



Sycamore
Informatics

SPA MDR CDR SCE

ET23

eProtocol and Promise of Automation

MAR 2025



The Clinical Data
Science Conference

US 2025

16–19 March

Renaissance Orlando at SeaWorld Florida



Agenda

- Why Are We Here?
- Challenges with the Current State of the Clinical Protocol
- Where Do We Go From Here?
- eProtocol: A New Paradigm
- Putting it All Together: End-to-End
- Q & A



Since 2000, Have We *Fundamentally* Changed Clinical Study Reporting?

- Invested significant amount of time, money, and effort in industry standards (e.g., CDISC) and new technologies (e.g., Cloud Computing)
- We've gained significant efficiencies optimizing the clinical trial data capture, analysis, and reporting processes
- But has it *really* changed?

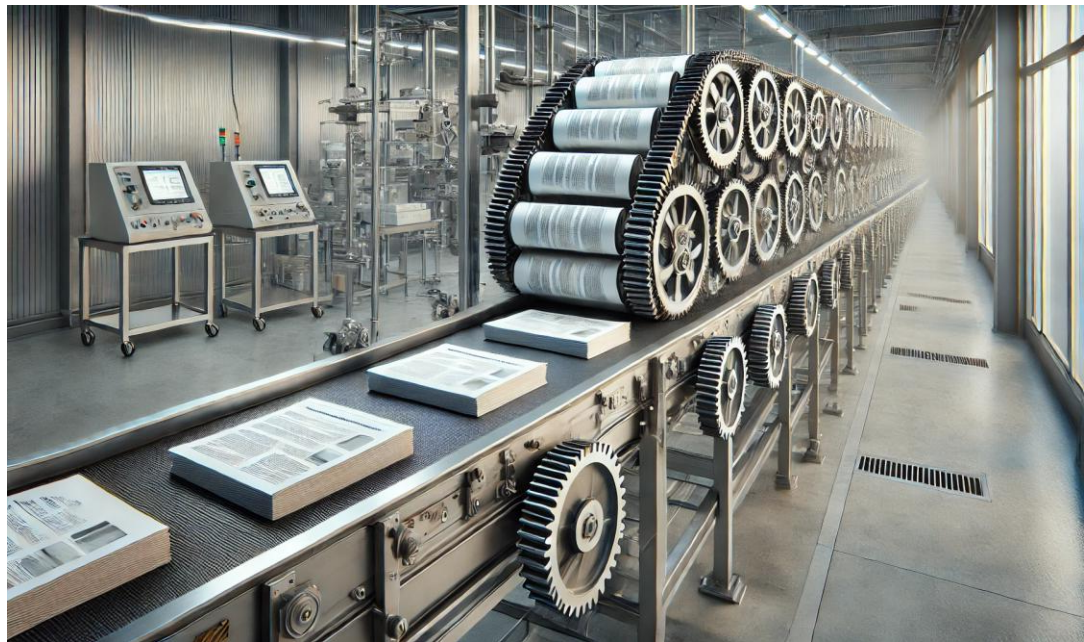


Image generated using AI (DALL·E, OpenAI)

Inflection Point for Industry Transformation

The Machine-Actionable Protocol

Protocol: “source of truth” & initiatives like Digital Data Flow further drive standardization and interoperability

