PhUSE

10-12 September 2005
Heidelberg, Germany

Setting the
Global Standard
for Clinical Data

CLINICAL DATA INTERCHANGE
STANDARDS CONSORTIUM

An Introduction to CDISC: Part One
"What is CDISC and Why Standards?"

Rebecca Kush, PhD, CDISC
David Handelsman, SAS

Lack of standards make our lives more complicated

- Electrical power

Standards make our lives easier

- ATMs
- Bancomat
- Geldautomat

CBSNEWS.com

April 10, 2005 4:42pm ET ▸ The Early Show ▸ CBS Evening News ▸ 48 Hours

HEALTH ▪ Section Front

E-mail This Story Printable Version

Arthritis Drug Vioxx Recalled

NEW YORK, Sept. 30, 2004

FREE VIDEO

Anti-Arthritis Rx Risks

A Merck lab technician checks Vioxx pills. (Photo: AP)

QUOTE

"If I were sitting on the FDA what I think what I would do is really urge physicians not to

(CBS/AP) Pharmaceutical giant Merc Co. is pulling its blockbuster arthritis Vioxx from the market worldwide bec new data from a clinical trial found ar increased risk of heart attack and str

Merck said Thursday that data from t trial showed the increased risk of he attack and other cardiovascular complications began 18 months afte patients started taking Vioxx.

FDA U.S. Food and Drug Administration

FDA Home Page | Search FDA Site | FDA A-Z Index | Contact FDA

Congressional Testimony

Te

▪ **November 18, 2004**

D., Acting Commissioner of Food and Drugs
to Ensure the Safety, Effectiveness, and Availability

n Energy and Commerce, United States House of

rector, Office of New Drugs

United States Senate

D., Acting Commissioner of Food and Drugs
to Ensure the Safety, Effectiveness, and Availability

n Government Reform, United States House of

Health - AP

Pfizer Takes Painkiller Bextra Off Market

AP Associated Press

Thu Apr 7, 7:48 PM ET MY Y! Health - AP

By LAURAN NEERGAARD, AP Medical Writer

WASHINGTON - The blockbuster painkiller Bextra was yanked off the market Thursday, and the government ordered that 19 other popular prescription competitors — from Celebrex to Mobic to high-dose naproxen — carry tough new warnings that they, too, may increase the risk of heart attacks and strokes.

AFP/File Photo

The warnings encompass an entire class of anti-inflammatory medicines called NSAIDs that are the backbone of U.S. pain treatment, not just newer versions of the painkillers initially suspected when the heart concerns made headlines last fall.

CDISC

Clinical Information Dispersion Today

- Healthcare information is found in:
  - paper medical records
  - disparate databases
  - hospital-based information systems
- Clinical research data exists in:
  - additional databases
  - research notebooks
- Clinical trial data collection:
  - 3-part NCR forms in ~85% of trials
  - multitude of electronic data capture applications
    - eCRF
    - IVRS
    - ePRO

The Move to Standards

"Faced with rapid changes, the nation's healthcare system has **fallen short of its ability to translate information into knowledge** that can be used in practice, and to apply new technology safely and appropriately.

The results are exactly what you would expect. Everyone who uses the current system **constantly confronts large information gaps**, whether it's at the doctor's office, on the hospital ward or at government agencies charged with protecting the public health. That goes for the FDA -- we're no exception."

Dr. Mark McClellan, former FDA Commissioner
CDISC Interchange, October 2003

"Innovation depends upon standardization."

Dr. Bob O'Neill, Director, Office of Biostatistics, CDER, FDA

Benefits of Standards: Operational

- Increase efficiencies of performing clinical trials
- Simplify processes among investigators, pharma companies, CROs, vendors, laboratories
- Streamline data collection at investigator sites
- Improve sponsor's access to data and ability to understand it
- Provide long-term means for electronic data archive
- Facilitate FDA review of submissions
- Improve links between healthcare delivery and clinical research

