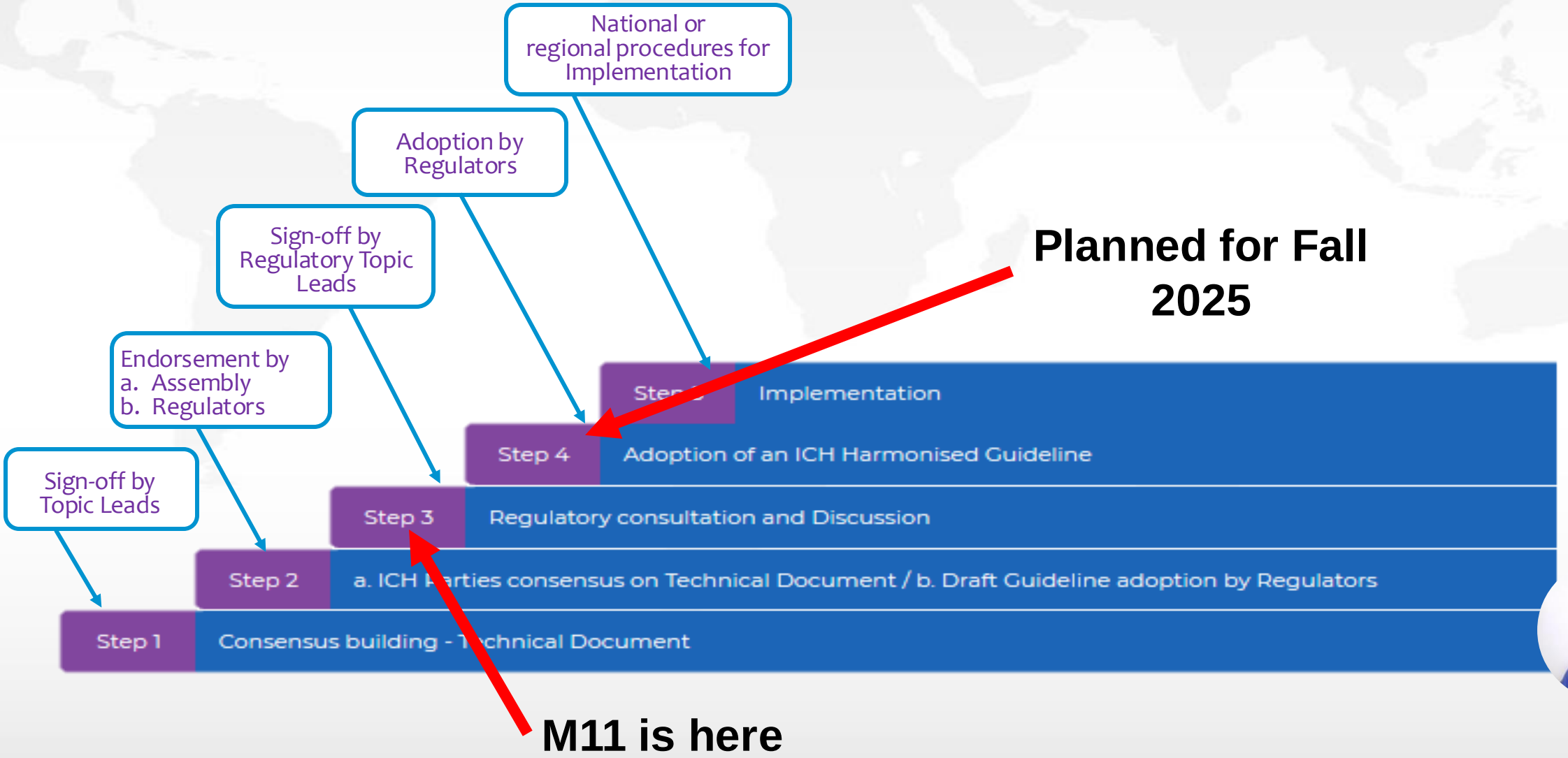
Term (Variable)	{<Clinical Safety Laboratory Assessments>}
Data Type	Text
Data (D), Value (V) or Header (H)	D
Definition	See CNEW For review context CNEW Trial assessments and Procedures related to participant safety.
User Guidance	
Conformance	Conditional Required
Cardinality	One to One
Relationship content from ToC representing the protocol hierarchy	TRIAL ASSESSMENTS AND PROCEDURES
Relationship (reference to high level conceptual model)	
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4.4 {Clinical Laboratory Assessments}

