PhUSE

10-12 September 2005
Heidelberg, Germany

CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

Introduction to CDISC: Part Three "Collaborations and Standards in Progress"

Rebecca Kush, PhD, CDISC

Mission Statement for CDISC

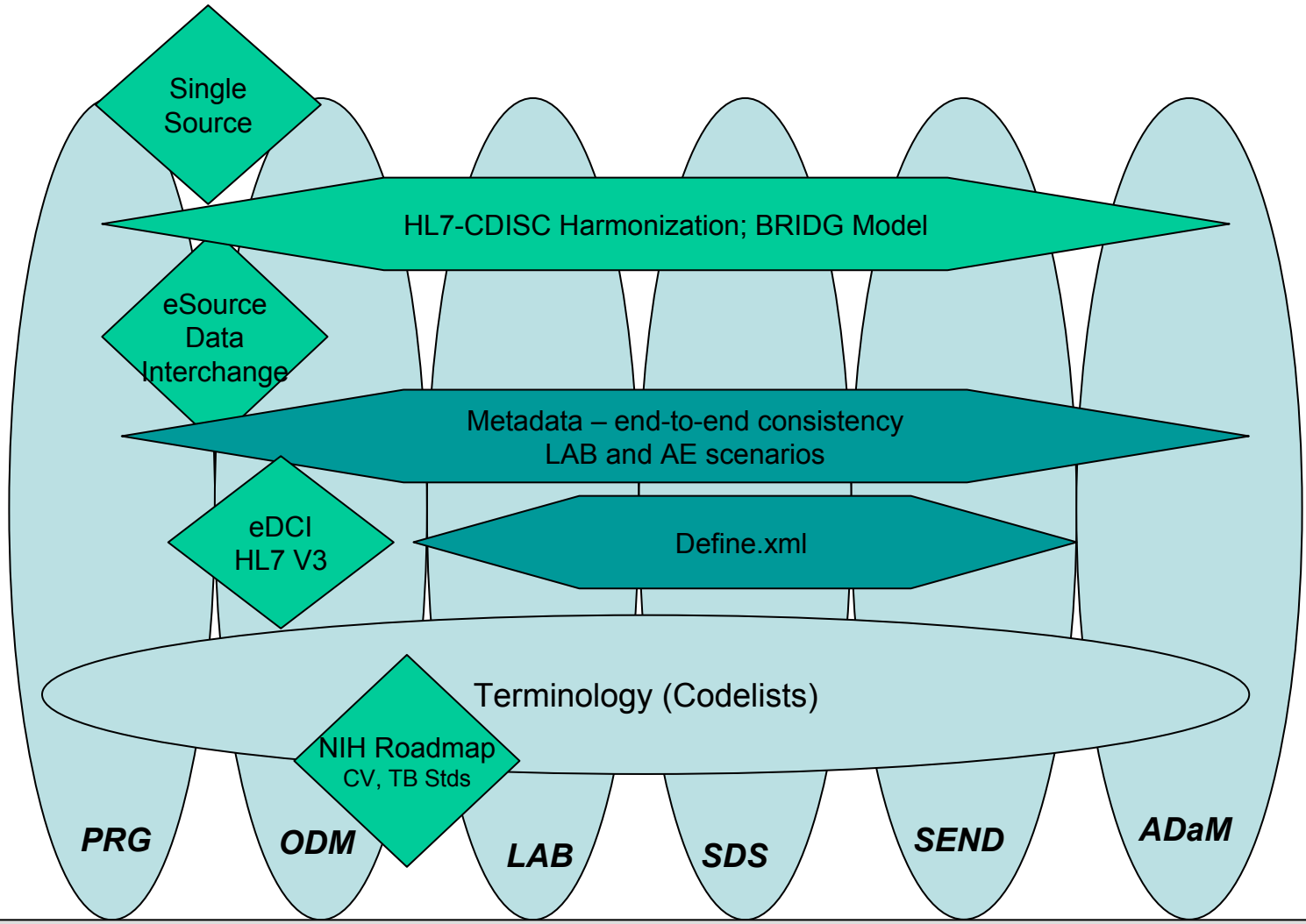
-as of October 2004

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.

CDISC Teams and Projects - 2005

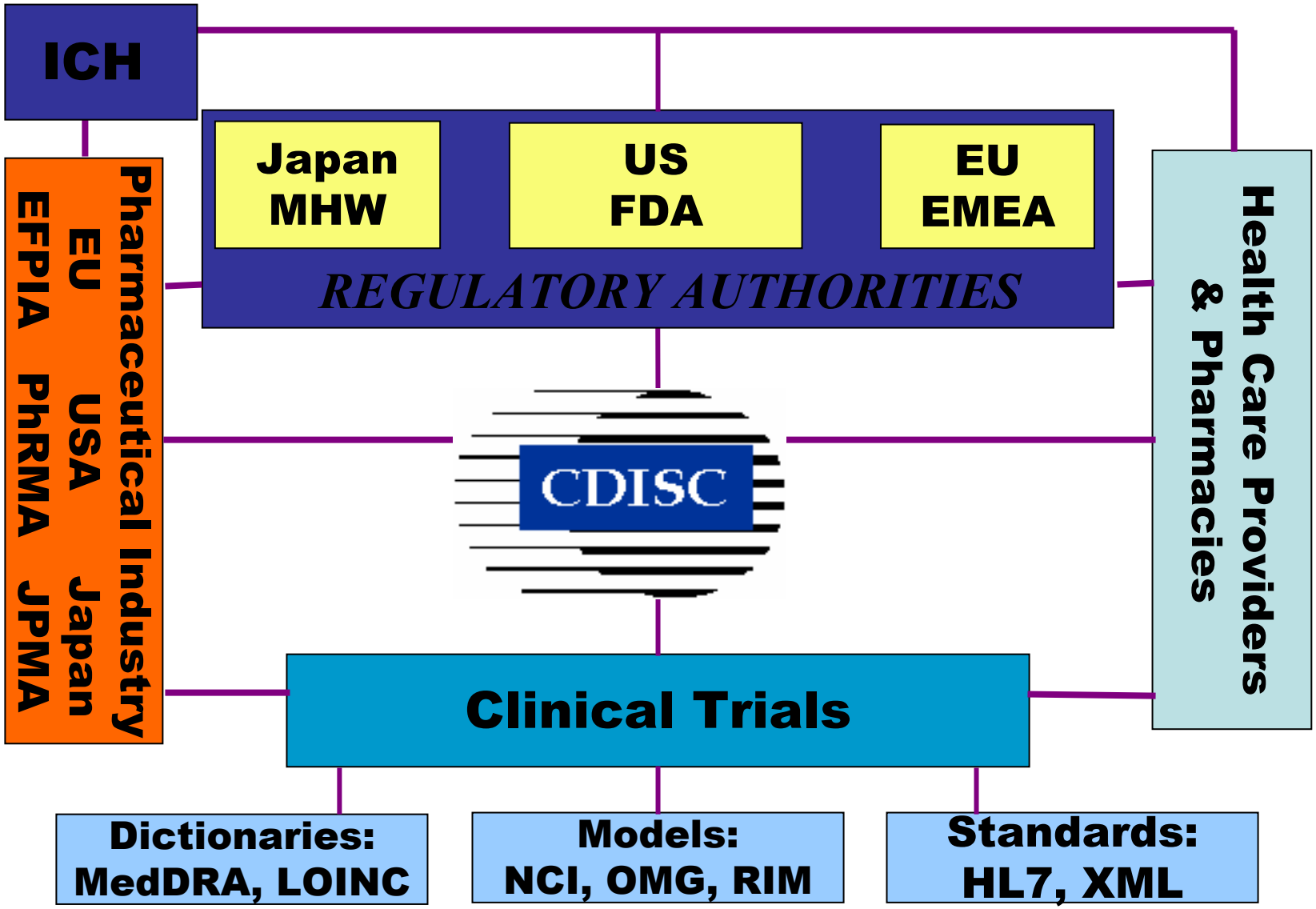


Maintenance, Member Relations, Education and Implementation Groups, Glossary

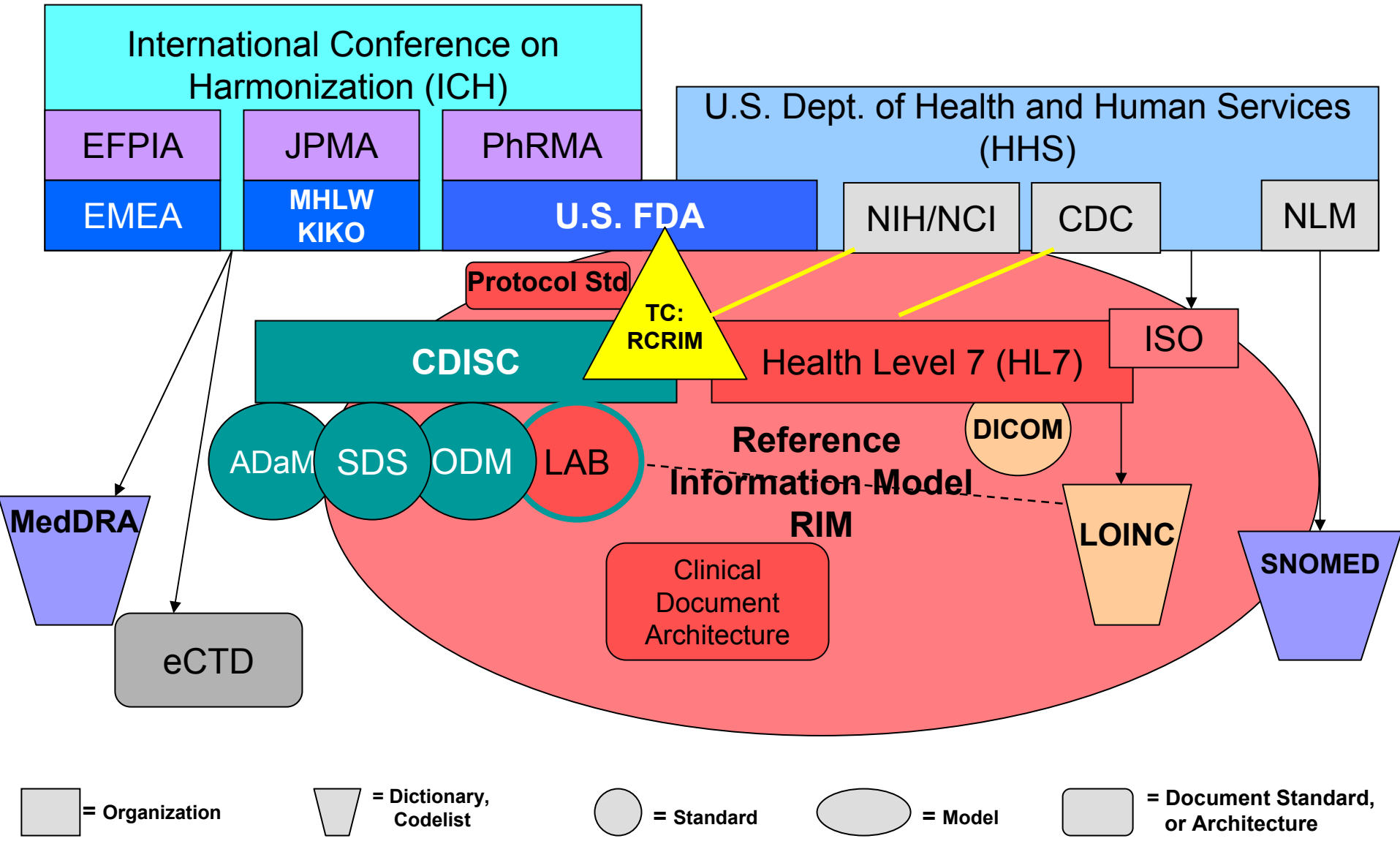
Outline

- CDISC Collaborations or Alliances
  - Health Level Seven (HL7)
  - NCI/NIH
  - Regulatory Authorities
  - Others
- Standards in Progress
  - Terminology
  - Protocol Representation

