Setting the
Global Standard
for Clinical Data

PhUSE

Heidelberg, Germany – 12 October 05

The Future of CDISC

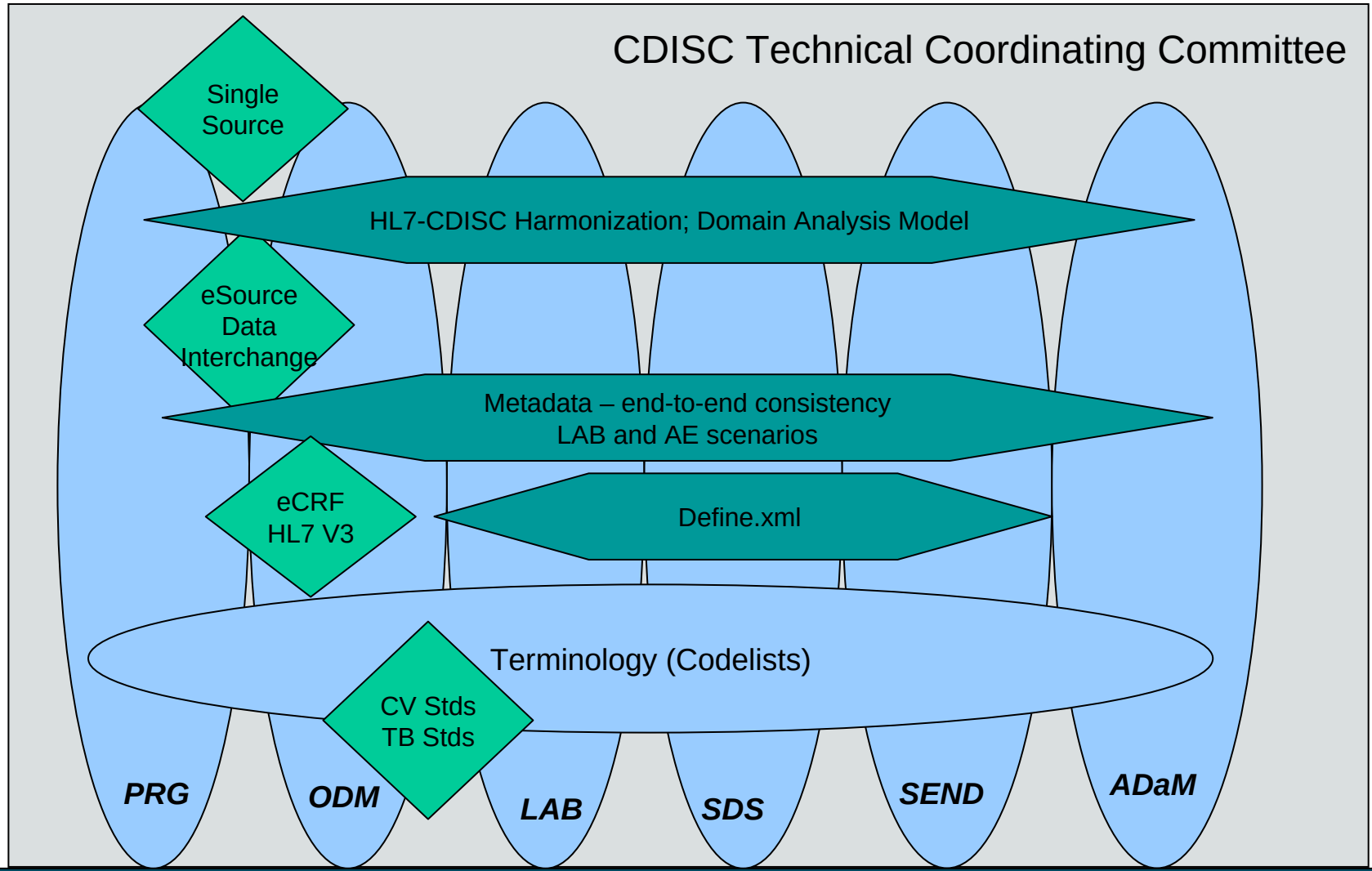
CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

Rebecca D. Kush, PhD
Founder and President, CDISC

The Future of CDISC

- The Remainder of 2005 (Q4)
- The CDISC Technical Roadmap (2006-08)
- Strategic Plans for the CDISC Future

CDISC Teams and Projects - 2005



OPS: Maintenance, Member Relations, Education and Implementation Groups, Glossary

Team; X-team Projects	Standard	Implementation Version Release Date
SDTM, SEND	Ready for regulatory submission of CRT 4,000 downloads as of mid-2005	2004*
ODM	CDISC Transport Standard for acquisition, exchange, submission (define.xml) and archive	2001
LAB	Content standard – available for transfer of clinical lab data to sponsors	2002
ADaM	General Considerations document and examples of datasets for submission	2004
Protocol Representation	Collaborative effort to develop machine-readable standard protocol with data layer	In progress
Terminology Codelists	Developing standard terminology to support all CDISC standards	In progress
Define.xml	Case Report Tabulation Data Definition Specification	2005*
Metadata End-to-end	(Harmonization activity among standards) – CDISC Roadmap	In progress

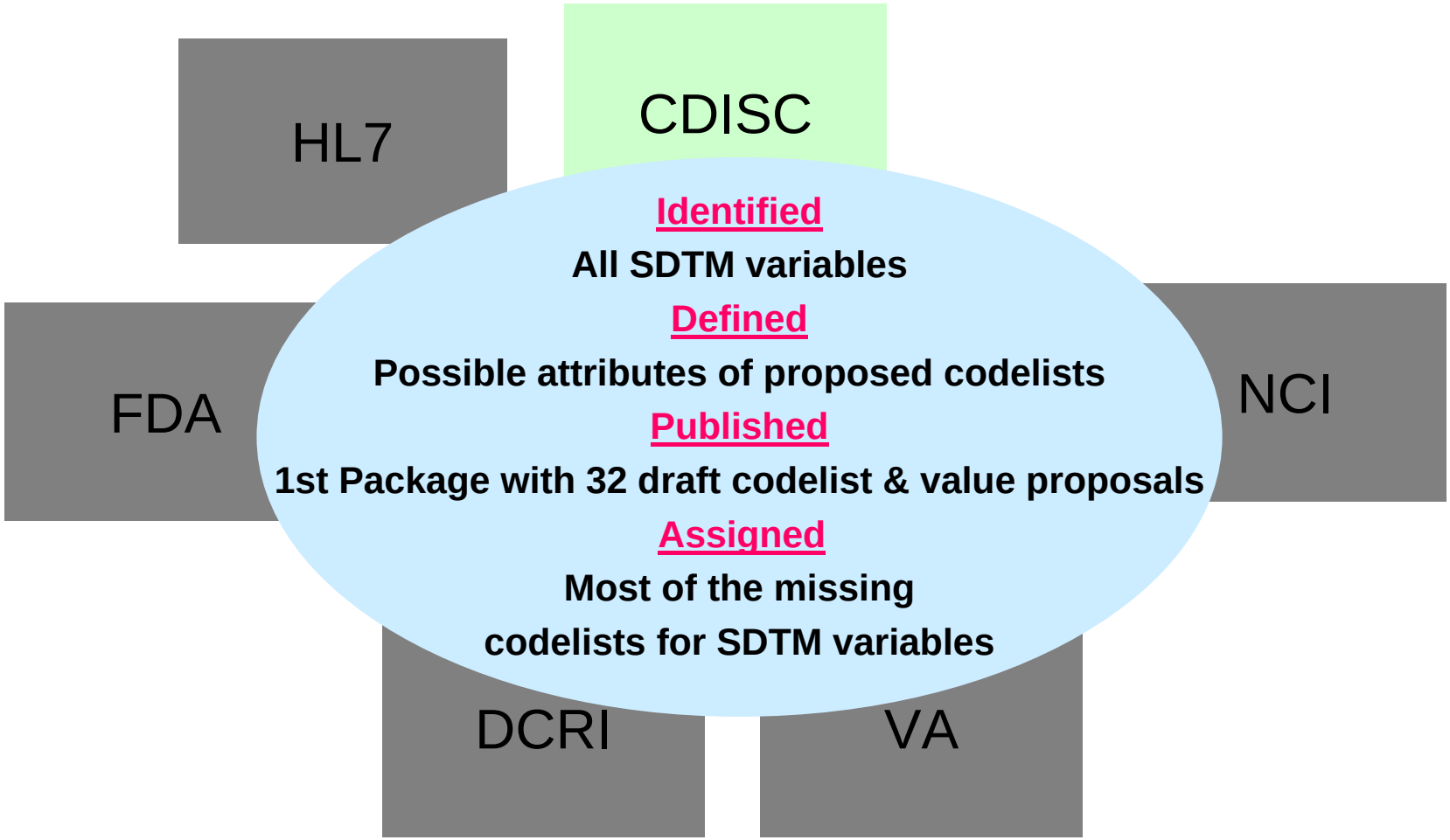
* Specification on FDA Guidance

Q4 CDISC Team Goals

- SDTM
  - SDTM IG 3.1.1 final released Sept 05; support implementations of SDTM
- SEND
  - Pilots for reproductive toxicity data in progress; likely to be released as separate IG
  - Working with SDS on PK domains
- ODM
  - Version 1.3 to be released by December 2005
  - Collaborating with NCI on HL7 Message for eData Collection Instrument (e.g. eCRF)
- ADaM
  - Completing analysis dataset examples
  - Collaborating with SDTM on SDTM-ADaM Pilot
- LAB
  - 1.1.0 update in progress (due Q4)
  - SDS Lab TESTCD names to be released Q4.

Terminology (Vocabulary)

A pillar of interoperability



NIH Grants

- NIH Roadmap contract: BAA-RM-04-23

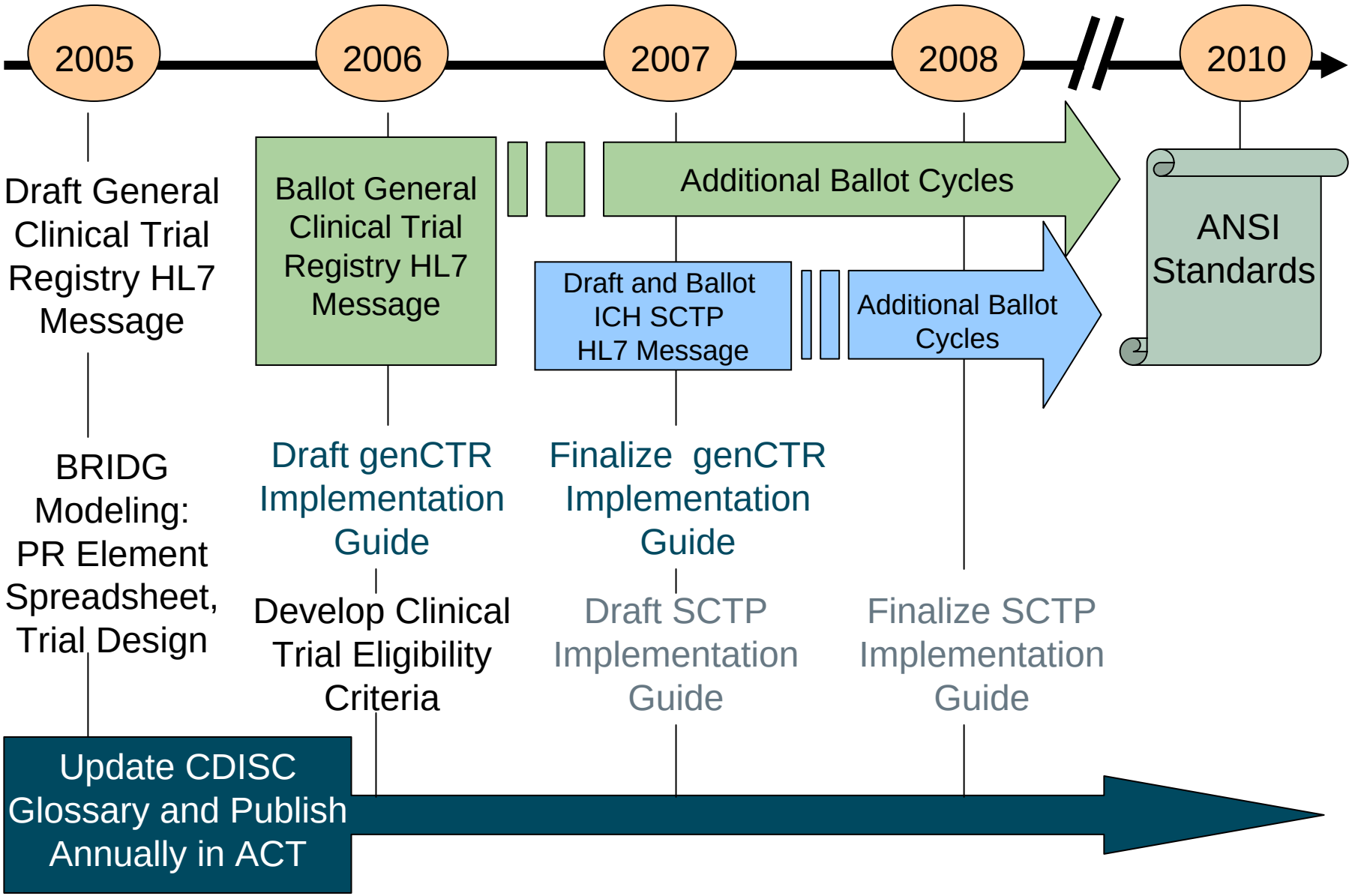
Re-engineering the Clinical Research Enterprise: Feasibility of Integrating and Expanding Clinical Research Networks

- Recognition that **therapeutic area standards (Cardiovascular and Tuberculosis)** development needs to be done in a public forum, formalized development process and broad participation from experts and stakeholders representing a variety of domains
- Focus on contributing to the public domain, not an specific implementation effort.