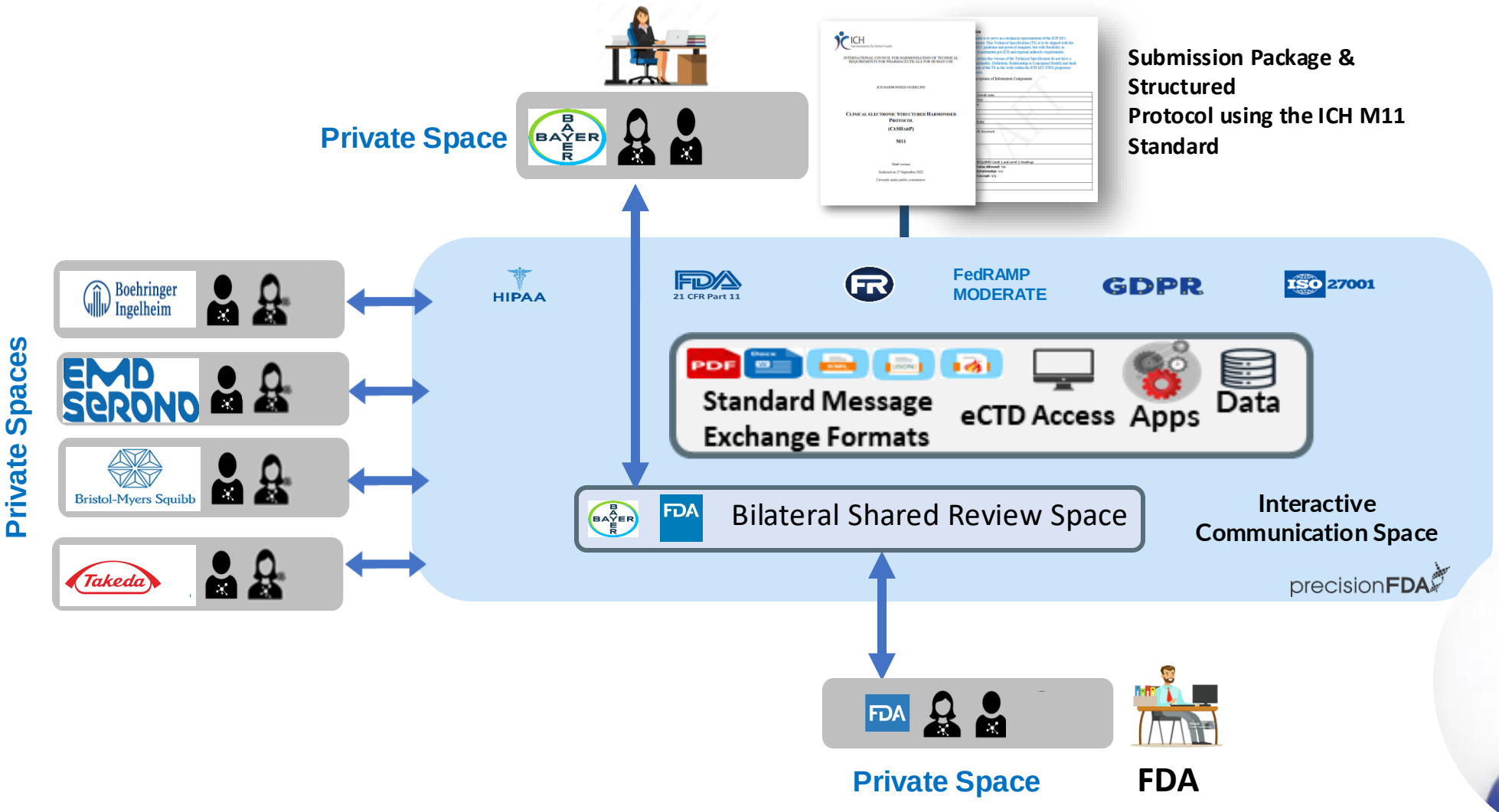
M11 & the ICH Step Process

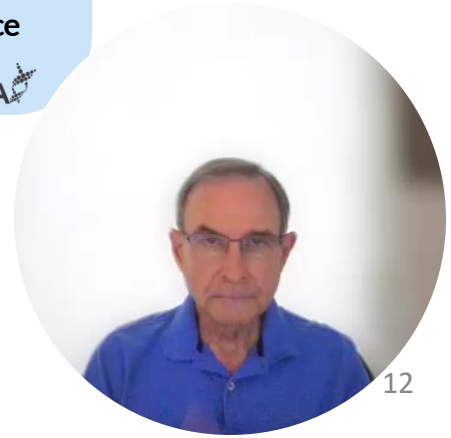


PRISM M11 Demonstration Use Case

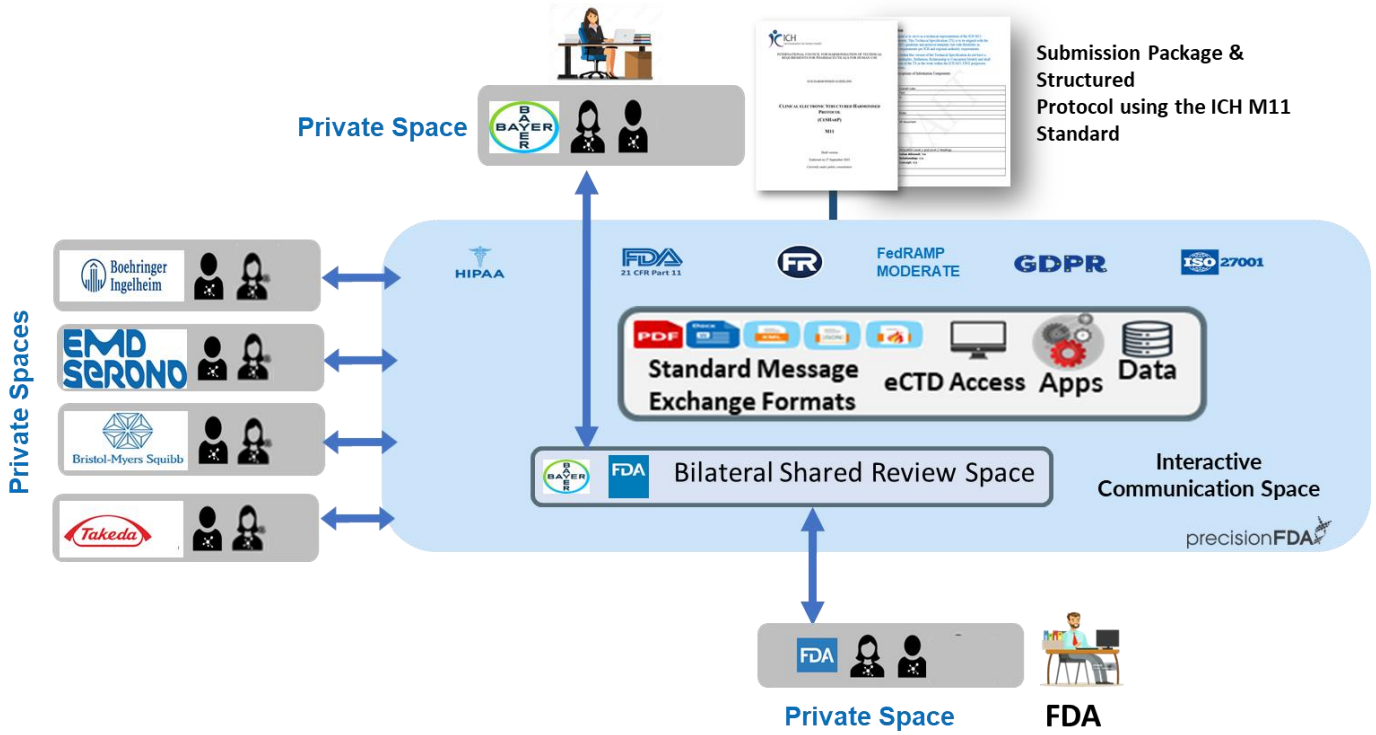
- **FDA and Sponsors:**
  - Demonstrate sponsor-to-regulator electronic exchange and viewing of a M11-compliant protocol in two parts.
  - In the **first part**, sponsors will create M11 protocols in two human-readable formats, DOCX and PDF.
  - In the **second part**, sponsors will create a machine-readable FHIR exchange format of the M11 protocols expressed as either XML or JSON XML.
  - 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 Interactive Communication on PrecisionFDA