CDISC in the "World of Standards" 2000



The Clinical Research "World of Standards" Today



CDISC

- The HL7 mission is: "*To provide standards for the exchange, management and integration of data that support clinical patient care and the management, delivery and evaluation of healthcare services. Specifically, to create flexible, cost effective approaches, standards, guidelines, methodologies, and related services for interoperability between healthcare information systems.*"

- History of HL7-CDISC Relationship
  - 2001 – HL7 and CDISC completed Associate Charter Agreement and initiated Clinical Trials Special Interest Group (CT-SIG); CDISC joined HL7 as organizational member
  - 2002 – FDA joined HL7 as a benefactor
  - 2002 – CT-SIG 'upgraded' to Technical Committee, Regulated Clinical Trial and Information Management (RCRIM), co-chaired by FDA, HL7 and CDISC
  - 2004 – HL7 and CDISC renewed Charter Agreement

HL7 RCRIM Technical Committee - Mission

This committee supports the HL7 mission to create and promote its standards by developing standards to improve or enhance information management during research and regulatory evaluation of the safety and efficacy of therapeutic products or procedures worldwide. The committee defines messages, document structures, and terminology to support the systems and processes used in the collection, storage, distribution, integration and analysis of such information. The work of this committee will facilitate the availability of safe and effective therapies by improving the processes and efficiencies associated with regulated clinical research.

- Shared Purposes
  - To improve the quality of public health
  - To have one overarching standard model for interoperability between healthcare and clinical research information systems

- Domain Expertise Contributions
  - CDISC and FDA: Regulated clinical research data acquisition, review and archive requirements
  - Health Level Seven (HL7): Healthcare information exchange standards and methodology; accreditation process

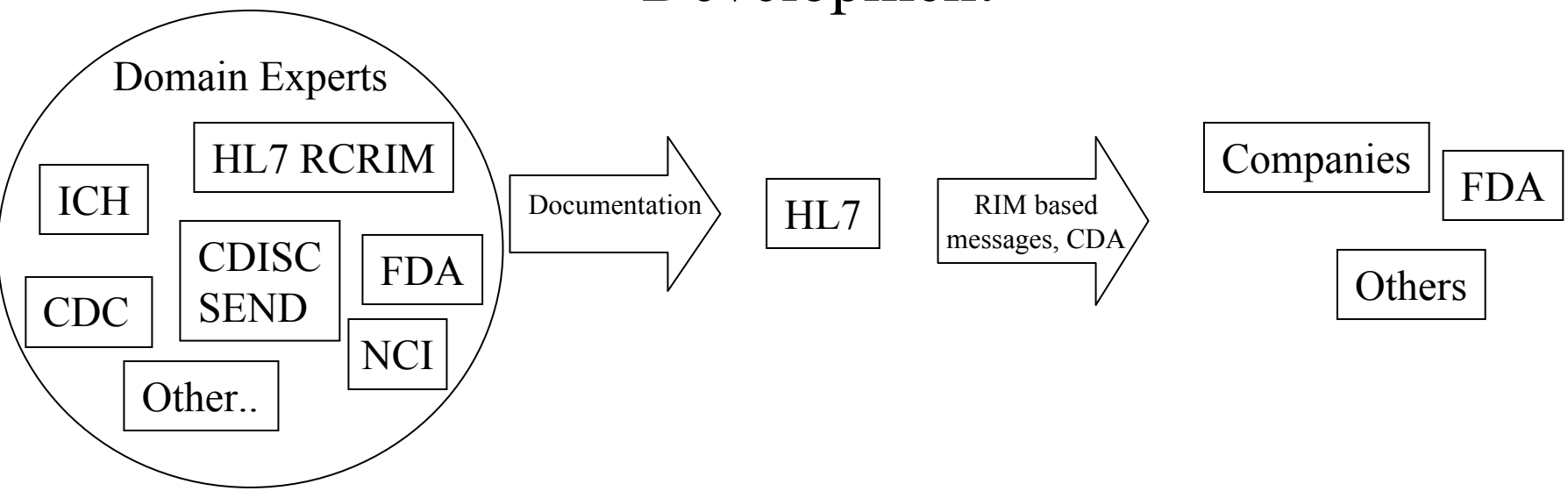
- Working Relationships
  - Regulated Clinical Research Information Management (RCRIM) Technical Committee (co-chaired by FDA, HL7, CDISC)
  - Renewed Associate Charter between CDISC and HL7
  - Organizational Memberships and Collaborations
  - Outreach Committee for Clinical Research (OCCR)
  - Commitment to harmonize the HL7 and CDISC standards

Standards Development

Requirements

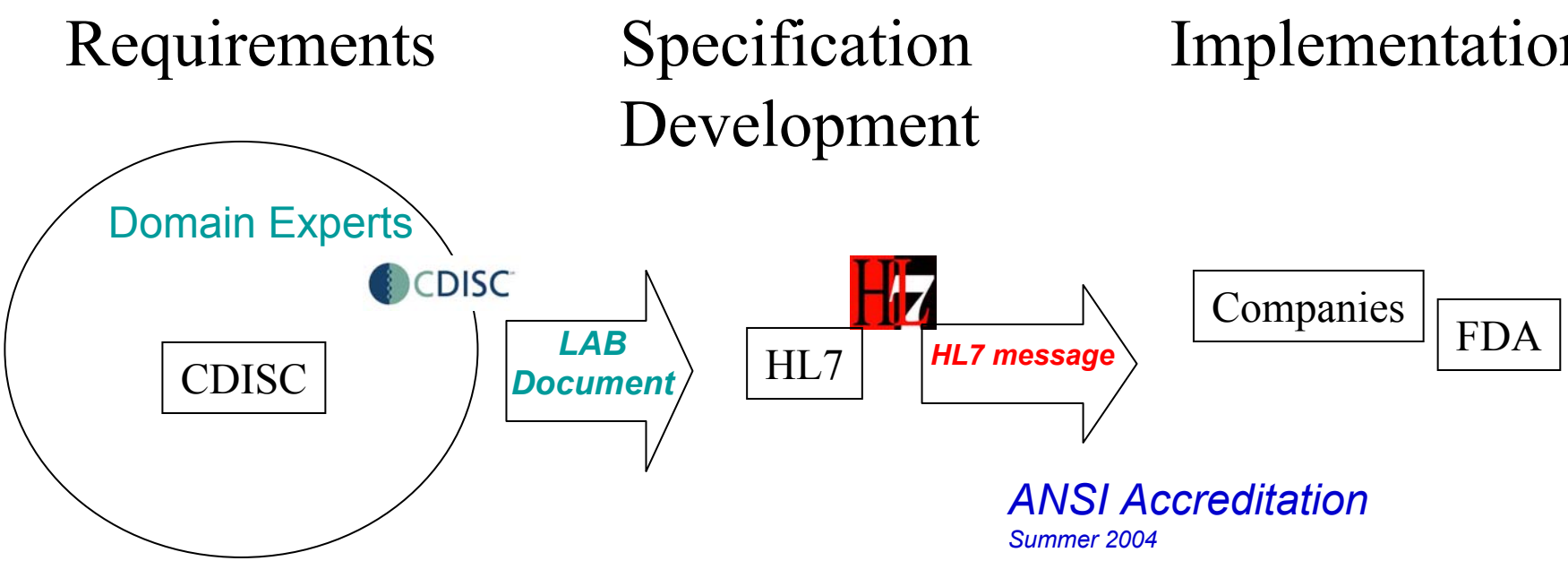
Specification Development

Implementation

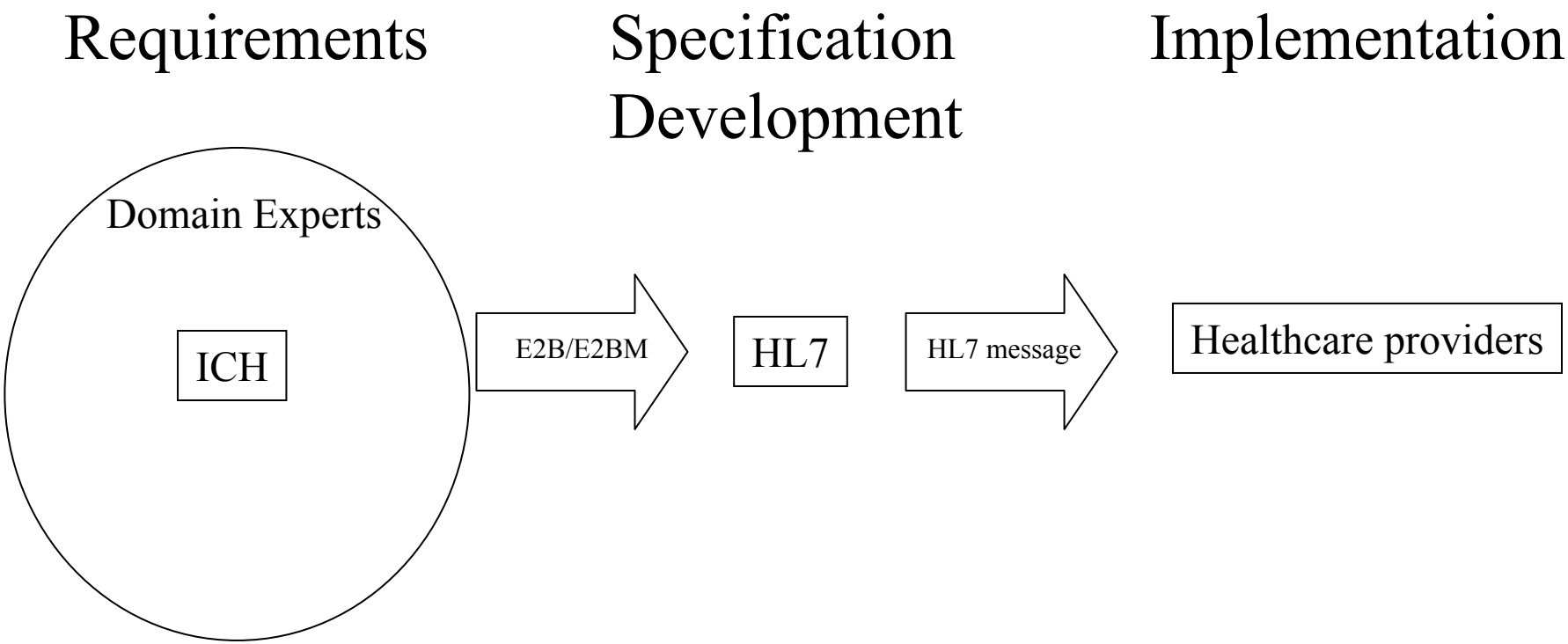


R. Levin, EuroInterchange, May 2004

Periodic reporting of clinical trial laboratory data (LAB)



Individual Case Safety Report



R. Levin, DIA Annual Meeting 2004

RCRIM Projects - 2005

- Clinical Trial Lab (CDISC LAB model → ANSI accredited HL7 V3 RIM message
- Individual Case Safety Report (ICSR- 'eMedWatch')
- Structured Product Label
- Annotated ECG→ANSI accredited HL7 V3 RIM message
- Stability Reporting
- Protocol Representation (Structured Clinical Trial Protocol) - also CDISC Team
  - Clinical Trial Registries (with PR Group)
- Registered Product Submission
- Patient Safety – Special Interest Group (SIG)
- Genomics – Special Interest Group (SIG)
- BRIDG to RIM Mapping and Reconciliation

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.