Resource-Constrained Industry

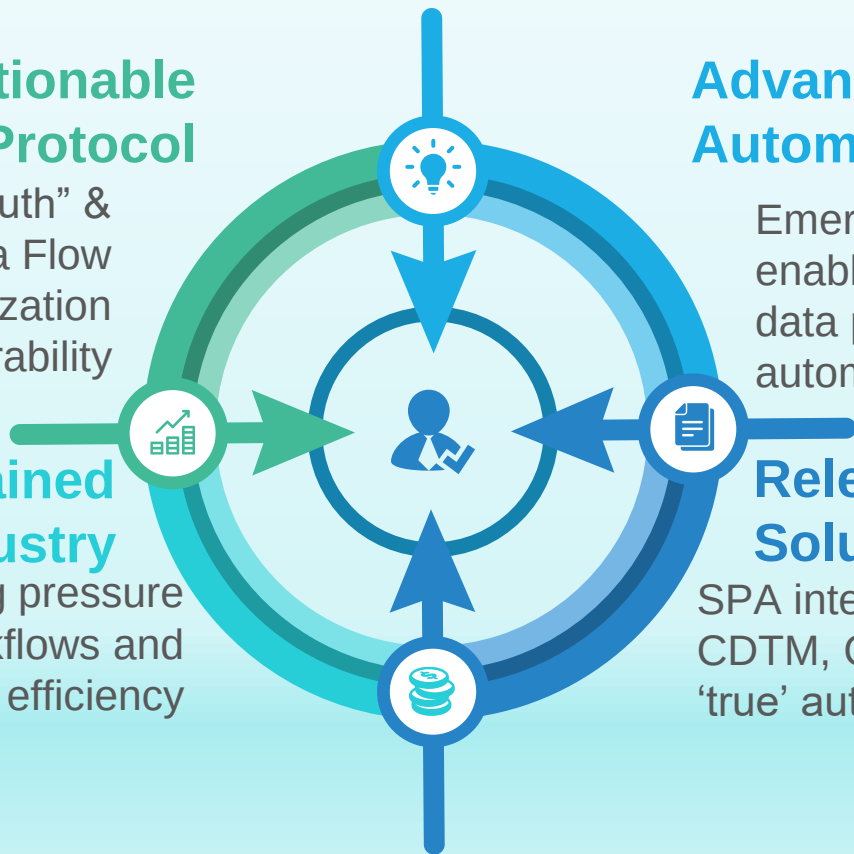
Organizations are facing pressure to streamline workflows and maximize efficiency

Advancements in AI & Automation

Emerging technologies now enable scalable, intelligent data processing and automation

Release of SPA Solutions

SPA integration with MDR, EDC, CDTM, CDR, SCE, etc. enables ‘true’ automation



What is a Clinical Protocol?

- A comprehensive plan that describes all aspects of a trial
- A blueprint how it will be conducted, ensuring patient safety and data integrity
- Key components include Synopsis, Background/Rationale, Objectives, Study Design, Eligibility Criteria, Treatment Plan, Schedule of Assessments, Safety Monitoring Plan, Statistical Analysis Plan
- The protocol is foundational and referenced by investigators, clinical operations, data managers, and regulators throughout the trial

It includes:



Study Objectives



Patient Population;
Inclusion &
Exclusions



Study Design,
Treatment Arms,
Randomization, etc.



Schedule of Activities



Statistical Considerations



Traditional Protocol Development Processes

- **Document-Centric Process:** Static protocols (Word, PDF) require manual data transcription, causing errors and inconsistencies
- **Fragmented Workflows:** Teams work in silos, causing duplication and version control issues
- **Inefficient Cycle Times:** Protocol development and approvals take months, delaying trials
- **Downstream Impacts:** Manual setup of CRFs and databases can lead to mismatches, errors, & rework



Current State: An example of clinical study Schedule of Activities (SoA)

- Read, interpret, & manually input information into various systems and deliverables
- AI models can accelerate this process; approach and constraints remain unchanged
- **Bottomline:** it is not machine-actionable. It remains locked within a doc – it is disjointed & siloed. Lacks relationships nor does it drive or influence downstream processes

	Vaccination Period						
	Clinic Visit	Phone Call	Clinic Visit	Phone Call	Clinic Visit		Clinic Visit
Clinic Visit Number	1 ^a	-	2	-	3	4	5
Visit Window (days)	n/a	-0/+0	-3/+7	-0/+0	-3/+3	-3/+7	-7/+7
Trial Day	1	2	29	30	43	57	120
Vaccination Day (Reference for post-vaccination time points)	-	1	1	29	29+14	29+28	29+91
Visit Week (Wk) / Month (M)			Wk 4		Wk 6	Wk 8	M 4
Signed informed consent	X						
Inclusion/exclusion criteria	X						
Demographics	X						
Smoking information	X						
Medical history	X						
Medication/vaccination history ^b	X						
Pregnancy test ^c	X		X				
Trial Vaccination							
Review criteria for delay or cancellation of trial vaccination ^d	X		X				

a. Procedures to establish subject eligibility may be performed within 21 days prior to trial vaccine administration, unless otherwise indicated. If all information to establish eligibility is available, these procedures can be done on the same day as trial vaccine administration. Eligibility criteria should be reviewed and confirmed prior to trial vaccine administration.