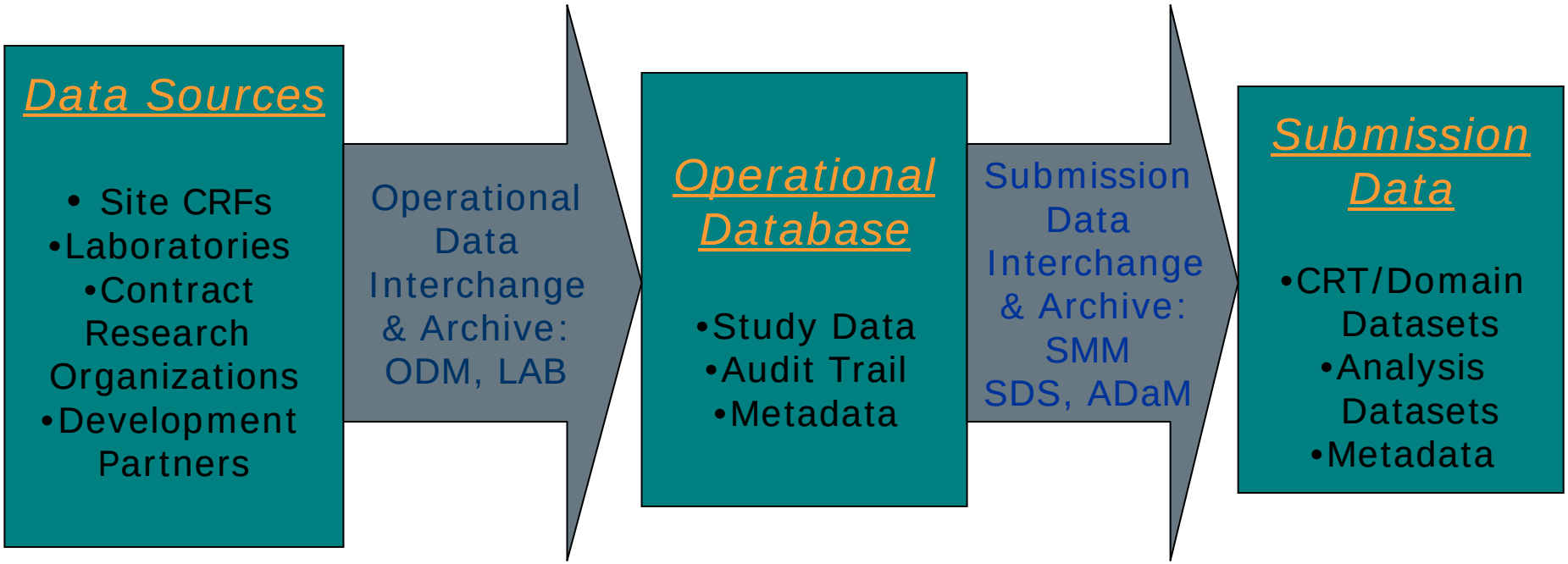
Protocol “Use Case” Priorities

1. To support CDISC **Study Data Tabulation Model (SDTM) V3.1**
   - Trial Design -Planned Assessments
   - Planned Interventions -Inclusion/Exclusion criteria
   - Statistical Analysis Plan
2. To **support study tracking databases**, e.g. EudraCT, clinicaltrials.gov, the protocol/trial tracking aspect of trial registry or results databases, or databases that support project management tools.
3. To support the development of the clinical trial protocol **document**

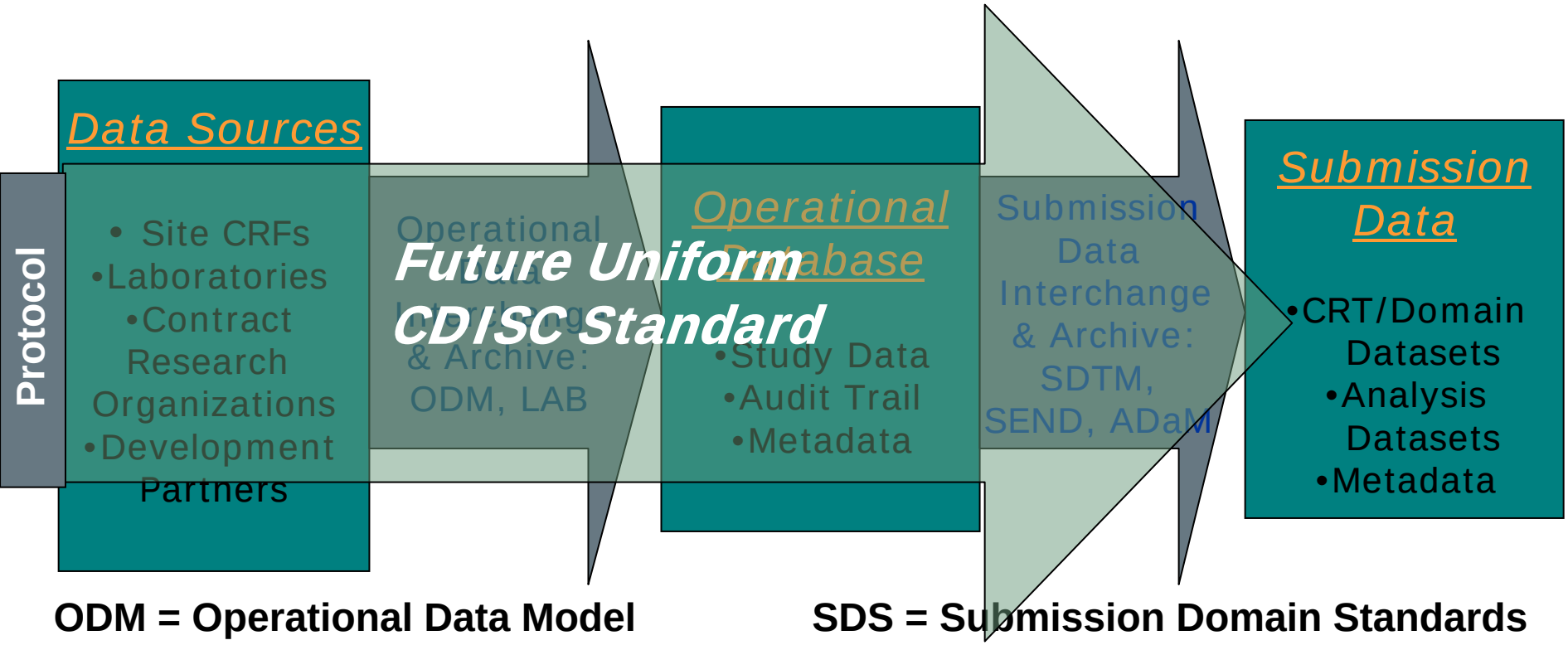
Protocol Representation Timeline



What's wrong with this picture?



Future of CDISC Models



ODM = Operational Data Model
LAB = Laboratory Data Model
SDS = Submission Domain Standards
ADaM = Analysis Dataset Models
SEND = Std. Exchg. Non-clinical Data

Standards Protocol Representation and Terminology

The CDISC Roadmap

- Purpose:
  - To provide a concise, common specification of all technical products to be developed by CDISC.
- Endpoint:
  - By 2008, there will be a **single CDISC standard** for the full life-cycle of a clinical trial or study from protocol representation through the capture of source data to submission and archive, comprising a set of fully integrated and consistent models which will form logically and organically from our current set.
- Success Criteria
  - **All submissions to the FDA** are being made using the CDISC standard;
  - The set of CDISC models in use across the **full life-cycle of clinical trials**; and
  - The CDISC standard being **globally adopted**.

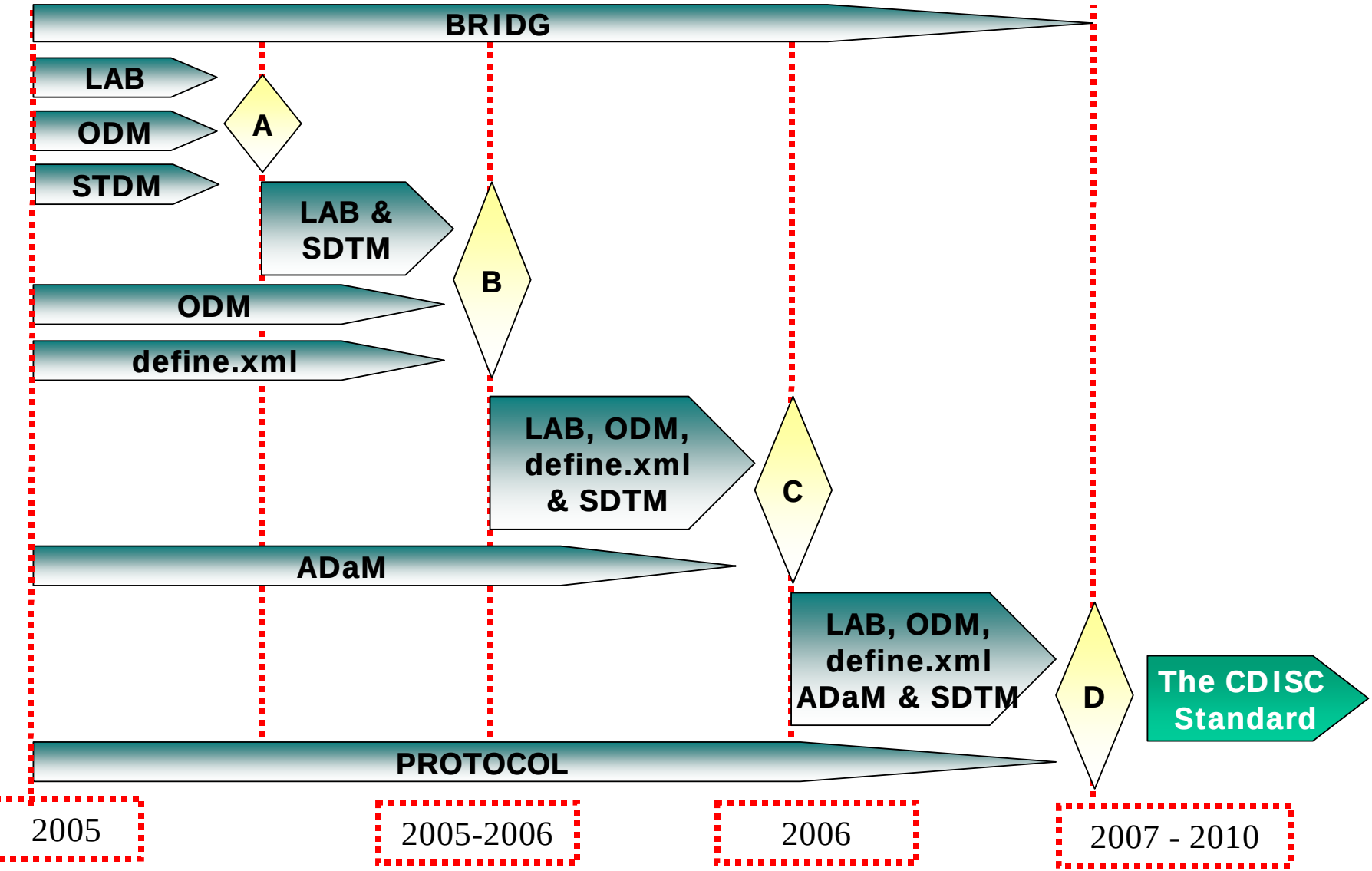
CDISC Roadmap - Guiding Principles

- Complete original mission, but focus on harmonization of CDISC models
- A single CDISC standard:
  - ODM XML defines format
    - Maintain Clinical Research scope while mapping to HL7
    - Remain platform-independent and platform-neutral
  - Define.xml describes common metadata
  - SDTM, LAB and AdaM define content
    - Standard ItemGroups and Items
    - Standard business rules and code lists
    - Metadata and information needed to support analysis

CDISC Roadmap – Guiding Principles

- Alignment with the BRIDG model
  - HL7 as portal to healthcare
- Leverage cross-functional teams
  - Fund projects not just teams, but assign teams as stewards and maintainers
  - Strive to achieve stability and maturity for current standards
- Prioritize processes over separate, individual models
- Support sites, sponsors and FDA as stakeholders.
- Expand Goals to include: Improving patient safety, process optimization, facilitating scientific and regulatory review.