Interchange vs Interoperability

- 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

Syntax → Structure

Semantics → Meaning

- **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

The Pillars of (Semantic) Interoperability

Necessary but not Sufficient

- **Common model across all domains-of-interest**
  - **Information model vs Data model**
- **Model grounded on robust data type specification**
- **Methodology for binding terms from concept-based terminologies**
- **A formally defined process for defining specific structures to be exchanged between machines, i.e. a "messaging standard"**

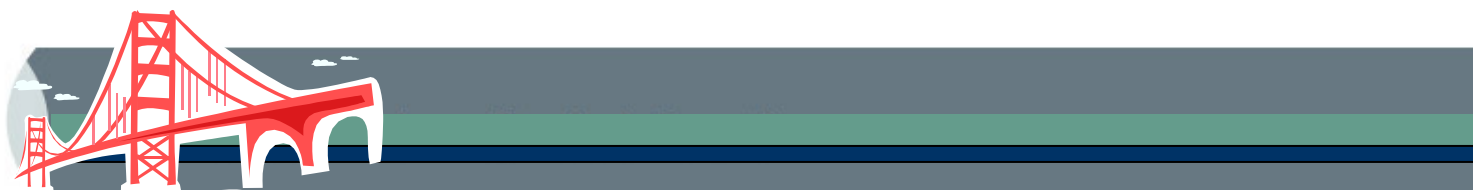
C. Mead, HL7

CDISC Domain Space Analysis Model, (now called BRIDG Model)

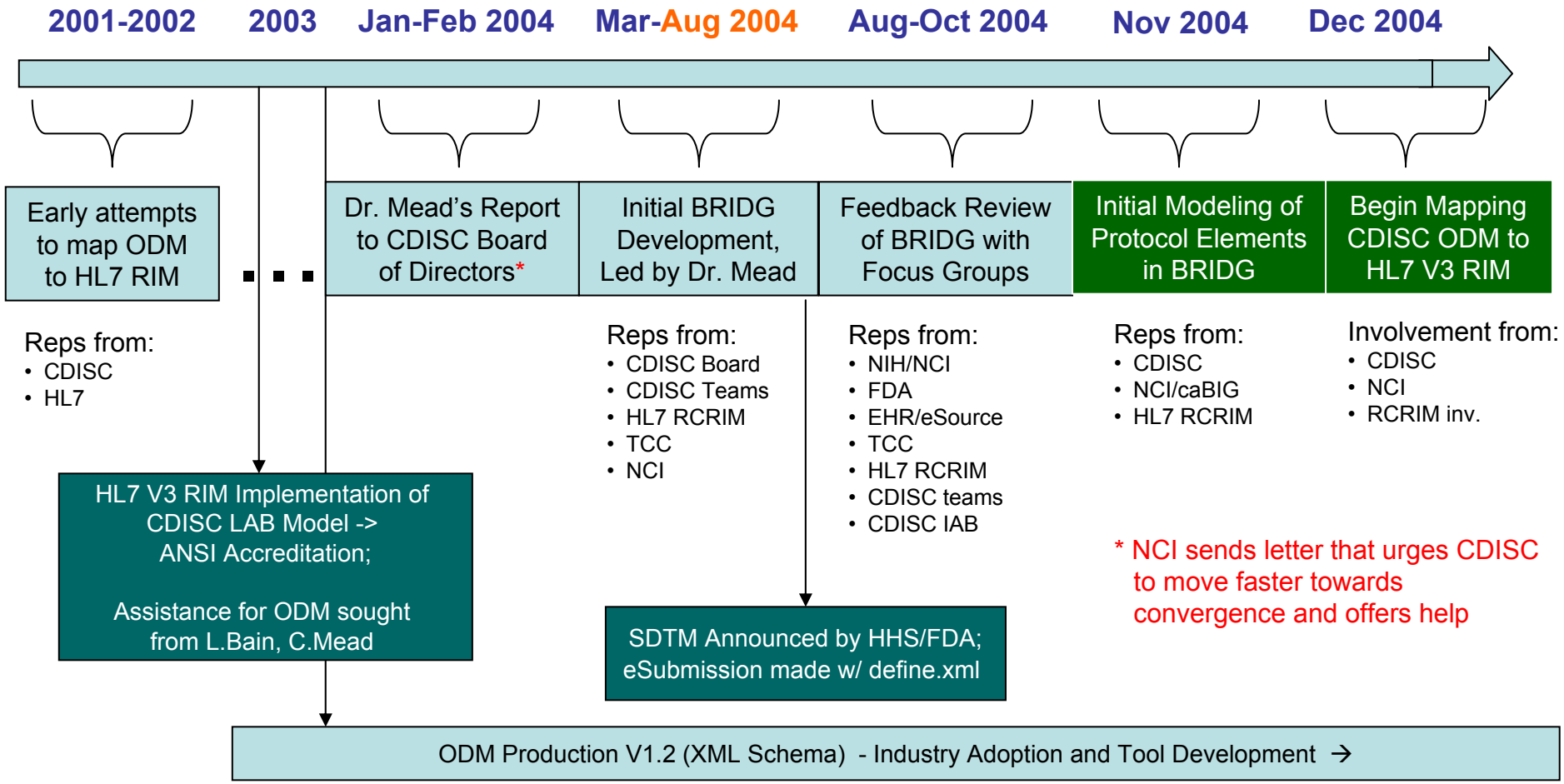
- Follows the HL7 Development Framework
- Initiated in January 2004 by CDISC Board
- Developed through numerous modeling sessions with domain experts and reviewed by CDISC, industry, FDA, NCI/NIH groups; led by HL7 RIM expert
- Purposes and Anticipated Benefits:
  - To help ensure harmonization among CDISC models (present and future)
  - To provide the industry with a standard model to represent the clinical research domain
  - To enable an HL7 implementation of the CDISC ODM
  - To help harmonize the CDISC and HL7 standards
  - To help enable interoperability between clinical research and healthcare systems

Biomedical Research Integrated Domain Group (BRIDG) Model

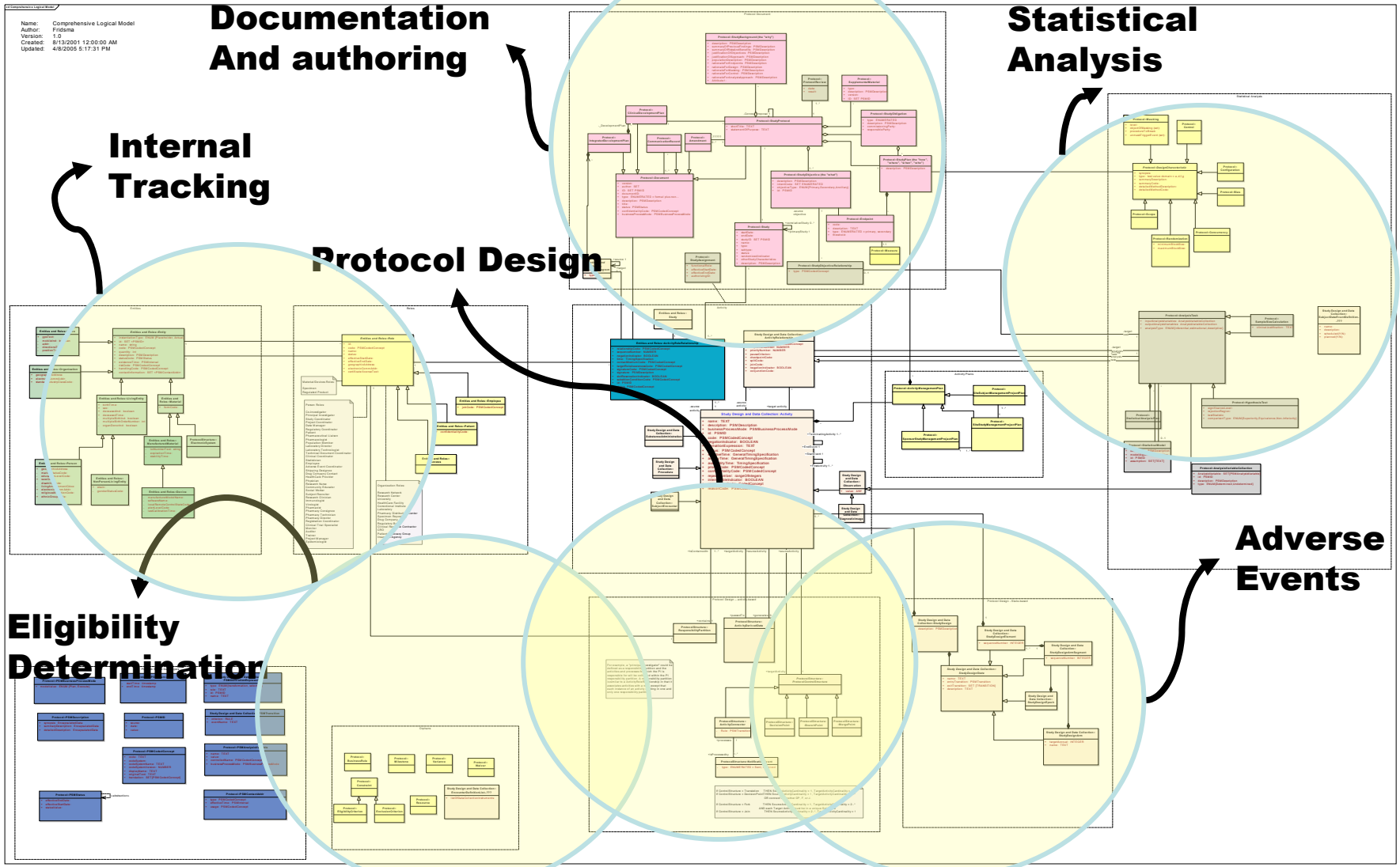
- A model that reflects the domain space of clinical/biomedical research using language domain experts comprehend
- Follows the HL7 Development Framework (HDF); led by HL7 RIM expert
- Initiated in January 2004 by CDISC Board
- Developed through numerous modeling sessions with domain experts from CDISC, FDA, and NCI/NIH
- Is being 'adopted' by the HL7 Regulated Clinical Research Information Management (RCRIM) Technical Committee and NCI
- A means of 'bridging' together the clinical research standards from CDISC and HL7 (towards interoperability)