b. Medication/vaccination history taken within 6 months prior to enrollment should be recorded to establish eligibility.

c. A urine pregnancy test will be performed before each trial vaccination on Day 1 and Day 29 for women of childbearing potential. Where required by local laws and regulations, the pregnancy test will be performed in blood (3 mL).

d. See Section 6.3 and Section 8.1 for an overview of the criteria leading to delay or cancellation of vaccine administration. In case of delay, the vaccination should take place within the allowed time windows, if feasible. The reasons for delay or cancellation should be documented in the subject chart.

e. Physical examination and vital signs must be performed/measured by a qualified healthcare professional. See Section 9.3.6 for an overview of the required assessments.

From: https://www.curevac.com/wp-content/uploads/2021/06/HERALD_CV-NCOV-004-Protocol.pdf



Current State: An example of clinical analysis and reporting (TFLs)

- Similar to SoAs: generation of the programs to process, analyze and report the clinical trial, the protocol must be read, interpreted, and implemented in code

Definition of Virologically-Confirmed COVID-19 Case for Primary Efficacy Analysis:

For the primary analysis of efficacy, the case must meet the following criteria:

- Must be a virologically-confirmed case of COVID-19 defined as a positive SARS-CoV-2 specific RT-PCR test in a person with clinically symptomatic COVID-19 as described above.
- Symptom onset must have occurred ≥ 15 days following the second trial vaccination.
- The subject must not have a history of virologically-confirmed COVID-19 illness at enrollment or have developed a case of virologically-confirmed COVID-19 before 15 days following the second trial vaccination.
- The subject must have been SARS-CoV-2 naïve at baseline and Day 43 (defined as seronegative to N protein in the blood samples collected at baseline and Day 43).

(Primary efficacy cases must be confirmed by the Adjudication Committee.)

From: https://www.curevac.com/wp-content/uploads/2021/06/HERALD_CV-NCOV-004-Protocol.pdf



Clinical Trials: Challenges and Automation

- Inefficiencies lead to delays & errors; protocol amendments delay over 57%
- Manual workflows create bottlenecks, key trial setup tasks require re-entering protocol data into multiple systems
- eProtocol is a digital approach that captures and stores content into machine-readable & actionable data
- eProtocol enables automation, faster study start-up, fewer errors, and reusability of protocol data



The Need for Protocol Automation and Standardization

Current clinical trial processes cannot keep up with increasingly complex trials

Automation addresses this by making protocols machine-readable datasets

This eliminates manual data re-entry, saving time and reducing errors

Standardized data is essential for effective automation

Industry groups are pushing for common protocol templates and data models

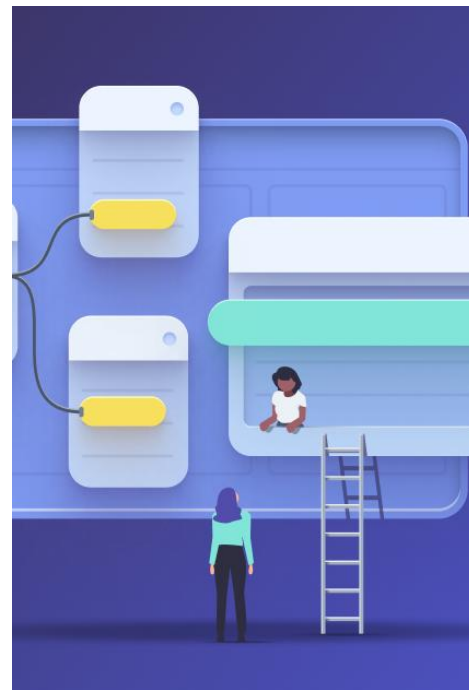
Standardization reduces ambiguity and speeds up regulatory review