CDISC Roadmap Timeline



Roadmap Destinations

- A = The final alignment of the LAB model with SDTM and ODM. At this point, Sponsors should be comfortable implementing all 3 of these models and understand how they work together.
- B = The ability to transport all CDISC submission data using the ODM transport mechanism and ensure consistency with the protocol representation standard. At this point, Sponsors should be comfortable submitting SDTM data in ODM format using Define.xml.
- C = The addition of the appropriate analysis datasets and analysis programs into the CDISC submission model and the alignment with the protocol representation standard and the statistical analysis plan. At this point, Sponsors will be able to submit both tabulation and analysis data as well as analysis programs in a standardized format using SDTM, AdaM, ODM and define.xml
- D = The final harmonisation of the models and the full protocol representation standard. At this point Sponsors will be able to define protocols that can be used to plan conduct and submit trials using the CDISC standard.

CDISC Models: The View Forward

- Keep models stable so industry can catch up
  - ODM, SDTM, LAB
- Support terminology team efforts to improve semantic interoperability
- More cross-team interactions focused on harmonization
  - More cross-team projects like Define.XML, Trial Design
- Complete End-2-End Traceability and SDTM/ADaM Projects
- Support the needs of existing users
  - Standard maintenance, support, implementation and evolution
  - Harmonmize, but maintain stable, backwards compatibility
- Support additional data uses based on CDISC standards
  - Integrated summary data, ECGs, Narratives, devices, etc . . . .
- Execute the roadmap
  - **All submissions to the FDA** use the CDISC standard;
  - CDISC models in use across the **full life-cycle of clinical trials**
  - The CDISC standard is **globally adopted**.

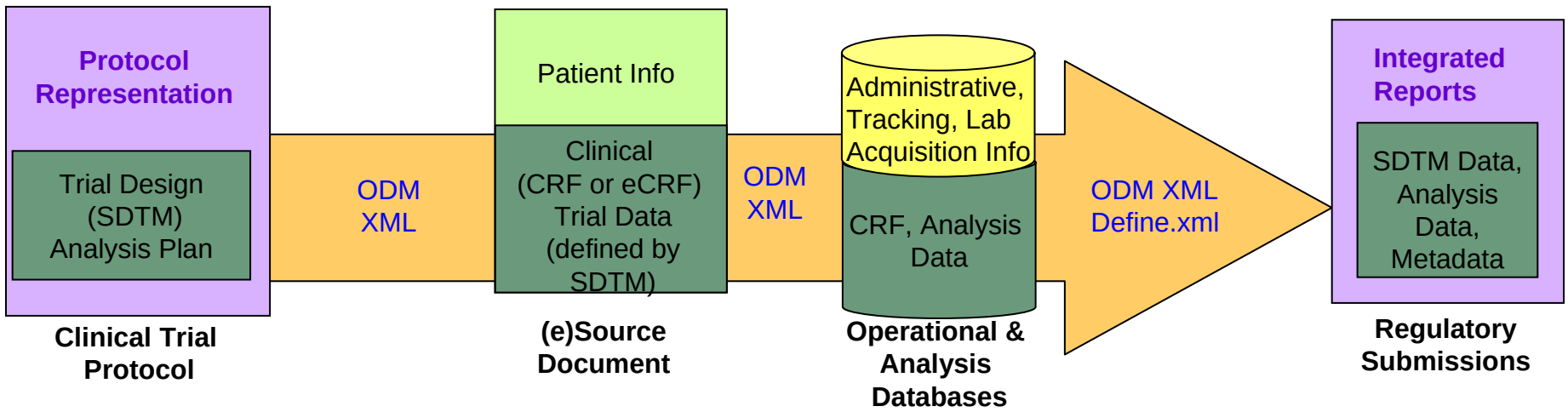
Data Flow Using THE CDISC Standard

= ODM (transport)

= SDTM and Analysis Data (content)

= Protocol information (content)

= Source data
(other than SDTM/CRF data)



Interchange Standards: Long-term Desired Outcomes

- A holistic approach to standards, facilitating data interchange from sites through regulatory submission, utilizing XML
- Standards for data acquisition supporting the population of a cross-trial warehouse within FDA
- HL7-CDISC models harmonized to yield value for both clinical research and healthcare – sharing of information between EMR and clinical trials
- Global adoption of CDISC data standards

CDISC Meeting with FDA Commissioner, April 2003

“Neither a wise man nor a brave man
lies down on the tracks of history to
wait for the train of the future
to run over him.”

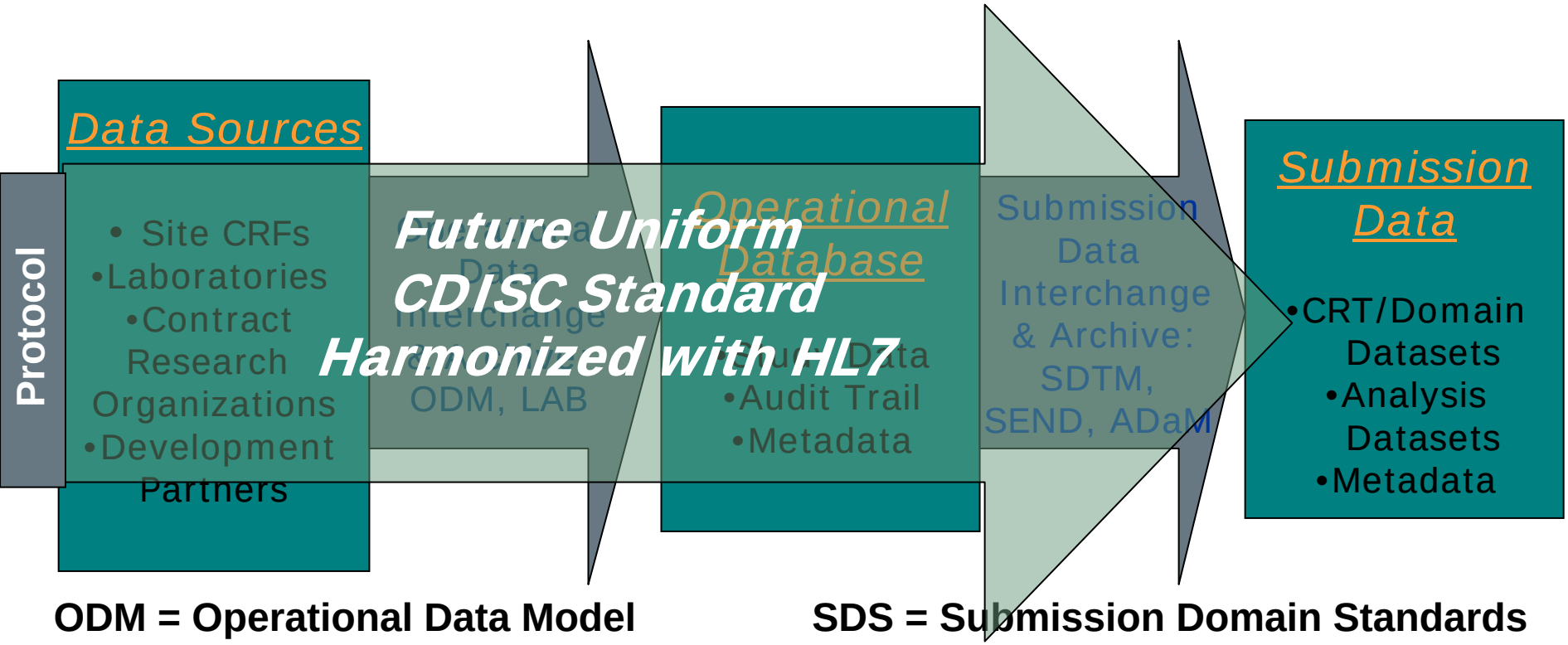
Dwight D. Eisenhower

The mission of CDISC is to develop and support global,

platform-independent data standards that enable information system interoperability

to improve medical research and related areas of healthcare.

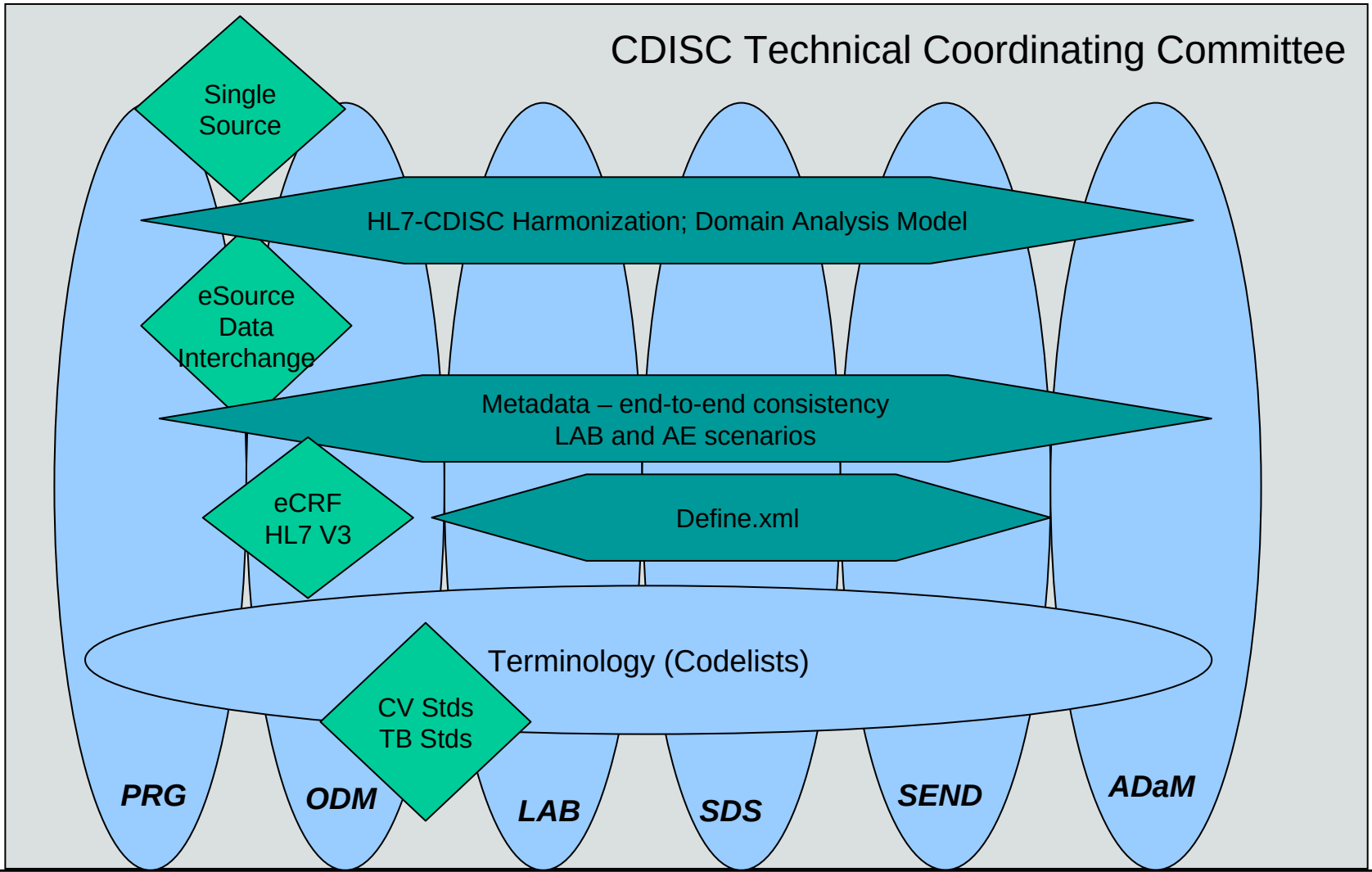
Future of CDISC Models



ODM = Operational Data Model
LAB = Laboratory Data Model
SDS = Submission Domain Standards
ADaM = Analysis Dataset Models
SEND = Std. Exchg. Non-clinical Data