BRIDG Model: Timeline



Biomedical Research Integrated Domain Group (BRIDG) Model



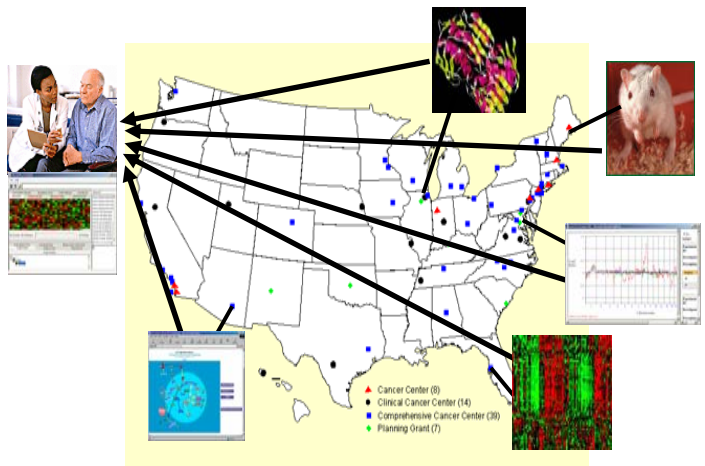
CDISC℠

NIH/NCI-CDISC Collaborations

- Harmonization of CDISC and HL7 standards
- Development of an overarching clinical research domain model
  - ODM to RIM mapping
  - Implementations of this model
- Vocabulary/terminology development and maintenance
- Development of a Protocol Representation standard
- Creating a shared environment for Janus database that can accept SDTM data

Cancer Biomedical Informatics Grid (caBIG™)

CaBIG Goal: Establish and/or adopt standards for semantic and syntactic interoperability to facilitate data and tools sharing and access across the caBIG community



- Common, widely distributed infrastructure permits research community to focus on innovation
- Shared vocabulary, data elements, data models facilitate information exchange
- Collection of interoperable applications developed to common standard
  - caBIG guidelines can be found at: http://cabig.nci.nih.gov

Clinical Research Information Exchange
CRIX 2.0: Janus Pilot

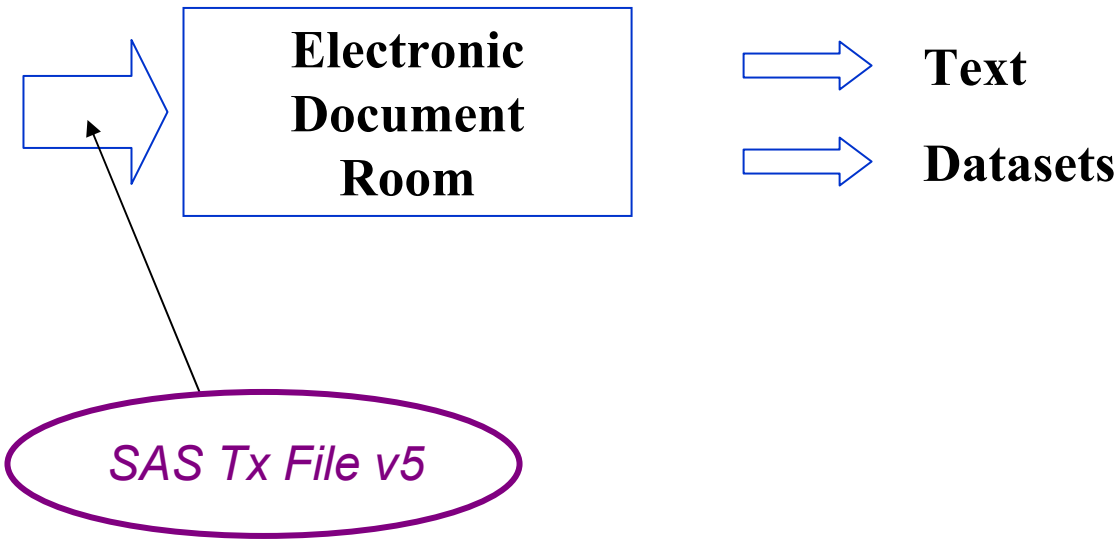
- NCI partnering with industry to implement the FDA Janus data model in a prototype data repository that is caBIG compliant
- Janus is based on CDISC's SDTM and includes data about:
  - "What Happened"
  - "What Was Supposed to Happen"

  As well as analysis plans and results

Transmitting and Using Data: Current Approach - FDA

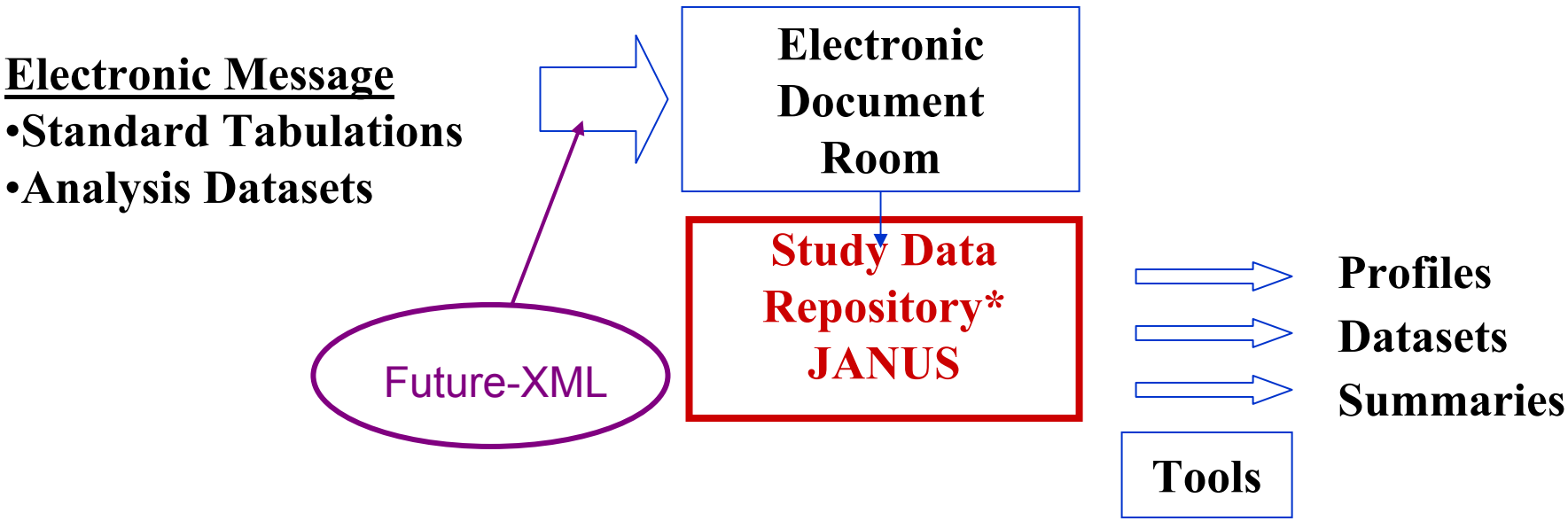
Data on Physical Media

- **Tabulation Datasets**
- **Analysis Datasets**
- **Data Listings Datasets**
- **Metadata Files**
- **Subject Profiles**
- **Summary Tables and Graphs**



Submission	Storage	Review

Transmitting and Using Data: Study Data Repository - FDA



*Planned and Actual

Submission	Storage	Review

MHLW, EMEA

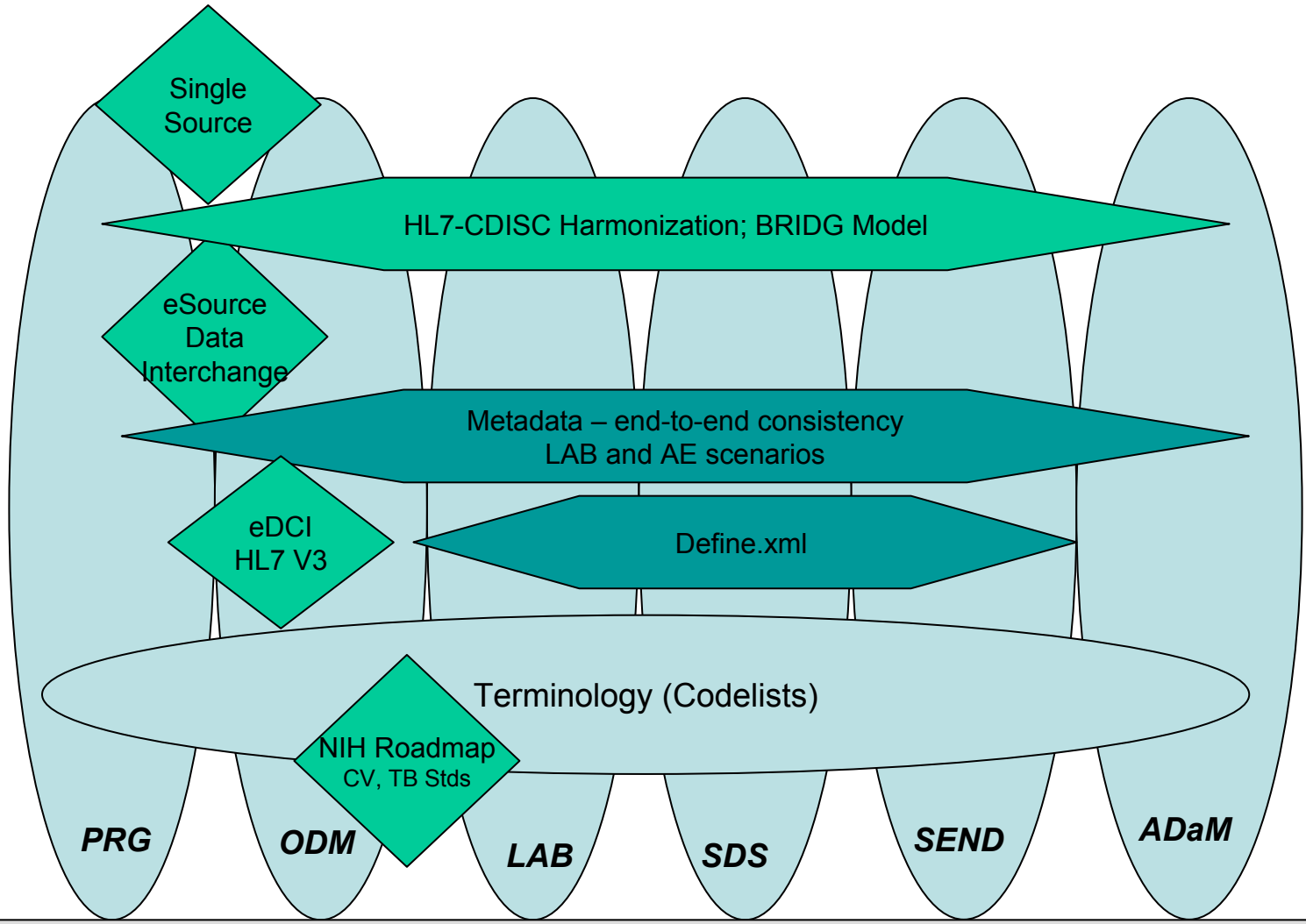
- Dr. Takahiro Kiuchi from the University of Tokyo, University Hospital Medical Information Network (UMIN) – work contracted by MHLW to study "Digitalization and Networking of Clinical Trials".
  - The recommendation was to leverage past achievements and use the CDISC standard, contribute to the development of the standard and ensure that the standard works in Japan, which may require extensions. (GOR, August 2005)

- EMEA – interested in harmonization of EudraCT requirements with Protocol Representation/Trial Tracking (and now WHO requirements)

NIH Roadmap Grants

- Grants to facilitate clinical research among sites doing cardiovascular or public health (TB) studies
- Collaborations of CDISC with Duke Clinical Research Institute and CDISC to develop therapeutic area standards (CV and TB)
- Also collaborated with DCRI and Duke University Medical Center and others on Single Source

CDISC Teams and Projects - 2005



Maintenance, Member Relations, Education and Implementation Groups, Glossary

Controlled Terminology for Clinical Trials

Objectives

To **select appropriate Controlled Vocabulary for each CDISC variable** that needs Controlled Terminology, an appropriate vocabulary is selected from available vocabularies **according to pre-defined criteria**.