It also enables cross-trial reuse and data sharing



Benefits of Structured Protocols

- Unified Study Definition Model (USDM): Standardizes each element (e.g., objective, inclusion criteria, study design and activities)
- Stored in a central repository, reused, and enforced across studies to ensure completeness, internal consistency, and easier updates
- Improves data integrity and supports advanced tools like automated consistency checks and AI.
- Regulators are encouraging structured, electronic protocol formats

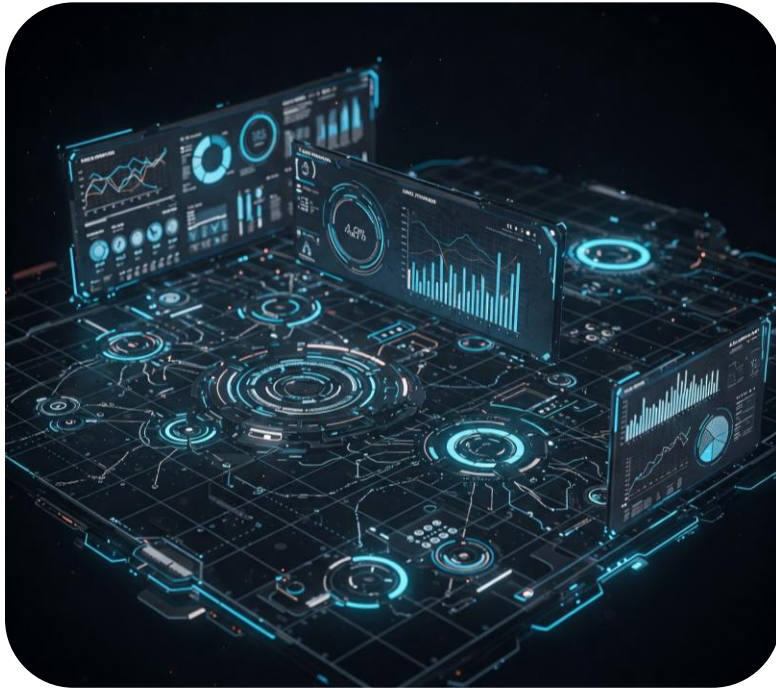