Standards Protocol Representation and Terminology

CDISC Teams and Projects - 2005



OPS: Maintenance, Member Relations, Education and Implementation Groups, Glossary

CDISC Projects - 2005 Initiatives towards the Mission

Initiative/Project	Deliverable(s)	Status
HL7 Harmoniz	CDISC standards harmonized with the HL7 RIM	In progress
eCRF HL7 V3 (eDCI)	V3 RIM Message representing data collection instrument for clinical research (eDCI)	In progress
Single Source	Proof-of-concept project to demonstrate feasibility of collecting data once (eSource) for multiple purposes (healthcare and clinical research)	Proof-of-concept done; pilots in progress
eSource Data Interchange	Document to describe the value and benefits of CDISC standards (particularly ODM) to facilitate the use of technology for eSource data collection	Document posted for open review and comment
CV and TB Standards	Standards to facilitate interactions among sites and sponsors for specific therapeutic areas (NIH Roadmap grants)	In progress

Interchange vs Interoperability

Syntax → Structure

Semantics → Meaning

- Main Entry: **in·ter·op·er·a·bil·i·ty**
  : ability of a system ... to use the parts or equipment of another system
  Source: Merriam-Webster web site

- **interoperability**
  : ability of two or more systems or components to exchange information and to *predictably* use the information that has been exchanged.
  - Source: IEEE Standard Computer Dictionary: A Compilation of IEEE Standard Computer Glossaries, IEEE, 1990]

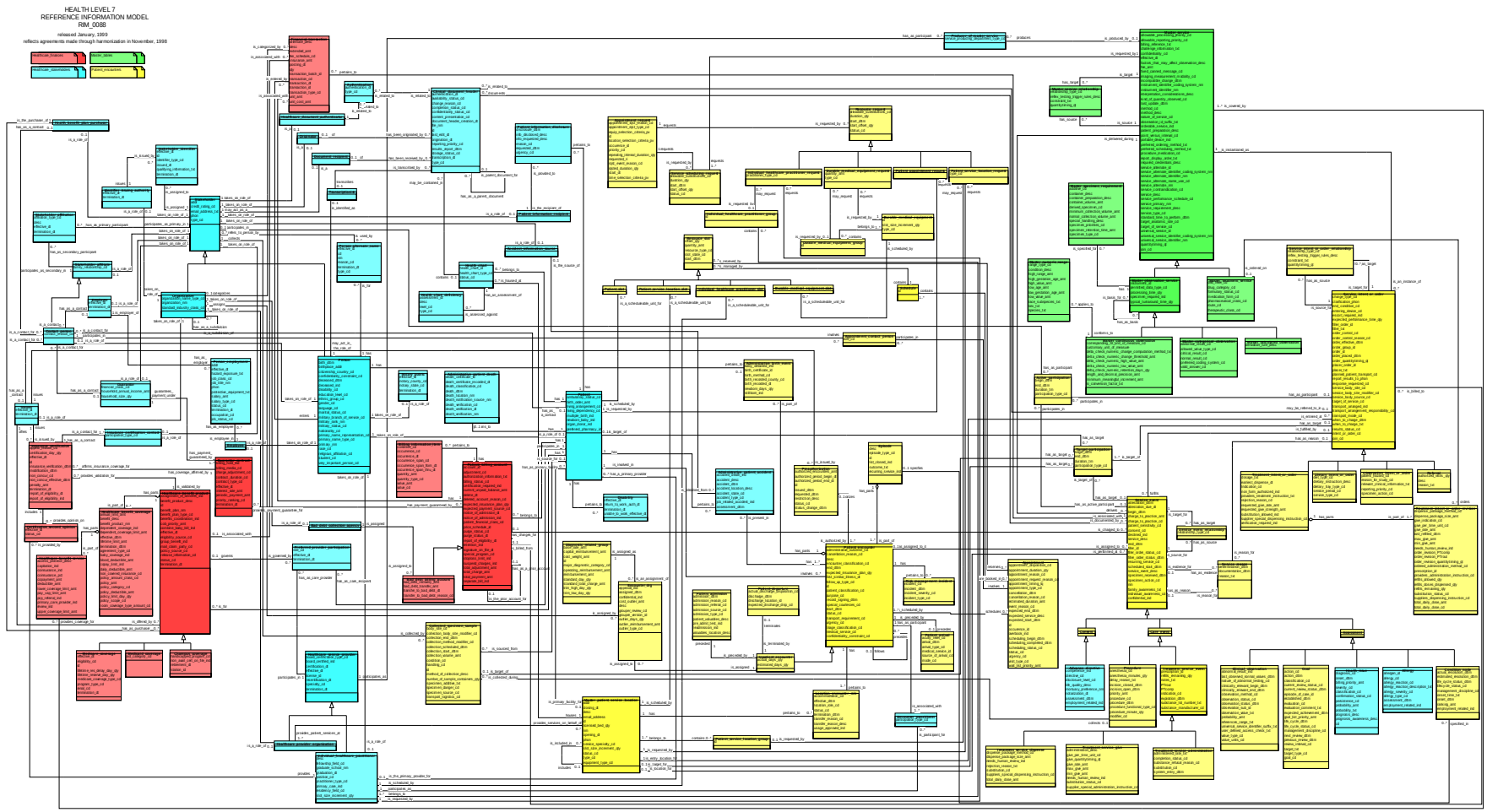
Syntactic interoperability

(interchange)

Semantic interoperability

Source: Charles Mead, MD, HL7

HL7 Reference Information Model (RIM)



The BRIDG Model

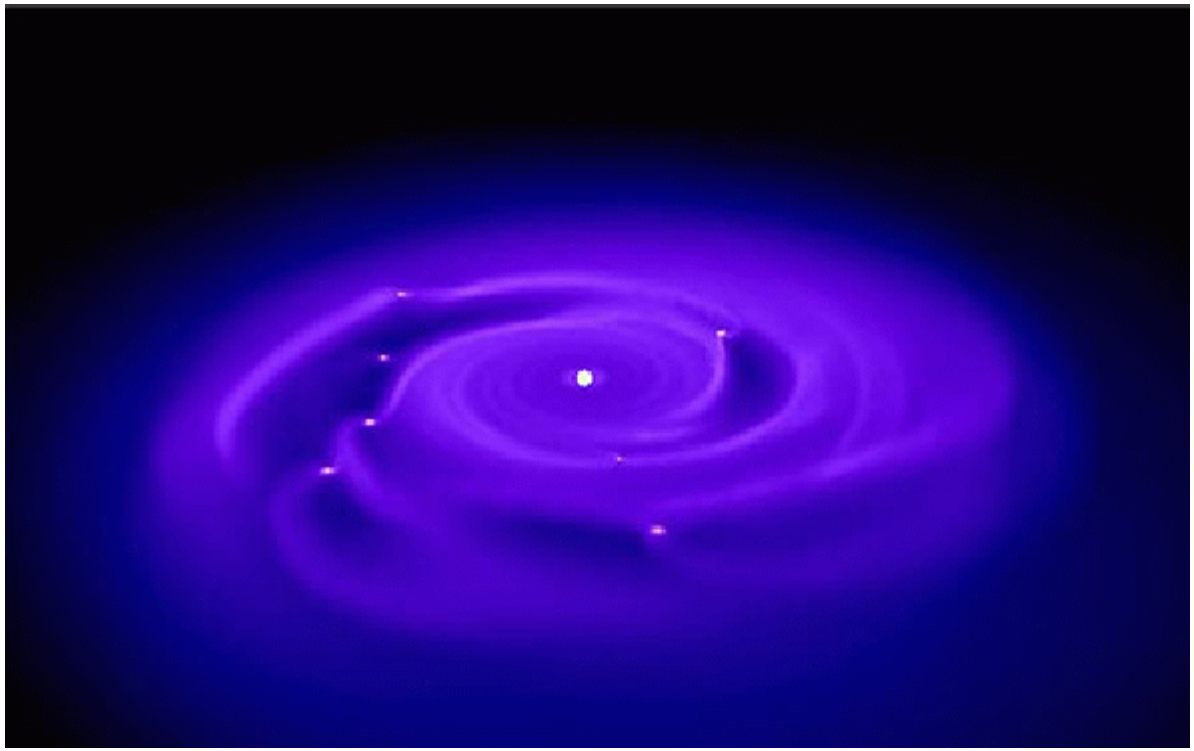
(a.k.a. PSM, DSAM, DAM)

- **Vision**: Create a domain analysis model for the clinical research domain to harmonize clinical research standards among each other and to harmonize standards between clinical research and healthcare

- **A Key Goal**: Define a structured computable protocol representation that supports the entire life-cycle of clinical trials protocol to achieve syntactic and semantic interoperability

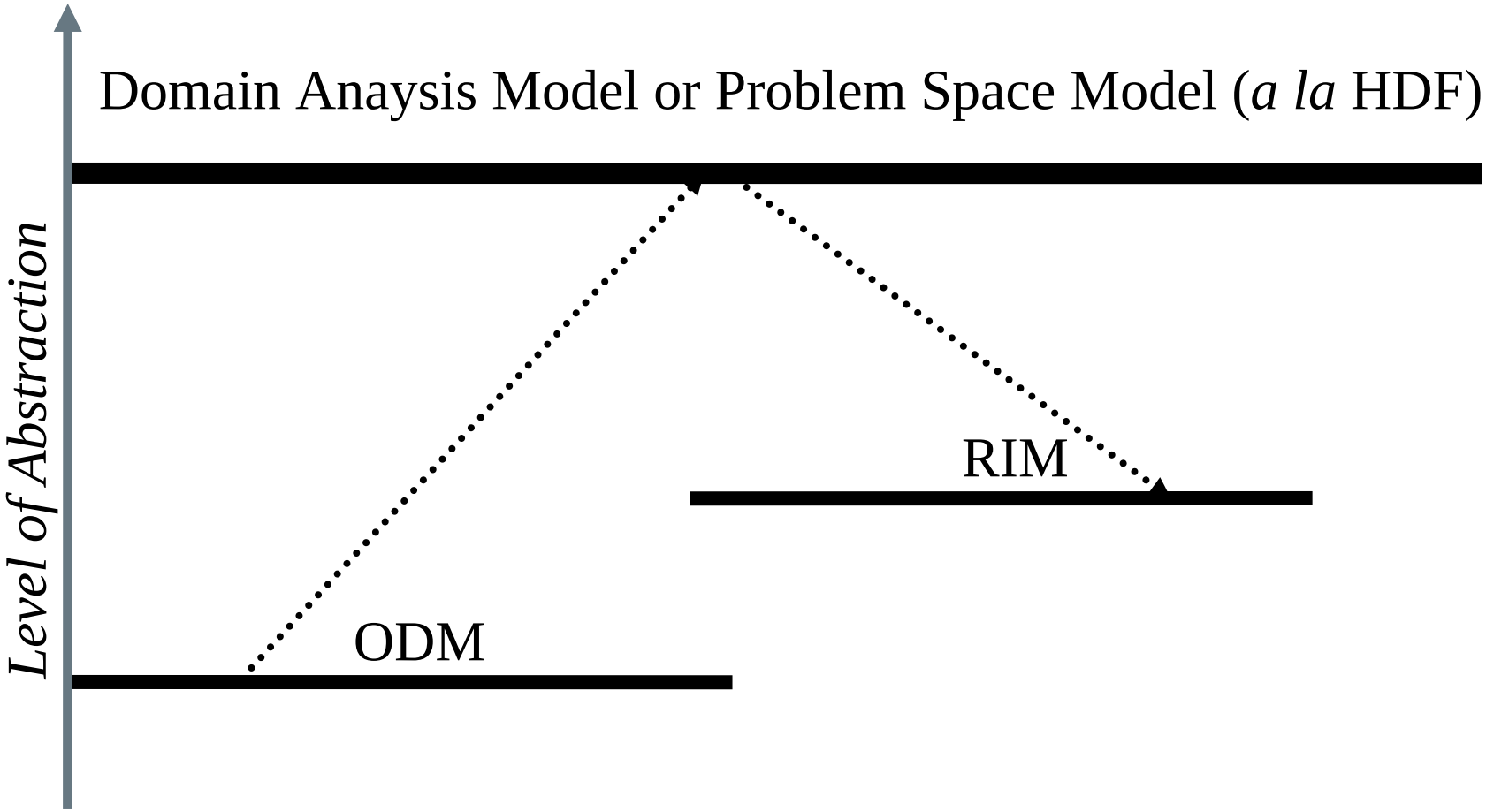
- **Milestones**:
  - January 2004 - **Initiated by CDISC Board**, with HL7 RIM expertise and leadership from Dr. Charlie Mead; followed HL7 Development Framework (HDF)
  - **Contributions of resources from NCI, HL7 RCRIM, FDA, CDISC, NIH and others** collaborated to create the Biomedical Research Integrated Domain Group (BRIDG) model
  - January 2005 – **Adopted by HL7 RCRIM** as Clinical Research Domain Analysis Model and posted on open source website
  - February 2005 – **CDISC ODM mapped to HL7 RIM** (collaborative effort among CDISC, NCI, HL7)