Controlled Terminology is created where none are available. The name and location of the Vocabulary is documented for each variable where it is required. The terminology selections will be **put forward through the CDISC review** process. ·

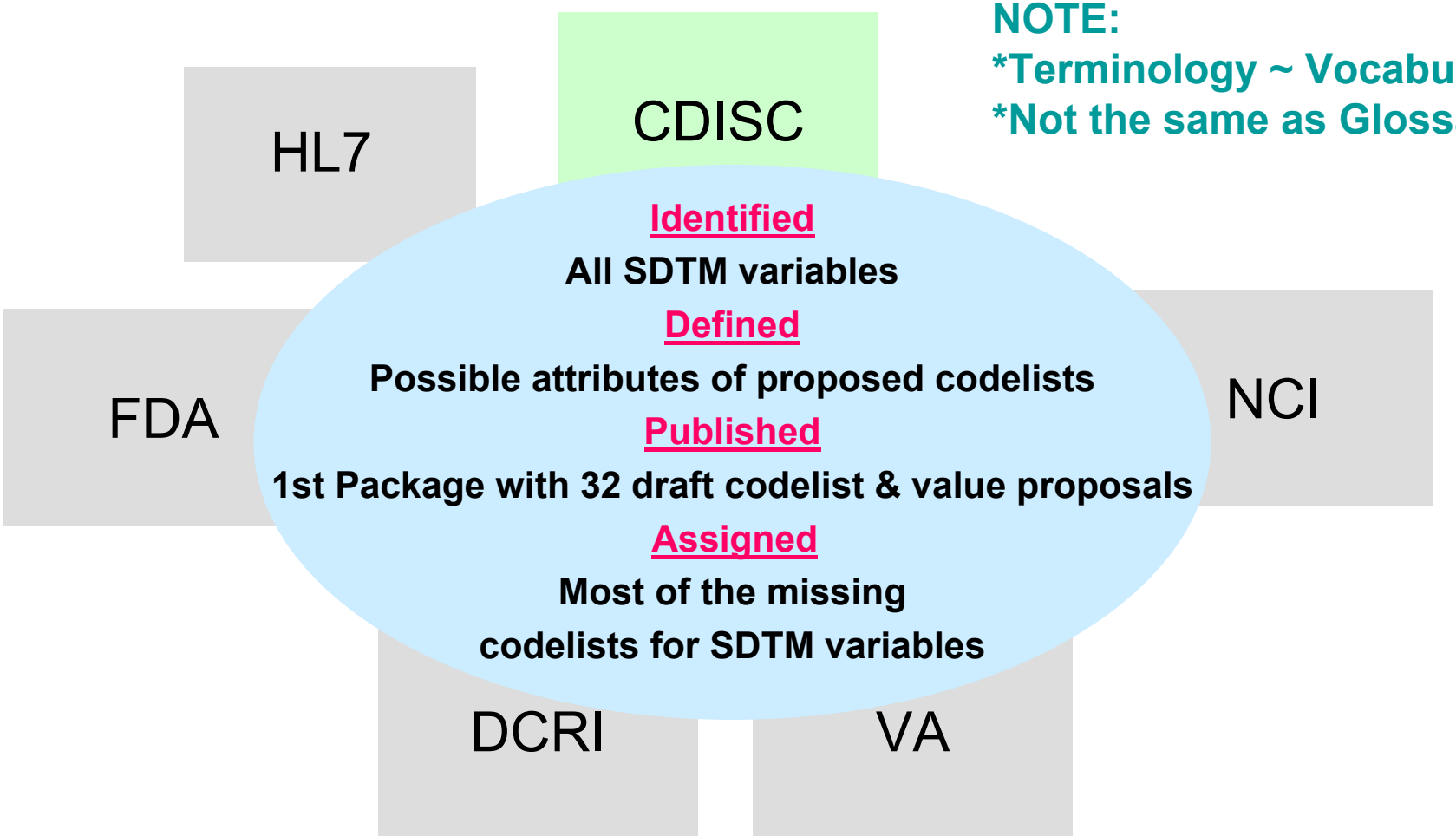
Principles

- To utilize **available terminology first**, before creating and maintaining our own
- To **harmonize** both within **CDISC models and with government efforts**
- To identify (point to) **ONE vocabulary for each CDISC variable** identified by the modeling team (SDM, ODM, LAB, ADaM) as needing Controlled Terminology

Andreas Gromen, EuroInterchange May 2004

CDISC is working with NCI on Terminology (caDSR – EVS) .

Terminology to support the CDISC standards (and related standards) is a key 2005-06 initiative.



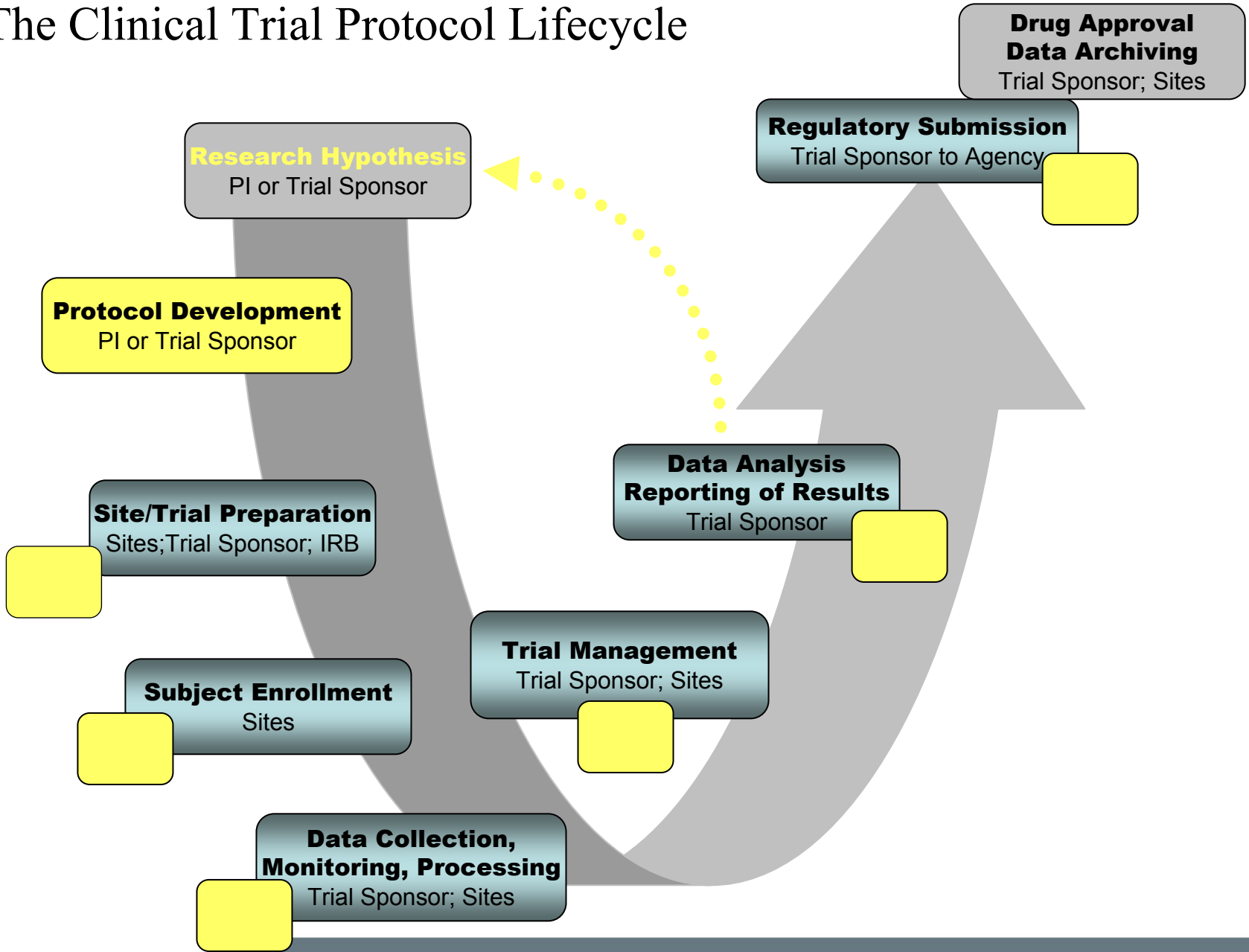
NOTE:
***Terminology ~ Vocabulary**
***Not the same as Glossary**

A.Gromen, modified, EuroInterchange 2005

CDISC Glossary
Objectives & Principles

- To harmonize word definitions used in the various standards initiatives undertaken by CDISC in clinical research.
- To serve the community of clinical researchers by selecting and defining terms pertaining to the conduct of federal and pharmaceutical industry-sponsored trials
- To produce a Glossary (not a terminology), that is publicly accessible, extensible through CDISC, and versioned to reflect its evolution.
  - Focus is on words, abbreviations, and acronyms used in clinical research, particularly in eClinical Trials and where clarification and standardization are required to reduce confusion or undisciplined usage.
  - Published in Applied Clinical Trials (December Resource Issue) and on CDISC website.