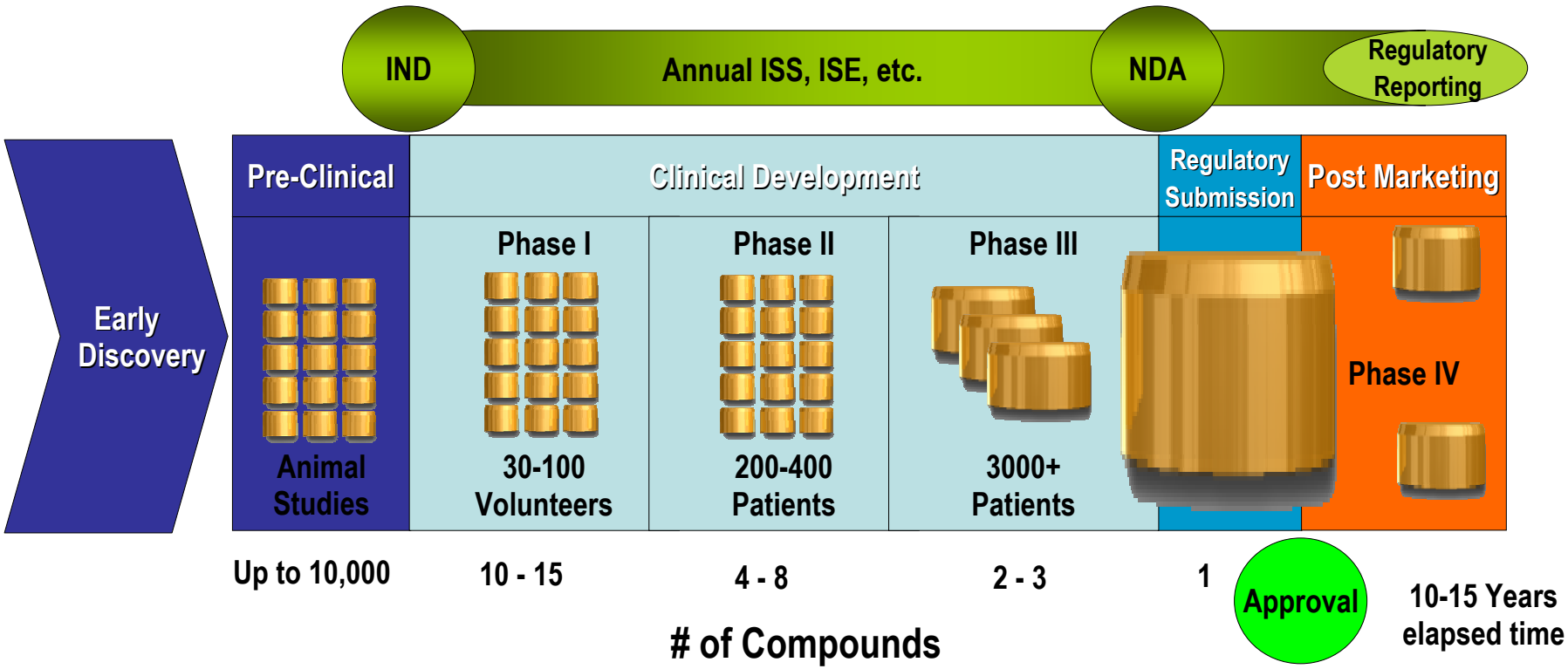
Benefits of Standards: Scientific

- Facilitate integration of data
  - Across trials, compounds, companies
- Enable assessment of trends and patterns in data
  - Public health benefit
  - Drug development benefit
  - Better guidance for studying disease states
- Allow companies to focus on their potential therapeutic products vs. data issues
- Improve safety monitoring and pharmacovigilance
- Support ad hoc analyses; enhance decision-making capabilities during data review