Mapping ODM to the RIM

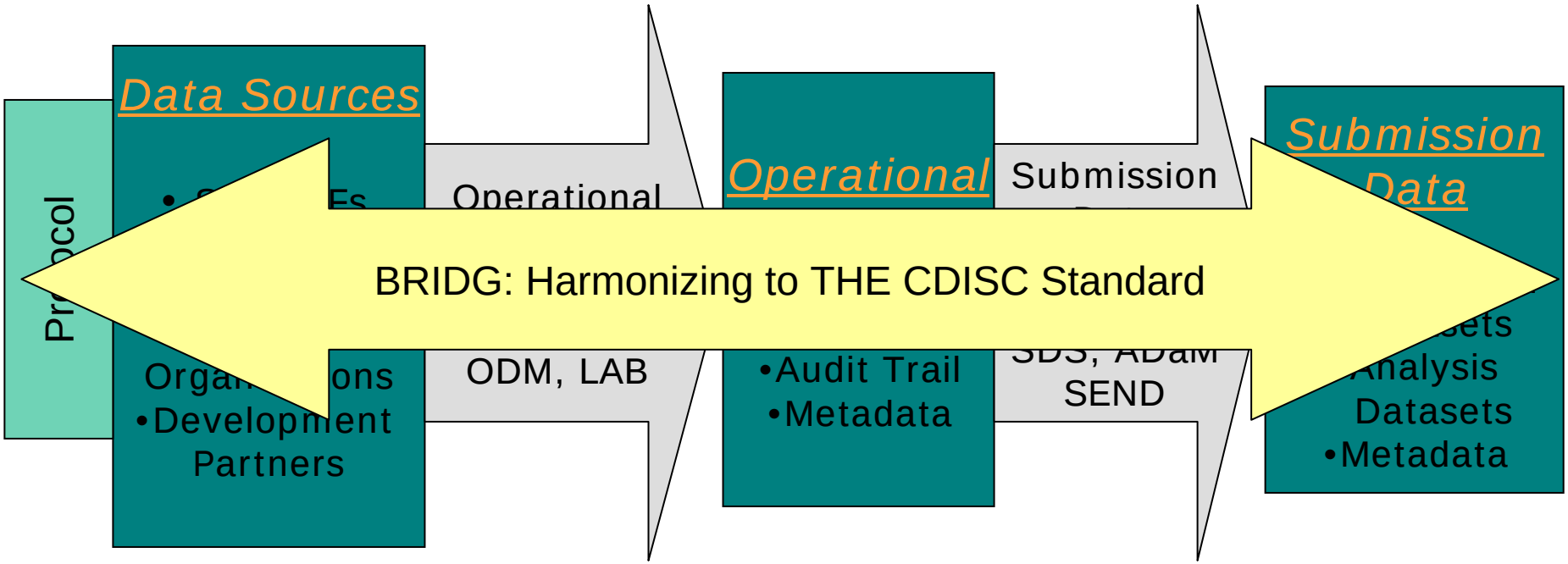


Sally Cassells, ODM Team Leader

CDISC and HL7:
Why BRIDG?

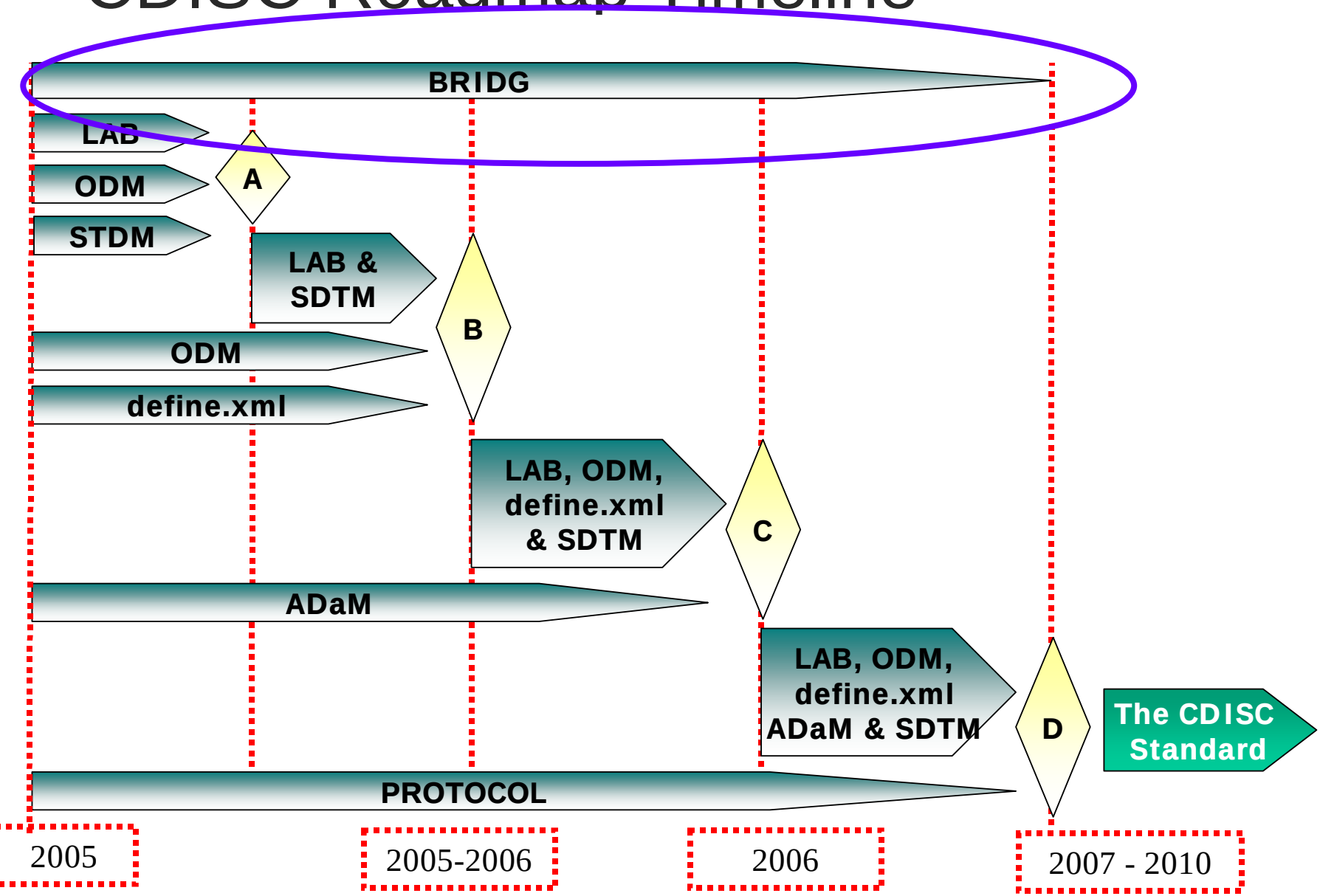


CDISC Standards Harmonization



ODM = Operational Data Model/Std
LAB = Laboratory Data Model/Std
SDS = Submission Domain Standards
ADaM = Analysis Data Models
SEND = Standards for the Exchange of Non-Clinical Data

CDISC Roadmap Timeline



Early BRIDG Implementations and Use Cases

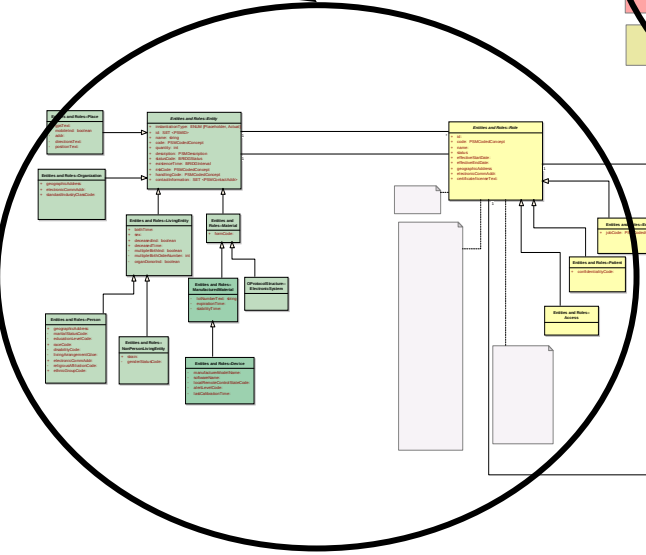
- NCI-CDISC: eData Collection Instrument (eDCI) Message Development
- CDISC-HL7 Protocol Representation Group: Trial Tracking and Registries
- NCI-CDISC: Clinical Trials Object Model (CTOM), a reference implementation of BRIDG to support collaborative research
- FDA-NCI: CRIX Clinical Data Repository based on Janus, populated with SDTM data, with data accessible via BRIDG
- caMATCH: Matching subjects to protocols – in implementation

Name: Comprehensive Logical Model
Author: Fridsma
Version: 1.0
Created: 7/22/2005 2:53:51 PM
Updated: 7/29/2005 2:33:32 PM

Clinical Trial Design

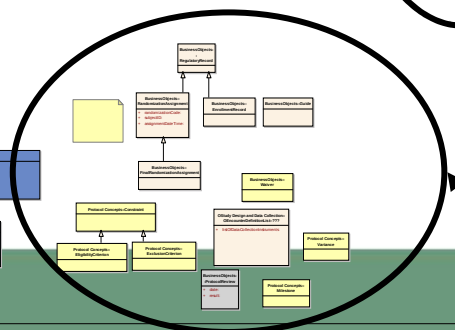
Protocol Authoring and Documentation

Clinical Trial Registration

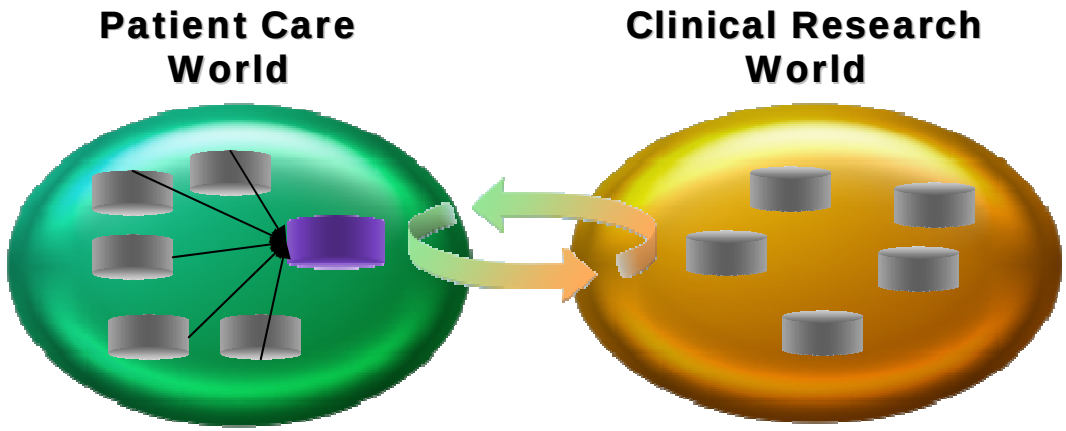


Protocol activities and Safety monitoring (AE)