The Clinical Trial Protocol Lifecycle

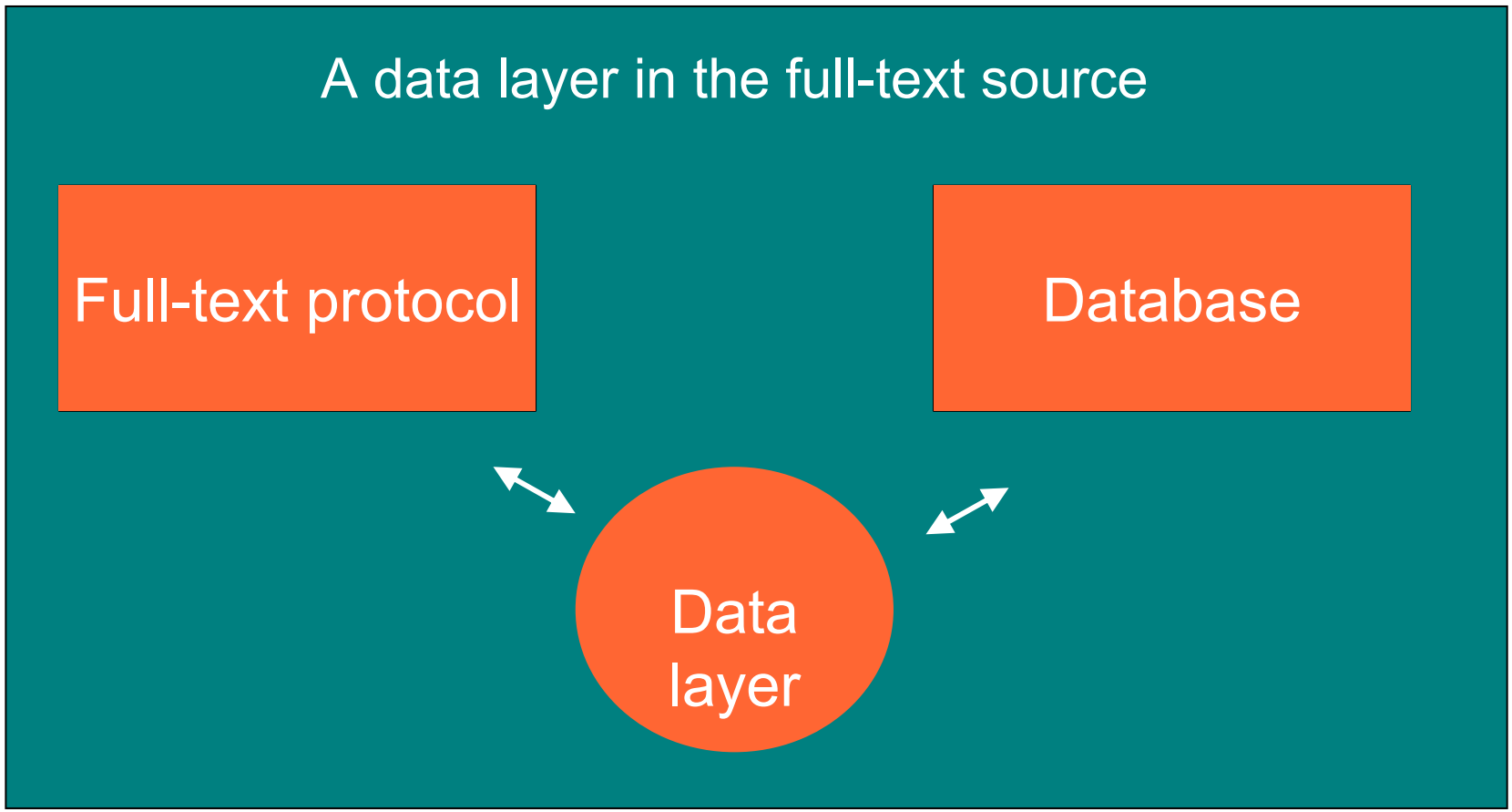


CDISC

Protocol Representation Standard

A human and machine-readable model that enables interchange of protocol data amongst systems and stakeholders

Goal: Structured Clinical Trial Protocol



Protocol Representation Standard

- Initiated as an HL7 project to develop standard representation of the protocol elements for support of interoperability
- CDISC team formed to provide domain expertise
- Spreadsheet of elements, with glossary definitions open for public review and comment; documentation available on CDISC website
- Initial CDA model developed and balloted through HL7

Protocol Representation - Hierarchy

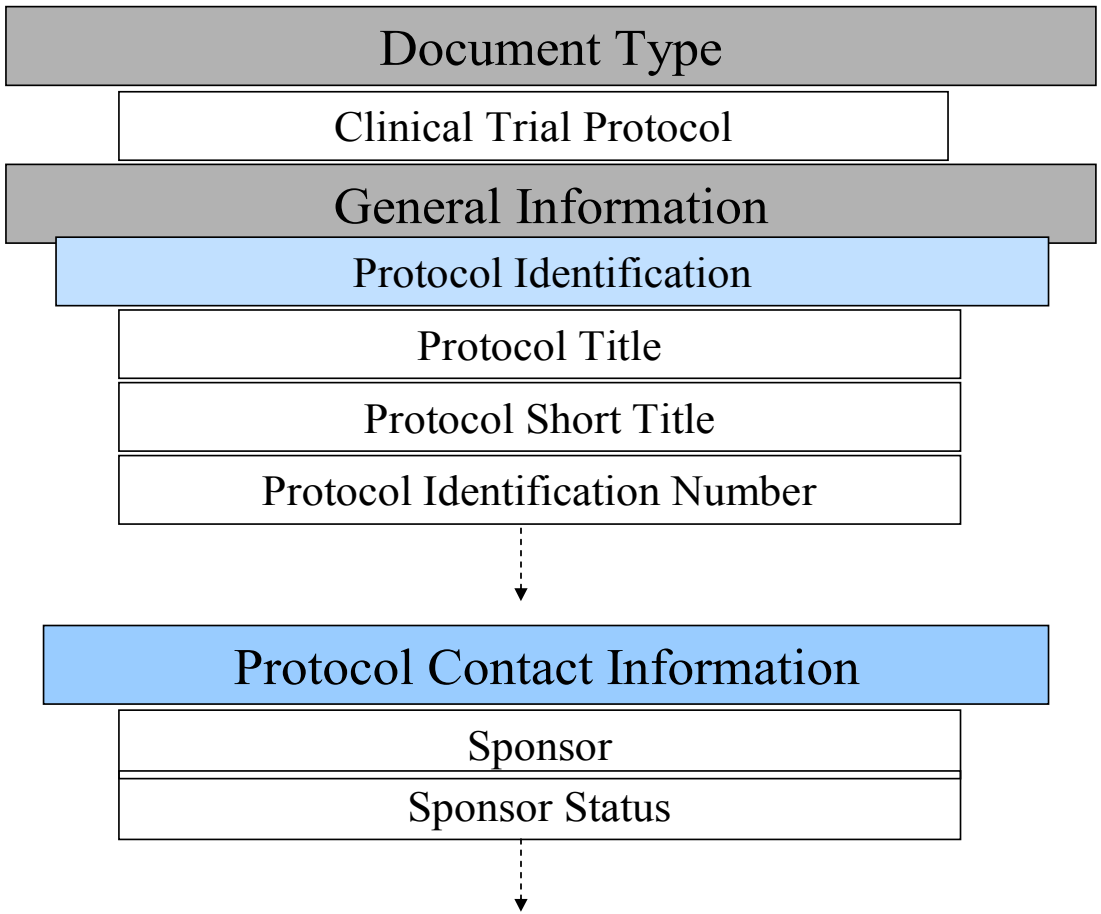
PR Group

Overall Structure based upon ICH E6, E3, E9

- Document Type
- General Information
- Background Information
- Trial Objectives and Purpose
- Trial Design
- Subject Selection and Withdrawal
- Subject Participation/Study Design
- Treatment of Subjects
- Efficacy Assessments
- Assessment of Safety
- Statistics
- Direct Access to Source Documents
- Quality Control and Quality Assurance
- Ethics
- Data Handling and Record Keeping
- Financing and Insurance
- Publication Policy
- Supplements

CDISC

Protocol Representation – Hierarchy
Sample: *Sections, Sub-sections, Elements*



Microsoft Excel - PR elements_revised JAN 2005_ready to post.xls

File Edit View Insert Format Tools Data Window Help

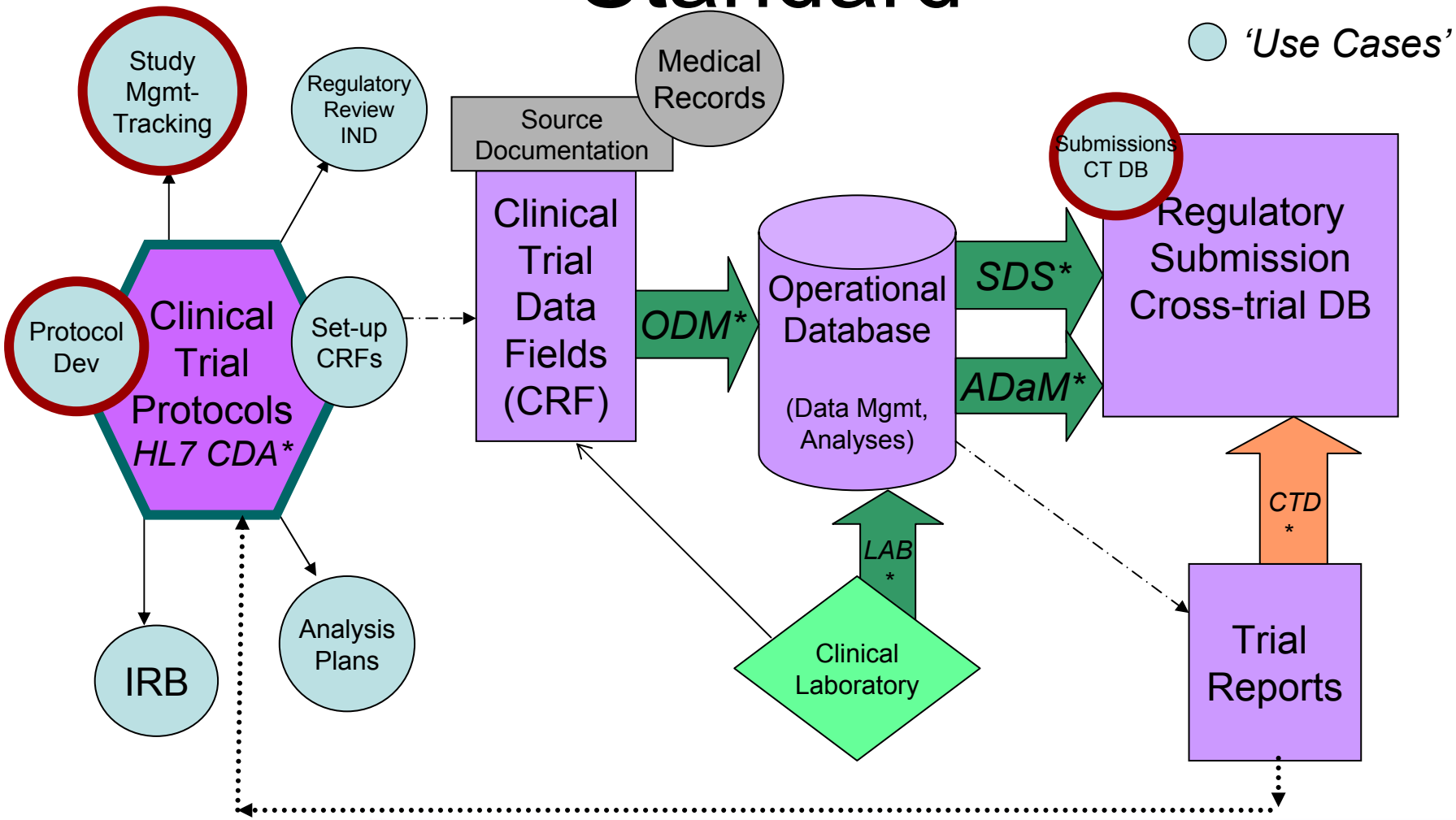
H83 = placebo, active, no treatment, dose response, external (excluding historical), multiple controls