Implementation of the M11 Protocol Standard for Interactive Communication in the Cloud



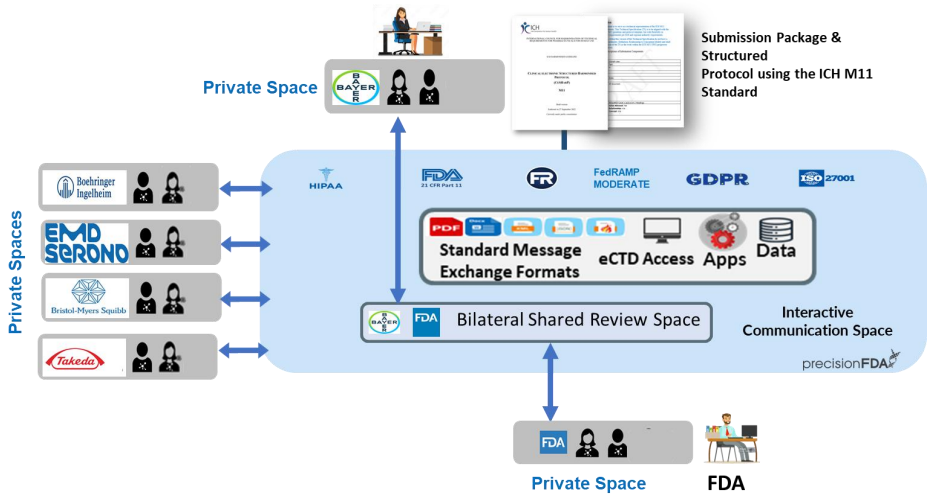
M11 Data Driven Protocols…

- Use a common data model & standards (e.g., CDISC)
- Can be exchanged using multiple standards: FHIR, XML, DOCX, PDF
- Can use common tools to access data repositories
- Can be real-time quality-checked
- Ensure consistency across protocol sections
- Ensure line of sight of trial objectives, endpoints, procedures and design.
- Facilitate downstream processes, e.g., SAP, CSR, CT Registries

Implementation of the M11 Protocol Standard for Interactive Communication in the Cloud

Regulators will be able to…

- Store thousands of protocol data and metadata in repositories across therapeutic areas
- Access to protocol data & metadata for analytics on trial design, procedures, IC/EC, populations
- Supports "What if Scenario Analysis" on, e.g., trial design, dosing, statistical methods