Eligibility Determination



Structured Statistical Analysis



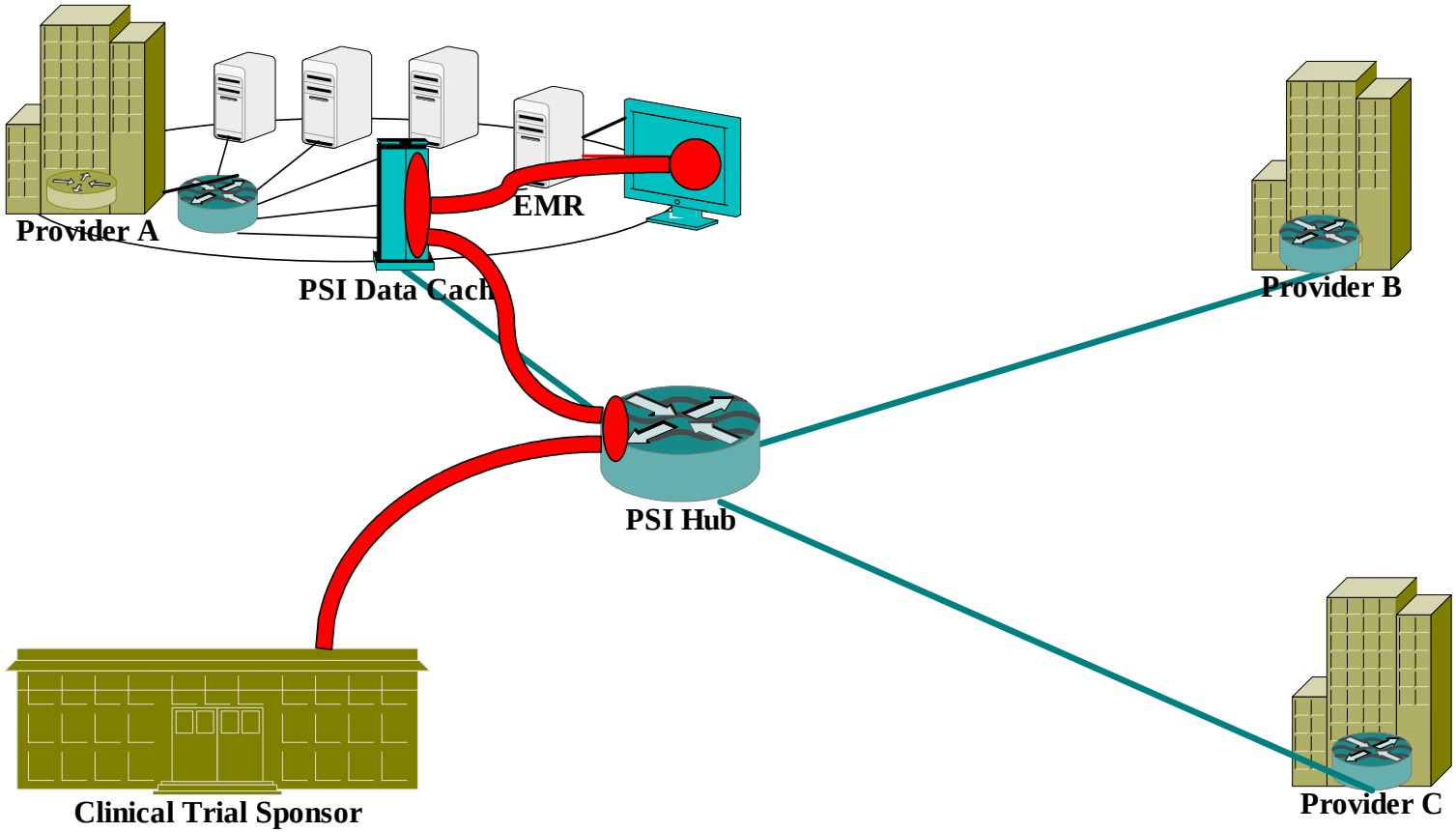
An industry initiative that has successfully demonstrated clinical information interoperability between physician clinical systems and pharmaceutical clinical trials systems based on open standards.

Data are collected once and subsequently rendered into multiple formats/systems using CDISC and HL7 standards – streamlines workflow.

Single Source creates one "source record" for medical data collection regardless of purpose (patient care or research).

Single Source opens the door for semantic interoperability

Patient Safety Institute/CDISC Proposed Single Source for Safety Monitoring in Clinical Care/Clinical Research

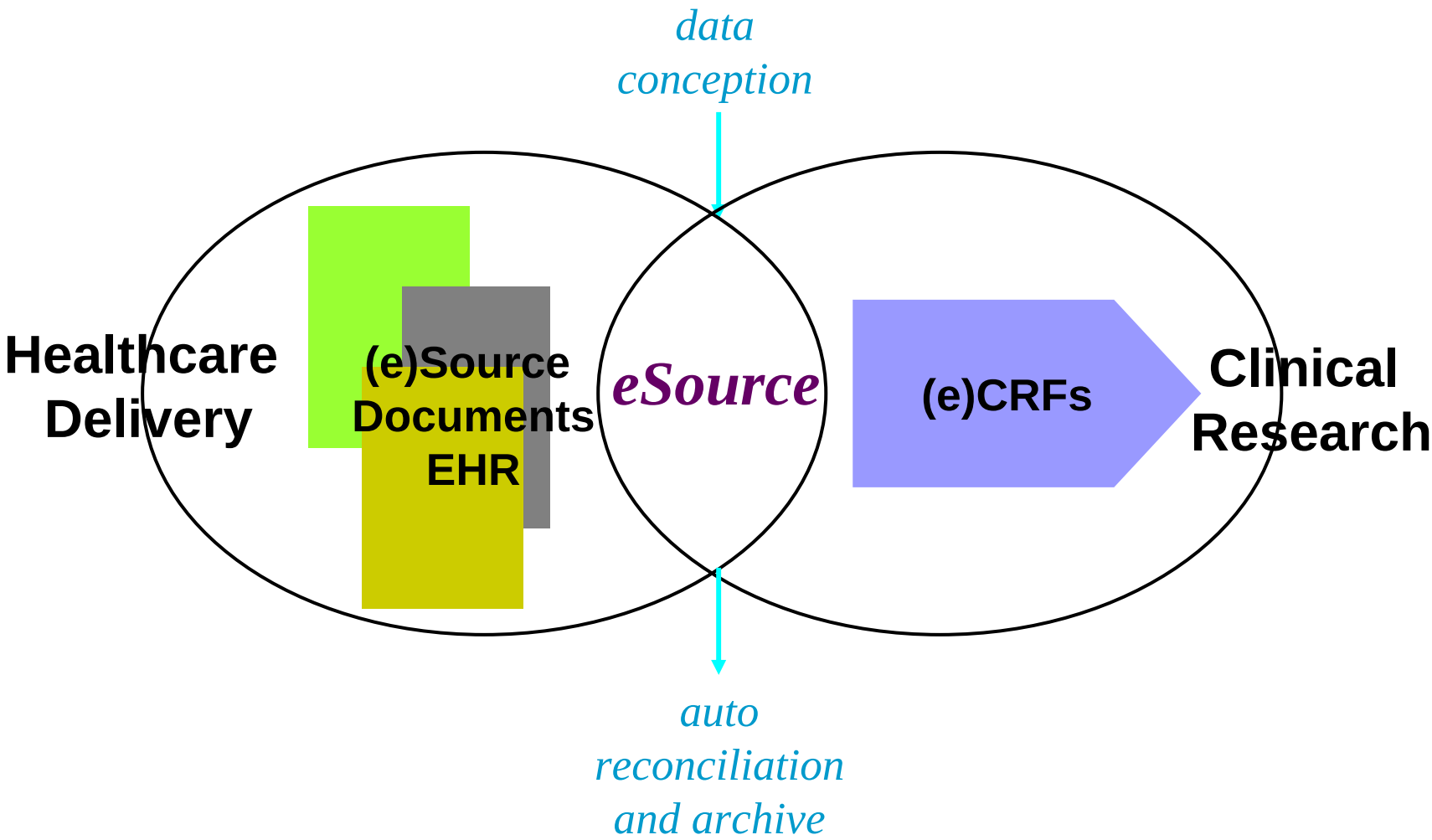


CONNECTIONS LEGEND:	
	PSI provided connections (HIPAA compliant)
	Provider site connections (HIPAA compliant)
	Single Source overlay (21 CFR -11 compliant)

Source: L. Bain

"The same EHR systems critical for improving patient care can also help accelerate clinical research and its impact on practice and improve pharmaceutical safety (pharmacovigilance) and biosurveillance for public health...dual use of EHR systems that could reduce total system costs."

Slide Courtesy Meredith Nahm



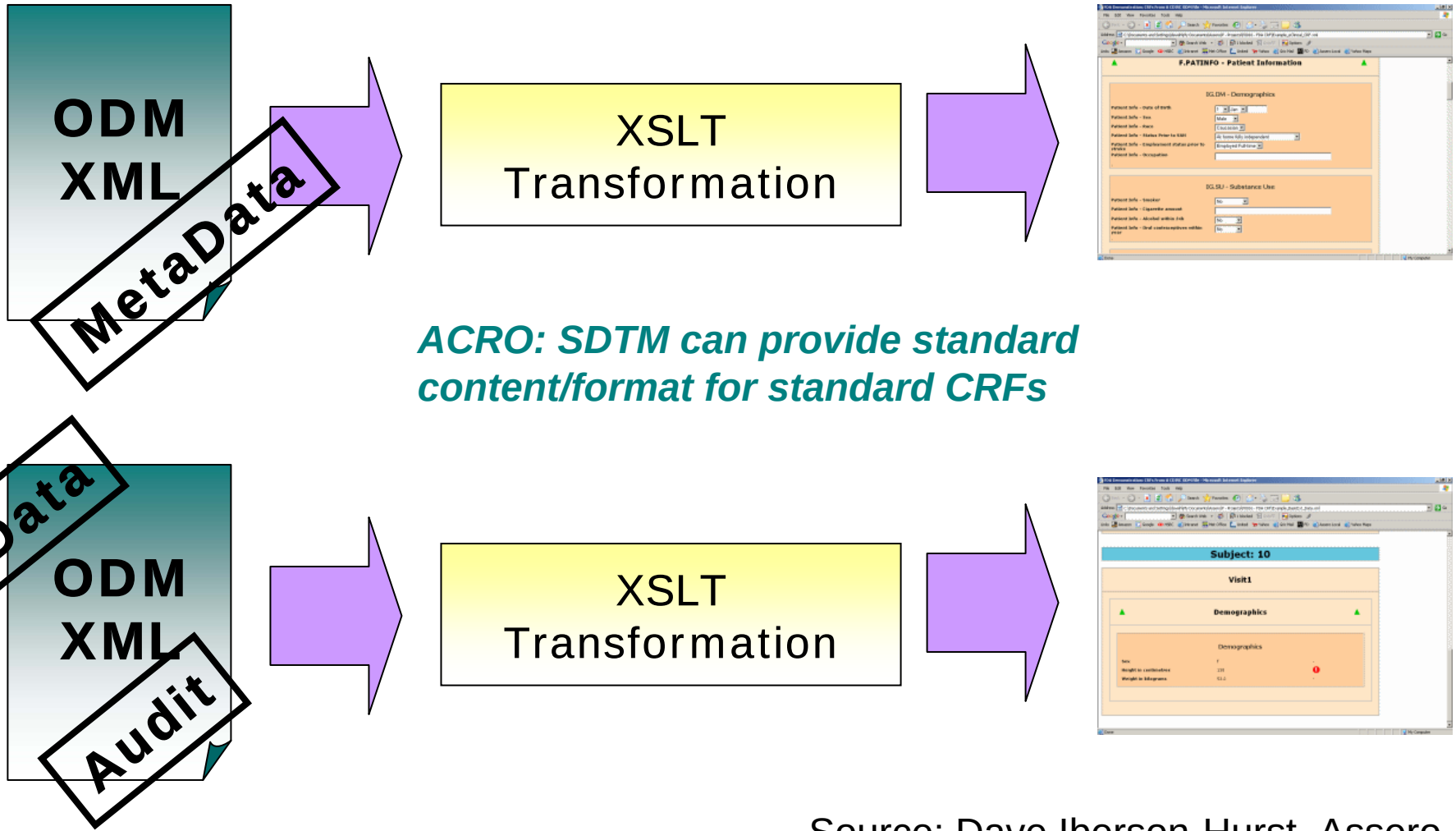
Can we not make it easier for the investigative sites and ourselves to do clinical trials?

eSource Data Interchange (eSDI)

- **Purpose of eSDI Initiative**
  - to facilitate the use of electronic technology in the context of existing regulations for the collection of source data in clinical trials for regulatory submission by leveraging the power of the CDISC standards, in particular the Operational Data Model (ODM).
  - **Note**: eSource pertains to eDiaries, ePRO, eDCI, Electronic Health Records…