eProtocol: A New Paradigm

- **eProtocol:** Digital, structured, interoperable clinical trial protocol
- **Core Functionalities:** Structured authoring, version control, rules engine, MDR integration
- **Export Formats:** Human-readable (PDF) and machine-readable (XML/JSON)
- **Interoperability:** Connects via APIs to EDC, CTMS, IRB submission portals
- **Impact:** Faster study startup, reduced errors, improved protocol quality, regulatory compliance



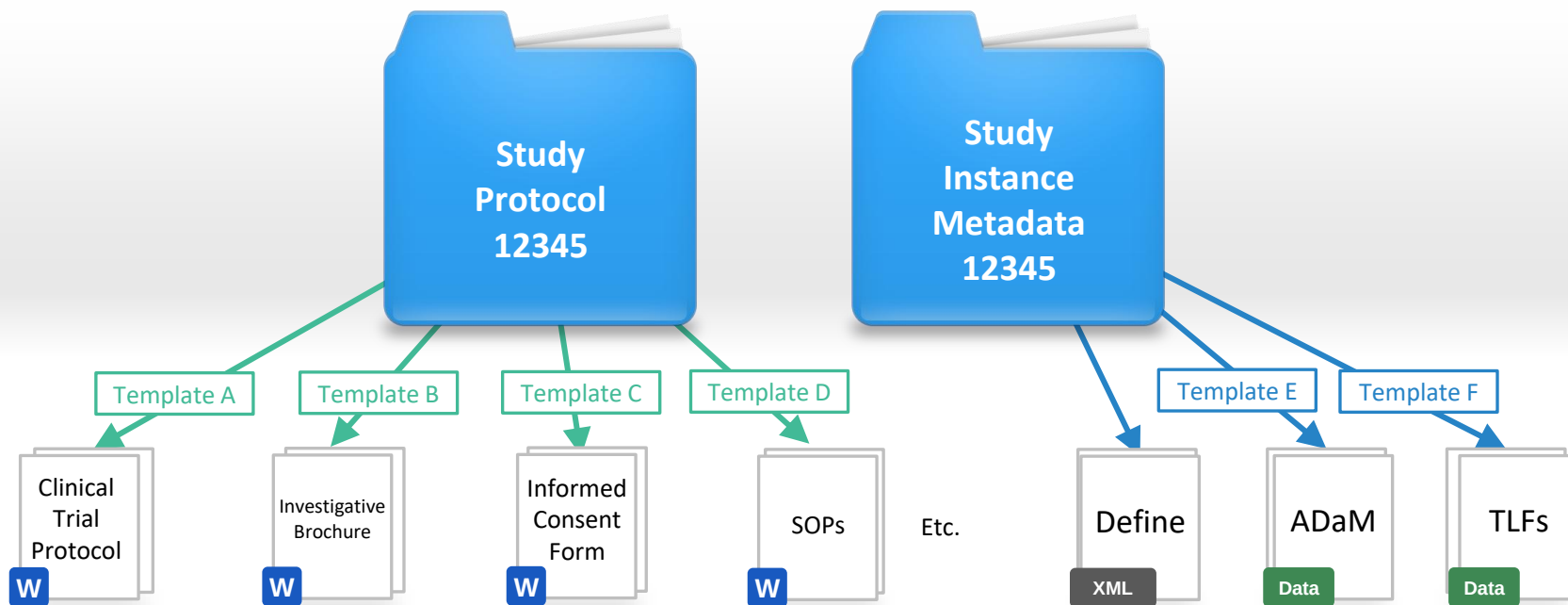
Structured Protocol Authoring (SPA)