M11
Data Driven Protocol

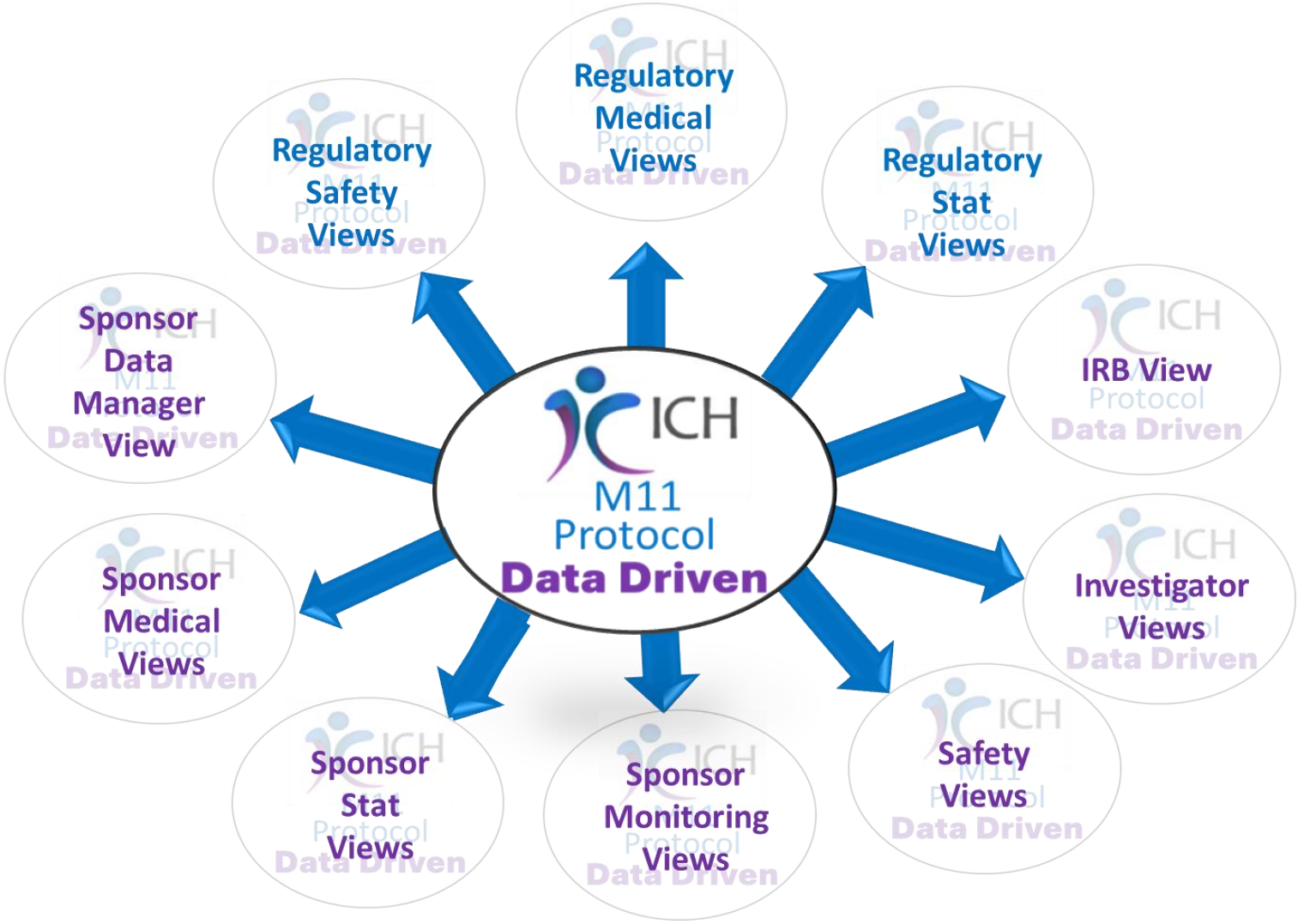
Regulators & Sponsors will be able to…

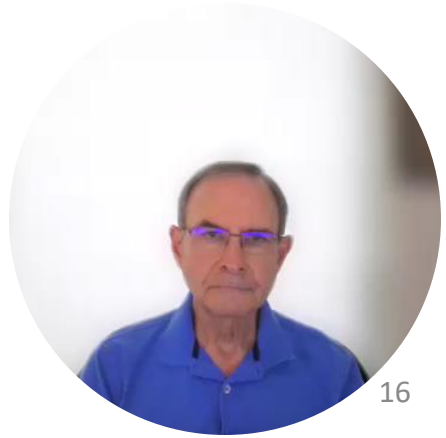
- Communicate more efficiently using M11 common terms and definitions and formats
- Reduce Information Requests to Sponsors
- Collaborate in real-time on protocol design points
- Perform collabor… if Scenario Analy… design, dosin… methods to o… protocol for gr…

Imagine a Future State…

- **Data driven Protocol opens in a protocol review tool**
  - Dashboard shows graphical display of study schematic, arms, epochs, visits.
  - A click, swipe or voice command takes you to the schedule of activities
  - Other protocol design features are clearly displayed, as well as metadata about the protocol.
  - Drill down ability to show more/less detail
  - Visually see the complete protocol document, as you want it / need it.

When the Protocol is Data Driven the Number of Views is Limitless





Thank You