- **Document Posted** for Open Public Review and Comment by 17 October

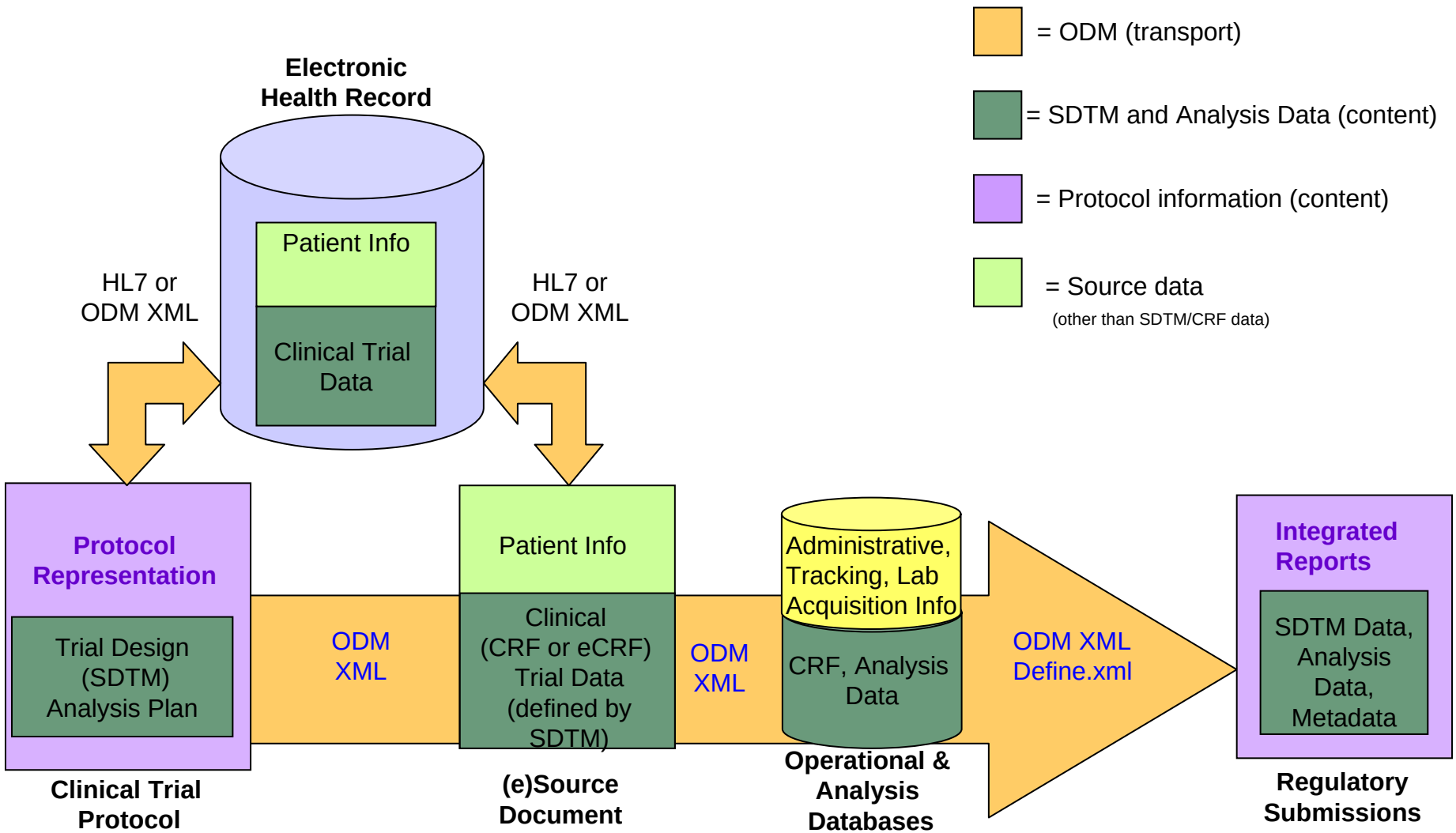
Standard CRF Generation, Viewing Metadata and Data Review and Archive



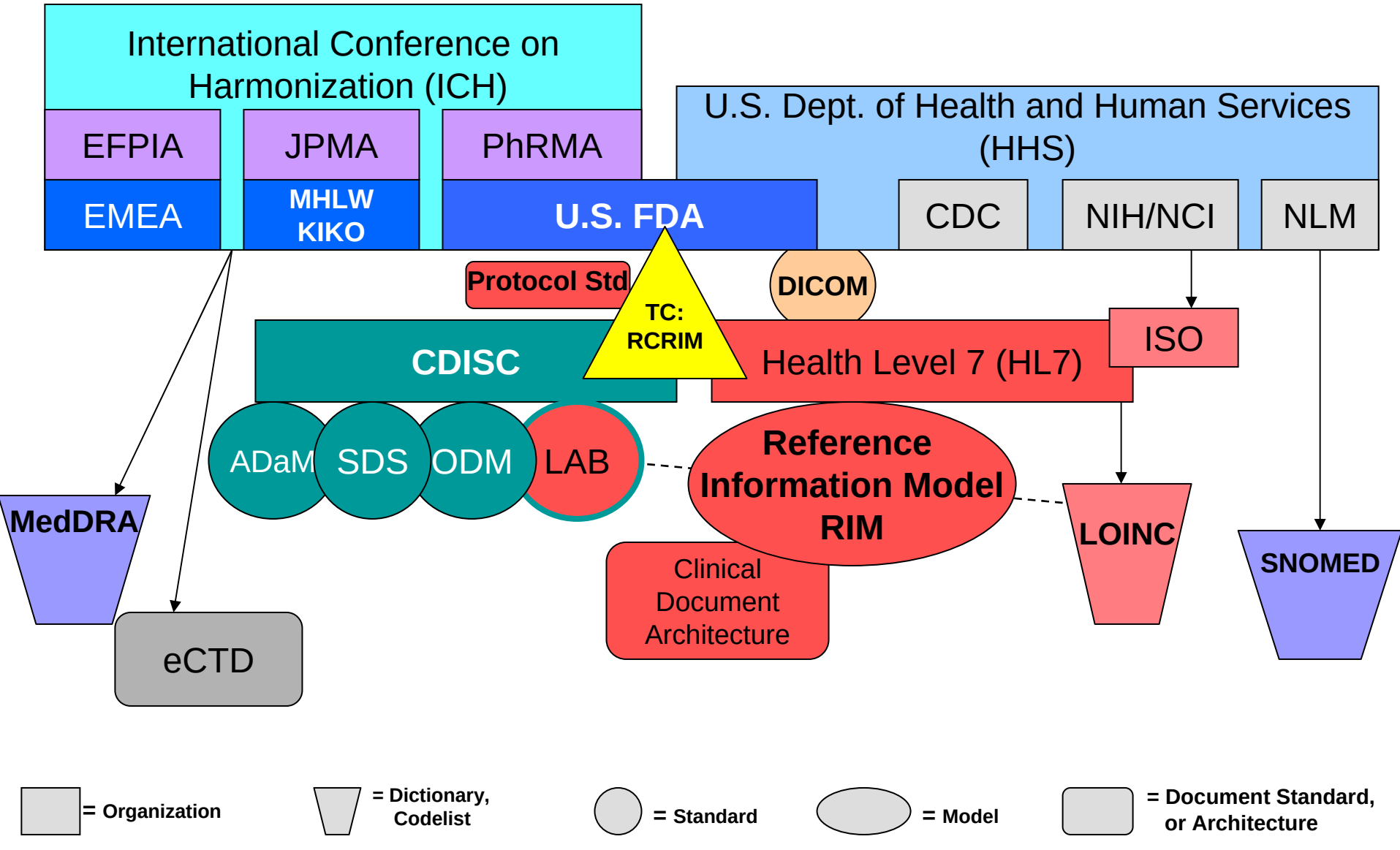
ACRO: SDTM can provide standard content/format for standard CRFs

Source: Dave Iberson-Hurst, Assero

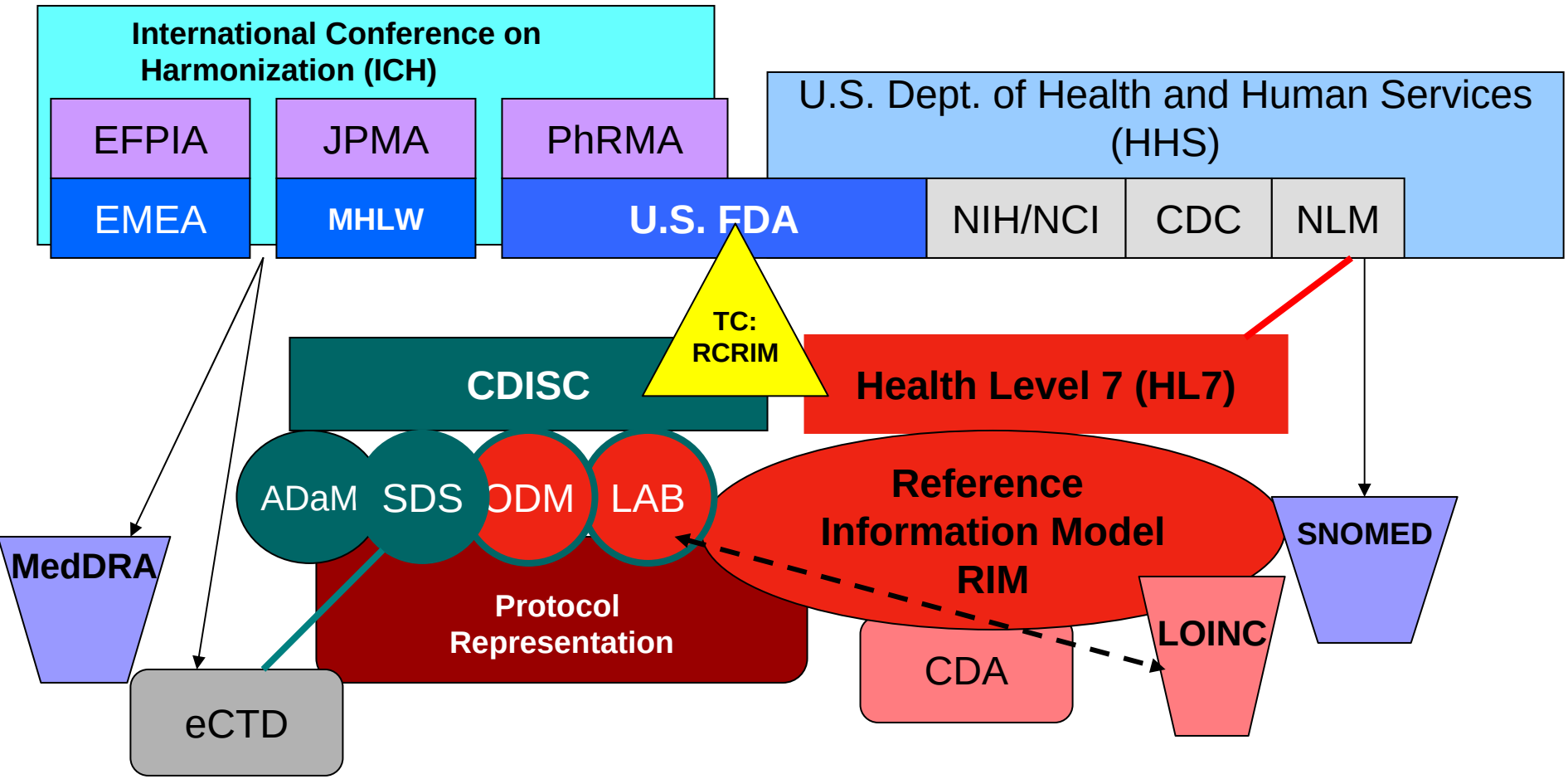
Data Flow Using CDISC Standard Linking Clinical Research and Healthcare