	A	B	C	D	E	F	G	H	I	
1	**ELEMENT NUM**	**ELEMENT NAME**	**ELEMENT DEFINITION (FROM GLOSSARY)**	**DEFINITION SOURCE**	**ELEMENT EXPLANATION (recommendations/ examples for usage)**	**ELEMENT SOURCE**	**ELEMENT SOURCE CONTENTS**	**SUGGESTED CODE LIST (terminology group)**	**CODE LIST GLOSSARY REFERENCE (terminology group)**	**SUG ATTI**
2	**Document Type**									
4	**GENERAL INFORMATION**									
5	1	Protocol Title			Full text of the protocol/study title	*ICH E6 6.1.1, EUDRACT*	*Appendix I A. Full title of the protocol*	NA		NA
6	2	Protocol Short Title			Name or abbreviated title of the trial wherever available	*EUDRACT*	*Appendix I A.Abbreviated title of the trial*	NA		NA
7	3	Protocol identifying number			Sponsor protocol number;and/or Unique EMEA code issued to sponsor by a central function within EMEA at the time of submission of clinical trial information to authorities. Any amendments will be reference this number also. The code will be used in reporting suspected serious adverse events. May include other numbers, e.g. national number, cooperative group protocol number)	ICH E6 6.1.1, EUDRACT	*National trial # reference, EUDRACT clinical trial number, Sponsor code = sponsor protocol number*	NA	CDISC, EUDRACT	Spons protoc identif numbe EUDR clinica numbe regula ISRCT nation other (cooper numbe
	4	Regulatory Investigational Product Number			Assigned by regulatory agency for the an investigational new product application with	ICH E6 6.1.1		NA		NA

PROTOCOL ELEMENTS | Supplements

Ready NUM

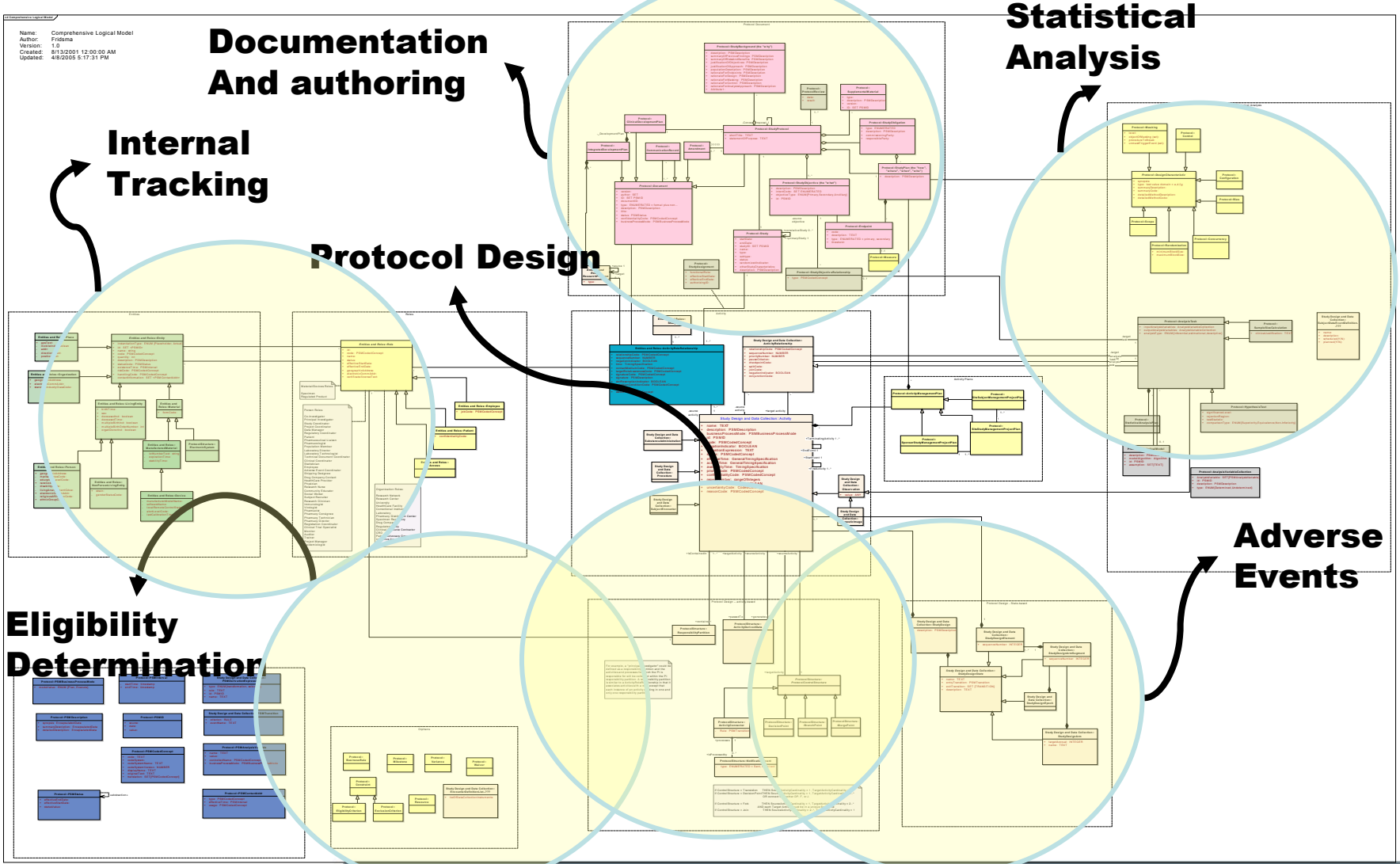
Protocol Representation Standard



PR Group: 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**

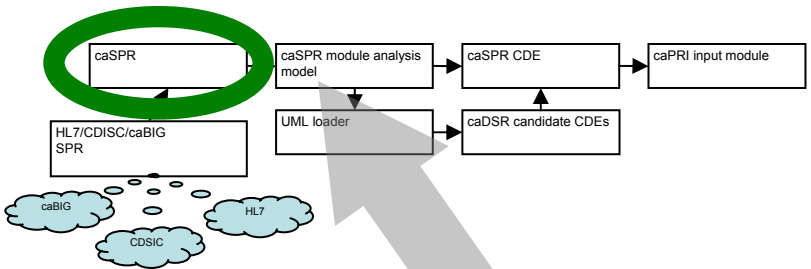
The Structured Protocol Representation



Source: Doug Fridsma, University of Pittsburgh, May 2005

CDISC℠

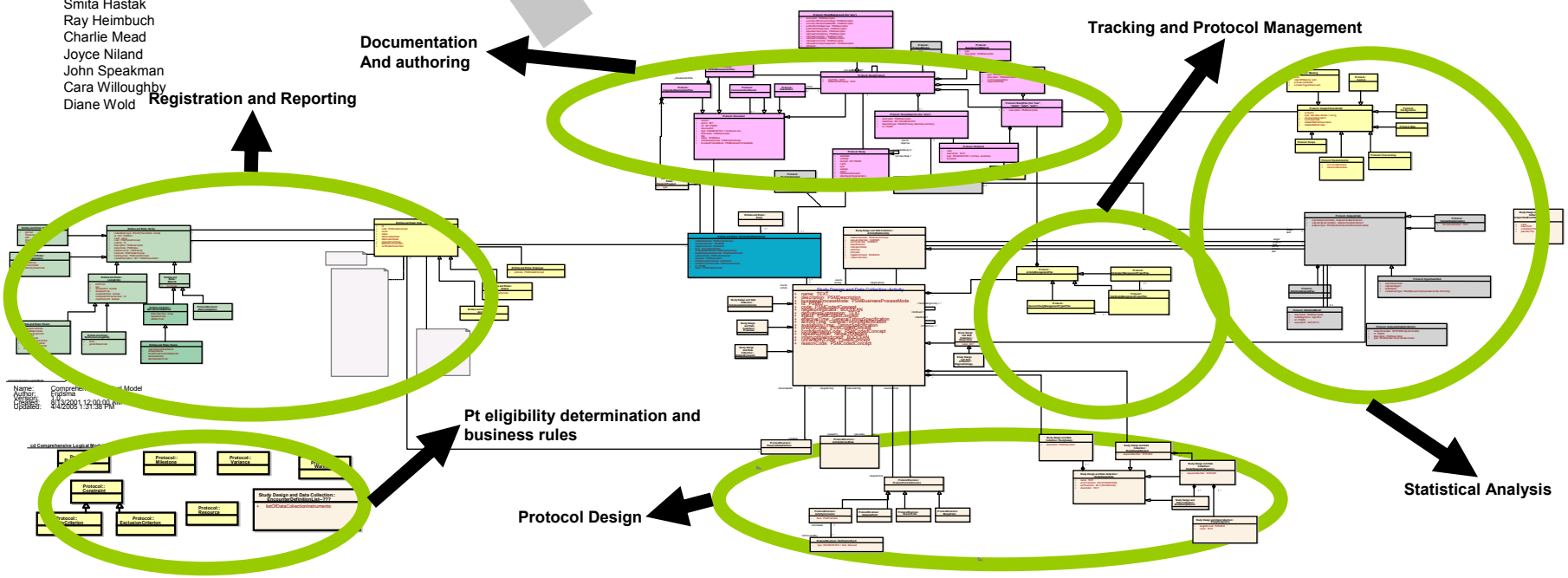
CDISC, HL7, and caBIG collaboration: The Cancer Biomedical Informatics Grid Structured Protocol Representation