- Structured Protocol Authoring (SPA) uses predefined structures (USDM) and fields for protocol creation
- SPA enhances standardization, compliance, and content reuse
- SPA tools include validation rules to catch errors early
- Streamlines collaboration and allows multiple contributors to work in parallel
- Enhances compliance and traceability



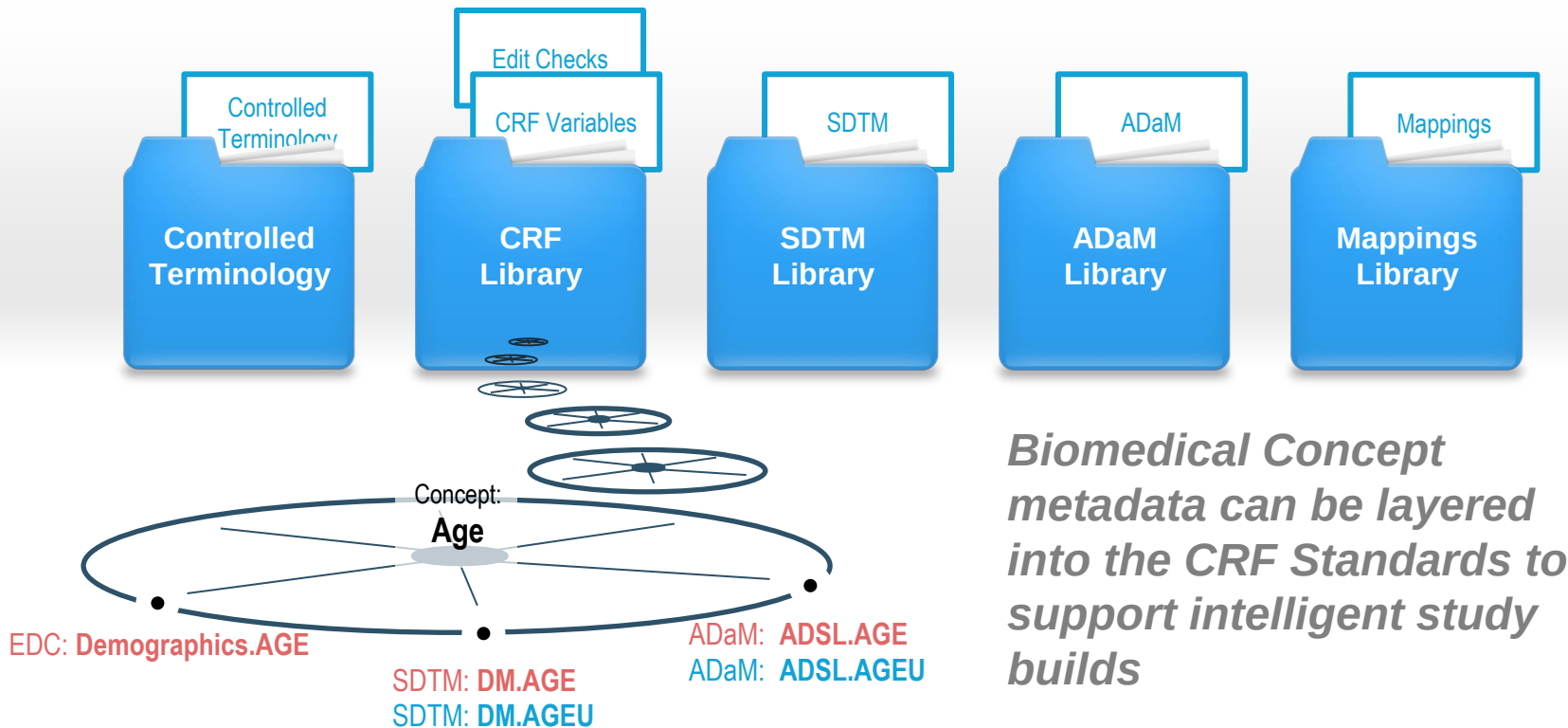
Production of Clinical Deliverables



Standards as the Foundation: Clinical Content & Reuse (CC&R) Initiative, formerly known as Common Protocol Template (CPT)