CDISC in the "World of Standards" 2003



CDISC in the "World of Standards" 2005



= Organization

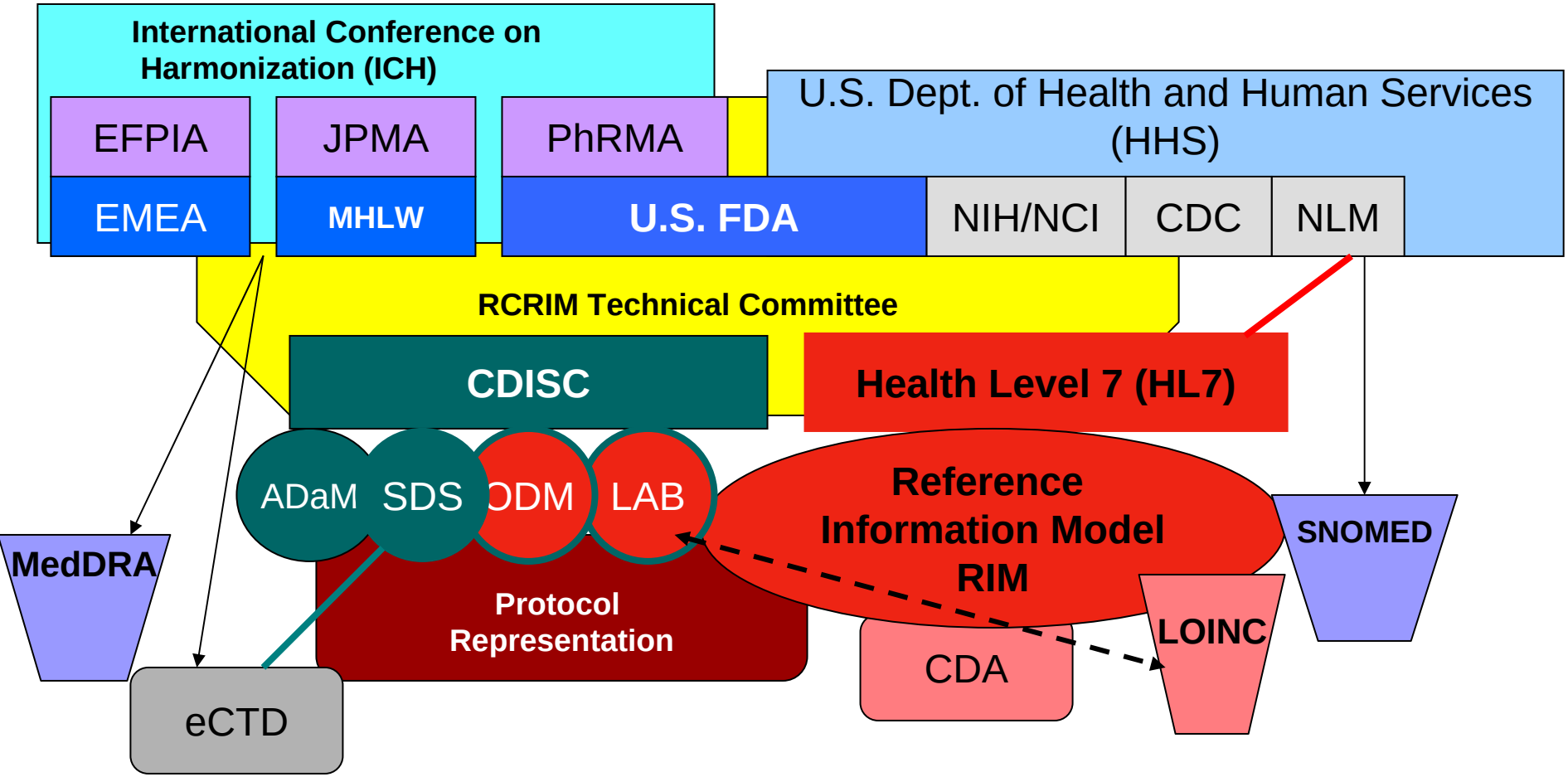
= Dictionary, Codelist

= Standard

= Model

= Document Standard, or Architecture

CDISC in the "World of Standards" 2005



= Organization

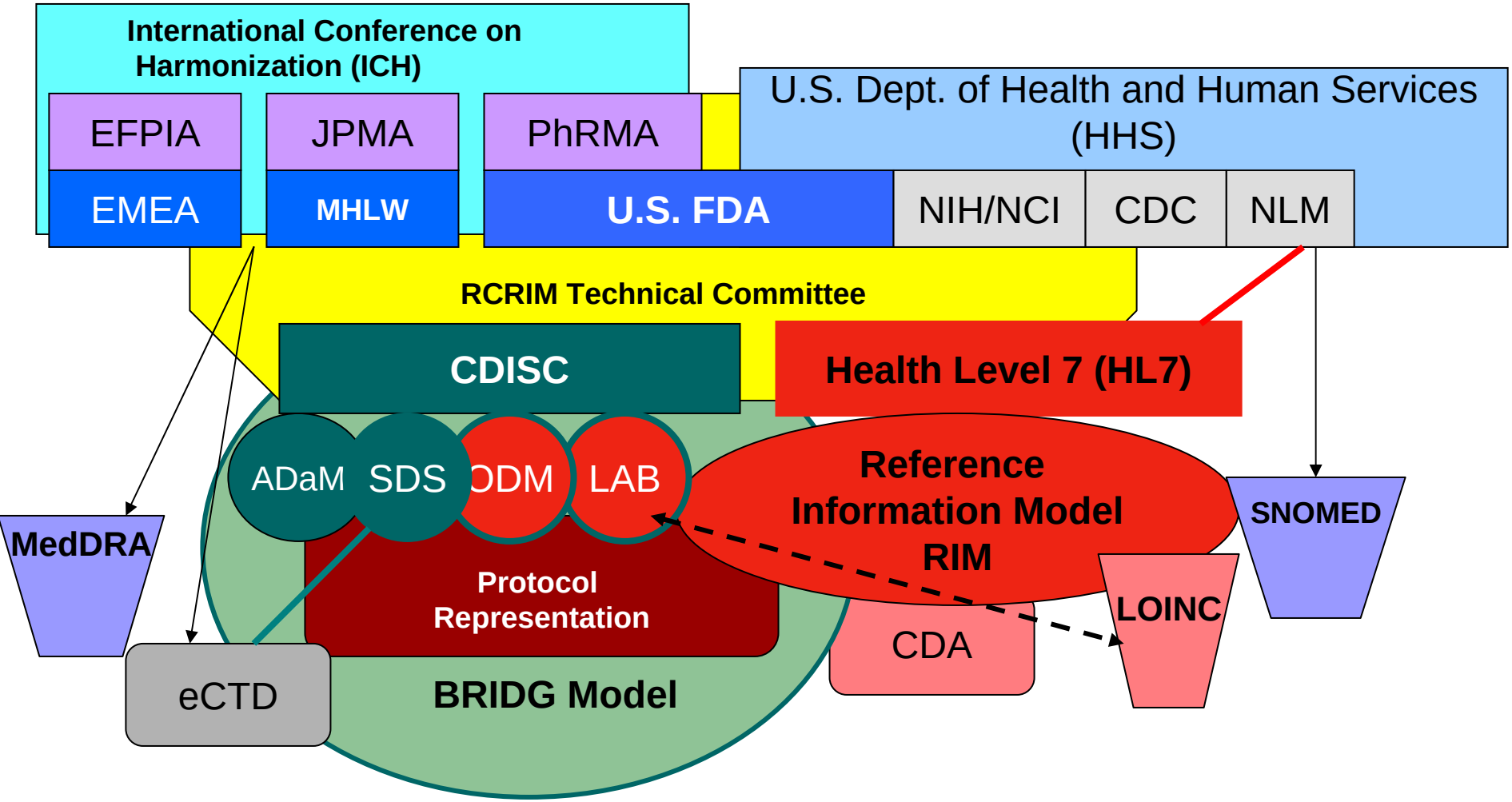
= Dictionary, Codelist

= Standard

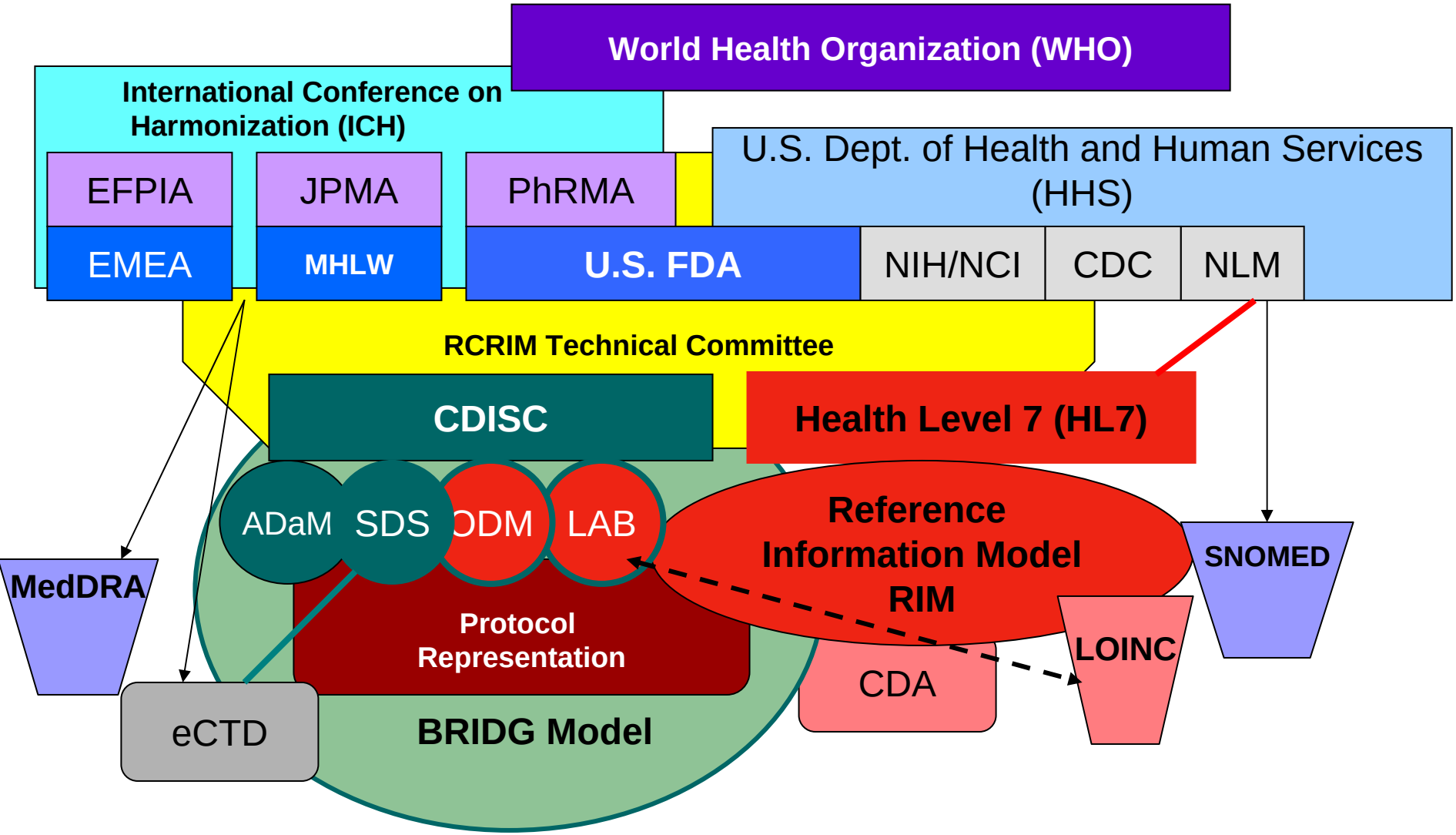
= Model

= Document Standard, or Architecture

CDISC in the "World of Standards" 2005



CDISC in the "World of Standards" 2005



“ Politics are almost as exciting as war, and quite as dangerous.

In war you can only be killed once, but in politics many times.”

> Winston Churchill

CDISC Board/IAB/TCC Strategic Planning: Today's Clinical Research Environment

- More intense focus on patient safety and pharmacovigilance
- Need for transparency of clinical information through publicly accessible registries and databases
- Direct data capture tools are now available
- Importance of interoperability
- Increasing focus on electronic healthcare records

CDISC Board/IAB/TCC Strategic Planning

- Board Committee, with input from Industry Advisory Board (3 Board Members, 2 IAB Co-chairs, 2 Operations), is working on CDISC Strategic Plan 2006 – 08
- CDISC Technical Roadmap and Input from IAB, TCC (environment and needs) will be incorporated
- To be completed by December 2005, with operational plan and budget
- David Hardison, PhD will be Board Chair 2006
- Ed Helton, PhD will be Board Chair-elect 2006

Knowing is not enough;
we must apply.
Willing is not enough;
we must do.

- Goethe-

To the gracious supporters who ‘apply’ and ‘do’….

THANK YOU!

Rebecca Kush
rkush@cdisc.org

Information and Contacts

- For standards and information, see www.cdisc.org
- eNewsletters available via e-mail; contact Shirley Williams swilliams@cdisc.org or sign up on the CDISC website.
- Technical questions: Julie Evans jevans@cdisc.org or Public Discussion Forum
- Education and Membership: Frank Newby fnewby@cdisc.org
- Rebecca Kush: rkush@cdisc.org