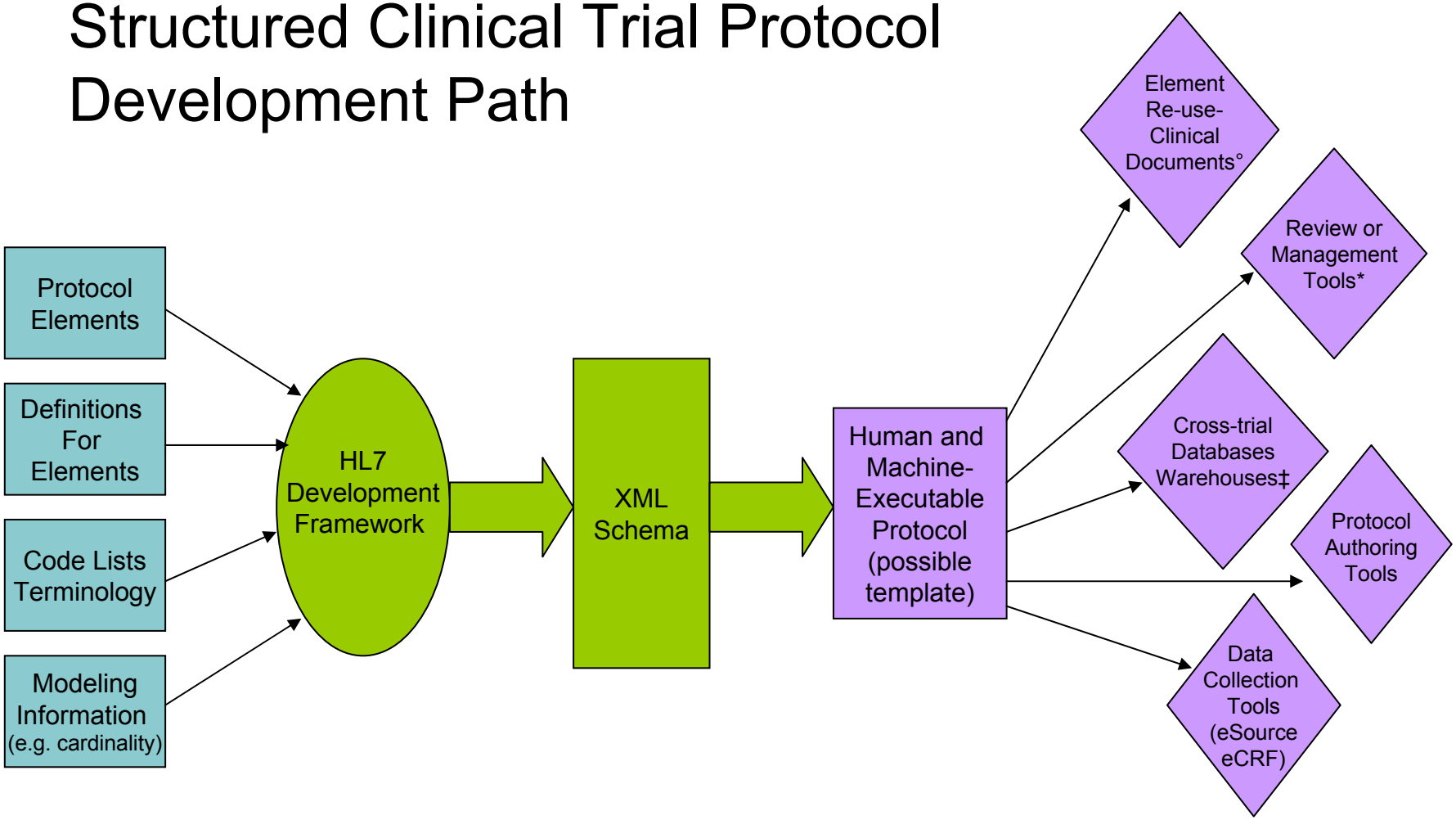
Increasing specificity and computability

The Clinical Data Interchange Standards Consortium (CDISC) Domain Space Analysis Modeling (DSAM) effort is a strategic initiative between CDISC, Health Level Seven (HL7) and caBIG to develop, support, influence and harmonize standards for data representation and exchange in clinical research.
A requirement for seamless syntactic and semantic interoperability in clinical research is a common, shared data representation. Such an exchange standard will facilitate data sharing and help to speed the delivery of innovative solutions to the cancer patient based on biological research, improve the efficiency and timeliness of data reporting, enhance patient safety during clinical trials, and improve the shared care of oncology patients.
Currently, there are two major standards for data exchange in healthcare. The CDISC group has focused on data exchange and reporting among pharmaceutical companies engaged in clinical research, while HL7 has developed healthcare messaging standards for all aspects of patient care. The caBIG community is playing an aggressive part in the activities associated with harmonizing these two models, and constructing a common model that can be shared among CDISC, HL7, and caBIG members. Specifically, caBIG participants have:
1. Participated in development of the CDISC Clinical Trials DSAM , a UML class model representing the common shared concepts of clinical research across the key communities – pharmaceutical companies, federal agencies and academic medical centers.
2. Supported the mapping of the CDISC DSAM to the HL7 v3 Reference Information Model (RIM) at the detail attribute level. This will ensure that all caBIG and CDISC data exchange requirements are addressed by the HL7 v3 messaging standards. Concepts identified in CDISC modeling may uncover new additions for the RIM, in turn making the RIM more robust
3. Participated in the CDISC Protocol Representation Group to develop a common terminology and vocabulary in support of clinical research data exchange standards. The CDSIC vocabulary is being maintained in the NCI's Cancer Data Standards Repository (caDSR) and will harmonize with the NCICB's Common Data Elements (CDEs).
This presentation focuses on the first of these three activities – the development of the UML DSAM, representing many hours of intensive interactive modeling by domain experts and modeling experts from pharmaceutical companies, HL7, and caBIG. The goal of the model is not only to facilitate seamless data exchange, but also to explore a computable representation of a clinical trial for planning, execution and analysis of clinical trials. In addition to data exchange, it is hoped this shared model will form the backbone for the applications developed in caBIG's Clinical Trials Management Systems (CTMS) domain-specific workspace. Such applications could include advanced protocol authoring tools, tools for data reporting and submissions, clinical trials management, and interfaces to clinical systems.
This initiative furthers the caBIG vision to provide a common informatics platform to exchange standardized data between disparate systems to support the cancer research community. The focus to promote data standardization and ability to exchange data seamlessly among the various stakeholders will put critical information in the hands of researchers, thus enabling them to broaden the scope of their research and allow hitherto unaddressable research directions to be pursued.

Participants
Christo Andonyadis
Greg Anglin
Lisa Chatterjee
Julie Evans
Douglas B Fridsma
Smita Hastak
Ray Heimbuch
Charlie Mead
Joyce Niland
John Speakman
Cara Willoughby
Diane Wold



Structured Clinical Trial Protocol Development Path



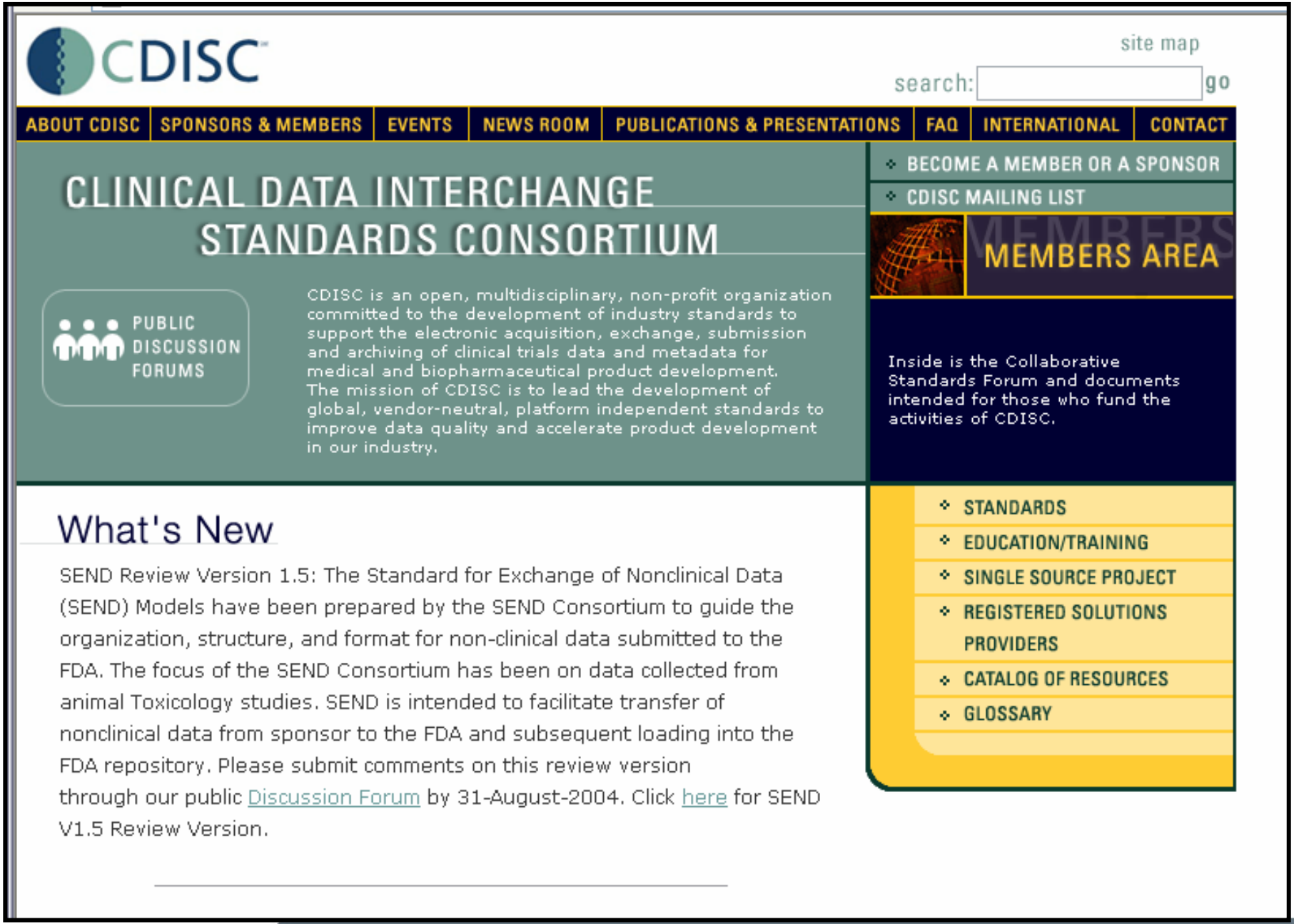
PR Group and Reviewers → HL7 Modeling → HL7 Balloting → Implementation/Tools

* e.g. Planned vs. Actual; Project Status

‡ e.g. Regulatory, Pharma Company, IRB

° e.g. Study Reports, PI Brochures

CDISC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FAQ
INTERNATIONAL
CONTACT
CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM
PUBLIC DISCUSSION FORUMS
CDISC is an open, multidisciplinary, non-profit organization committed to the development of industry standards to support the electronic acquisition, exchange, submission and archiving of clinical trials data and metadata for medical and biopharmaceutical product development. The mission of CDISC is to lead the development of global, vendor-neutral, platform independent standards to improve data quality and accelerate product development in our industry.
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Inside is the Collaborative Standards Forum and documents intended for those who fund the activities of CDISC.
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EDUCATION/TRAINING
SINGLE SOURCE PROJECT
REGISTERED SOLUTIONS PROVIDERS
CATALOG OF RESOURCES
GLOSSARY
What's New
SEND Review Version 1.5: The Standard for Exchange of Nonclinical Data (SEND) Models have been prepared by the SEND Consortium to guide the organization, structure, and format for non-clinical data submitted to the FDA. The focus of the SEND Consortium has been on data collected from animal Toxicology studies. SEND is intended to facilitate transfer of nonclinical data from sponsor to the FDA and subsequent loading into the FDA repository. Please submit comments on this review version through our public Discussion Forum by 31-August-2004. Click here for SEND V1.5 Review Version.

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

CDISC

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