MDR: Clinical Data Standards and Bio-Medical Concepts

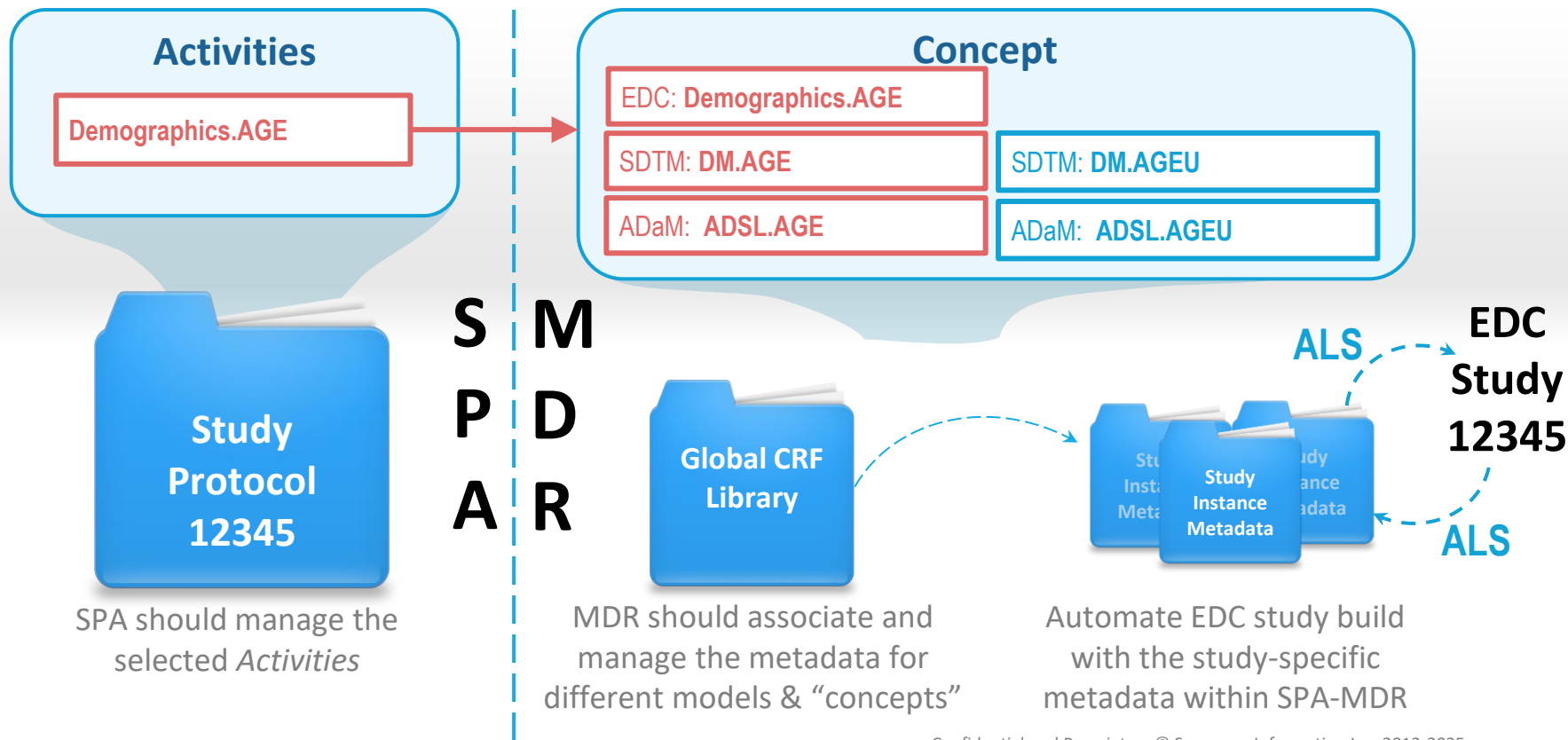


Biomedical Concept metadata can be layered into the CRF Standards to support intelligent study builds



Leveraging MDR's Bio-Medical Concepts in SPA

Establish Linkage between SPA & EDC Builds



Must-Have Features of a Structured Protocol Authoring (SPA) System



Standards-Driven, Structured Protocol Development

- Enforce consistency, reusability, and alignment with industry standards (CDISC, TransCelerate, NIH-FDA Templates)



Machine-Readable, Structured Content

- Protocol information in a digital format to eliminate redundancy and improve downstream integration



MDR Integration

- Ensure compliance with standards & maintain data integrity



Integration with Downstream Clinical Systems

- Automation & establish linkage across EDC, CTMS, CRF builds, etc.



Document Generation Capable

- Provide Clinical Development Plans (CDPs) and Study Protocols in Word, PDF, etc. and in with Medical Writing tools



Must-Have Features of a Structured Protocol Authoring (SPA) System, Continued



Protocol Benchmarking & Reuse

- Enable comparison and best practices for improved study design



Real-Time Collaboration & Review Workflow

- Support multiple stakeholders (medical writers, clinical teams, regulatory reviewers) with structured review and approval processes



Audit Trails, Version Control, & Role-Based Access

- Track changes, maintain document traceability, and ensures controlled access for security and compliance



Operational Planning and Budgeting

- Tool to determine Patient and Site Burden, Cost

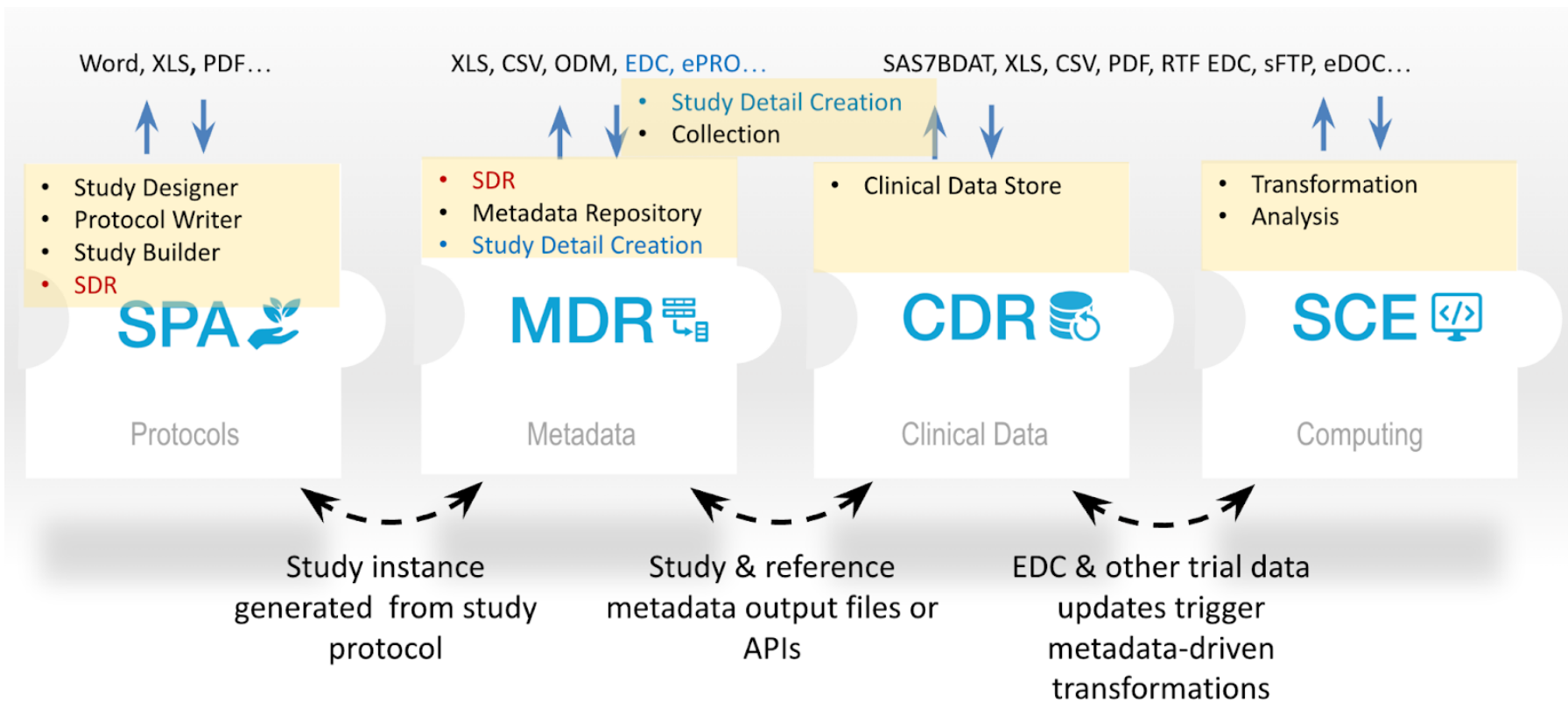


User-Friendly Interface & Enhanced Usability

- Provide an intuitive, efficient platform for protocol authoring, collaboration, and regulatory submission



End-to-End Facilitation of Processes is within Reach Today (SPA, MDR, CDR & SCE)



Wrap-up

- The clinical trial industry can no longer afford to rely on document-heavy workflows
- ***eProtocol is the future:*** a fully digital, structured, and automated approach that integrates with clinical trial execution systems
- Implementing Structured Protocol Authoring, Metadata Repository, and Digital Data Flow, we can:
 - Reduce protocol timelines (e.g., automate study builds)
 - Eliminate inefficiencies (e.g., redundant data entry)
 - Ensure synchronization of protocol data across clinical trial systems
- Adoption of eProtocol is a strategic necessity. As the industry moves toward a digital-first clinical trial ecosystem, organizations that fail to modernize will face increasing inefficiencies, rising costs, and delays in bringing new therapies to market
- Now is the time to embrace structured protocol automation and unlock the full potential of eProtocol-driven clinical research

Q & A



Bill Qubeck

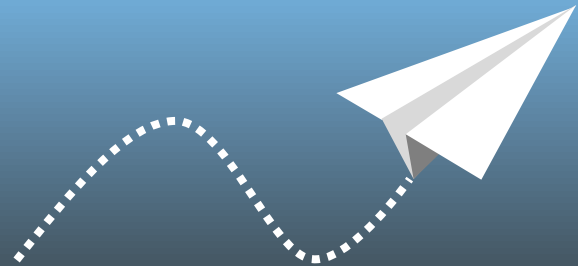


Suhas Giriraj



Thank You

<https://www.sycamoreinformatics.com>



Bill Qubeck

Bill.Qubeck@SycamoreInformatics.com
<https://www.linkedin.com/in/williamqubeck/>

Suhas Giriraj

Suhas.Giriraj@SycamoreInformatics.com
<https://www.linkedin.com/in/suhasgiriraj/>