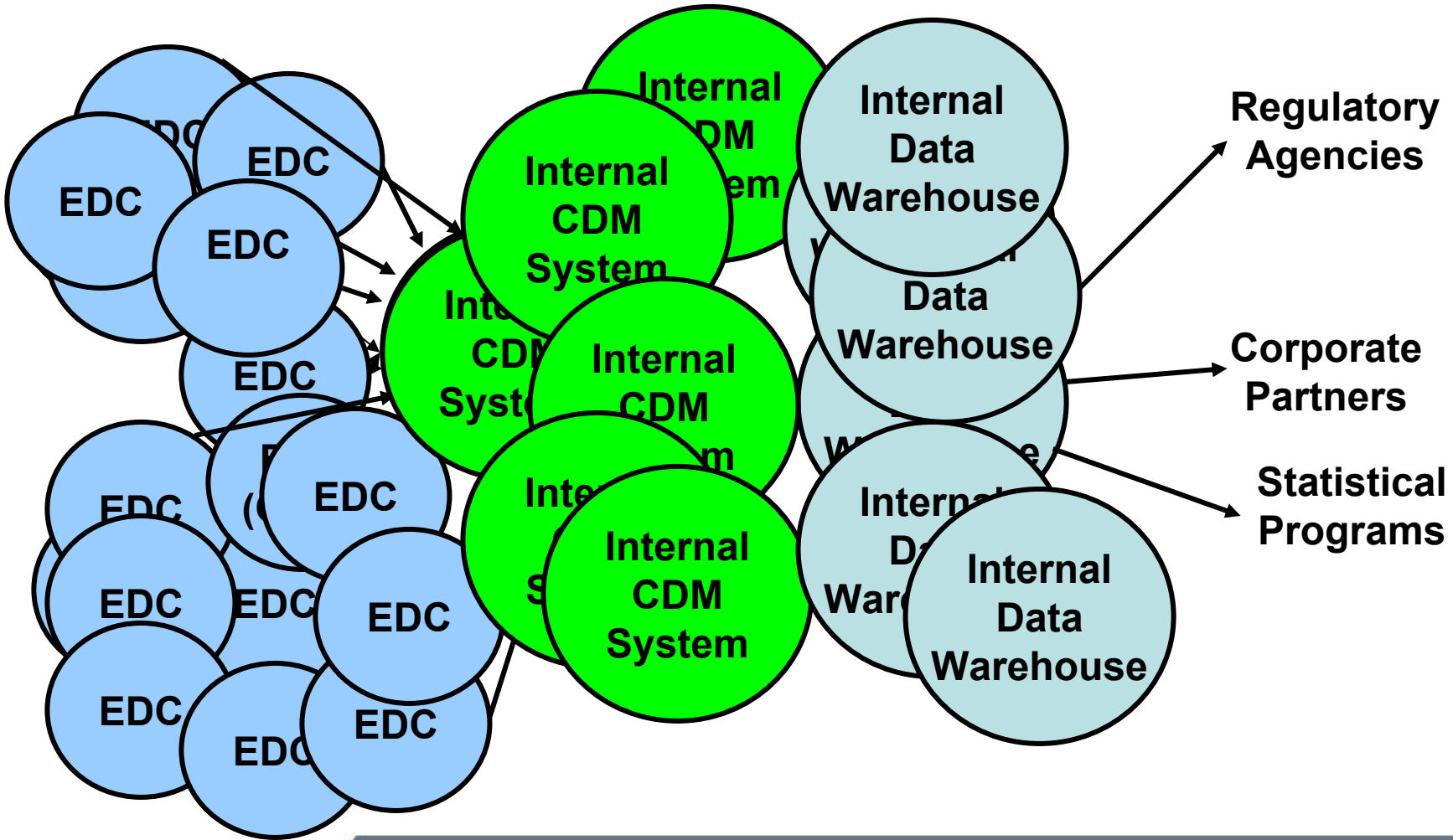
Standards: Yours, Mine, Ours

- Internal standards are a good first step, but are insufficient
  - Streamline internal processes
  - Little effect of data transfer and interoperability with external organizations
  - CROs are a classic example of the limits of internal standards
- Development and adoption of public standards are the next logical steps
  - Increase data efficiency of all participating organizations
  - Brings a renewed focus to the science of clinical research

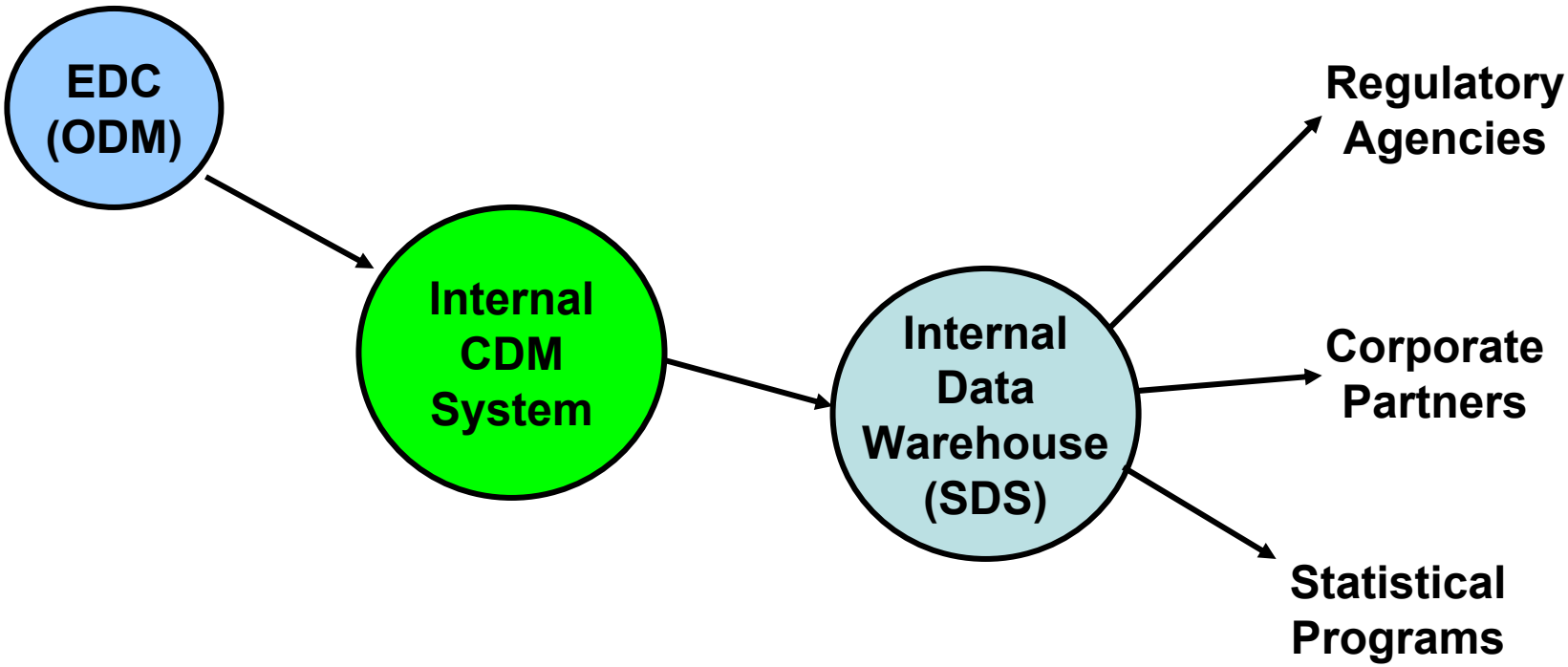
Why Are Standards Important?



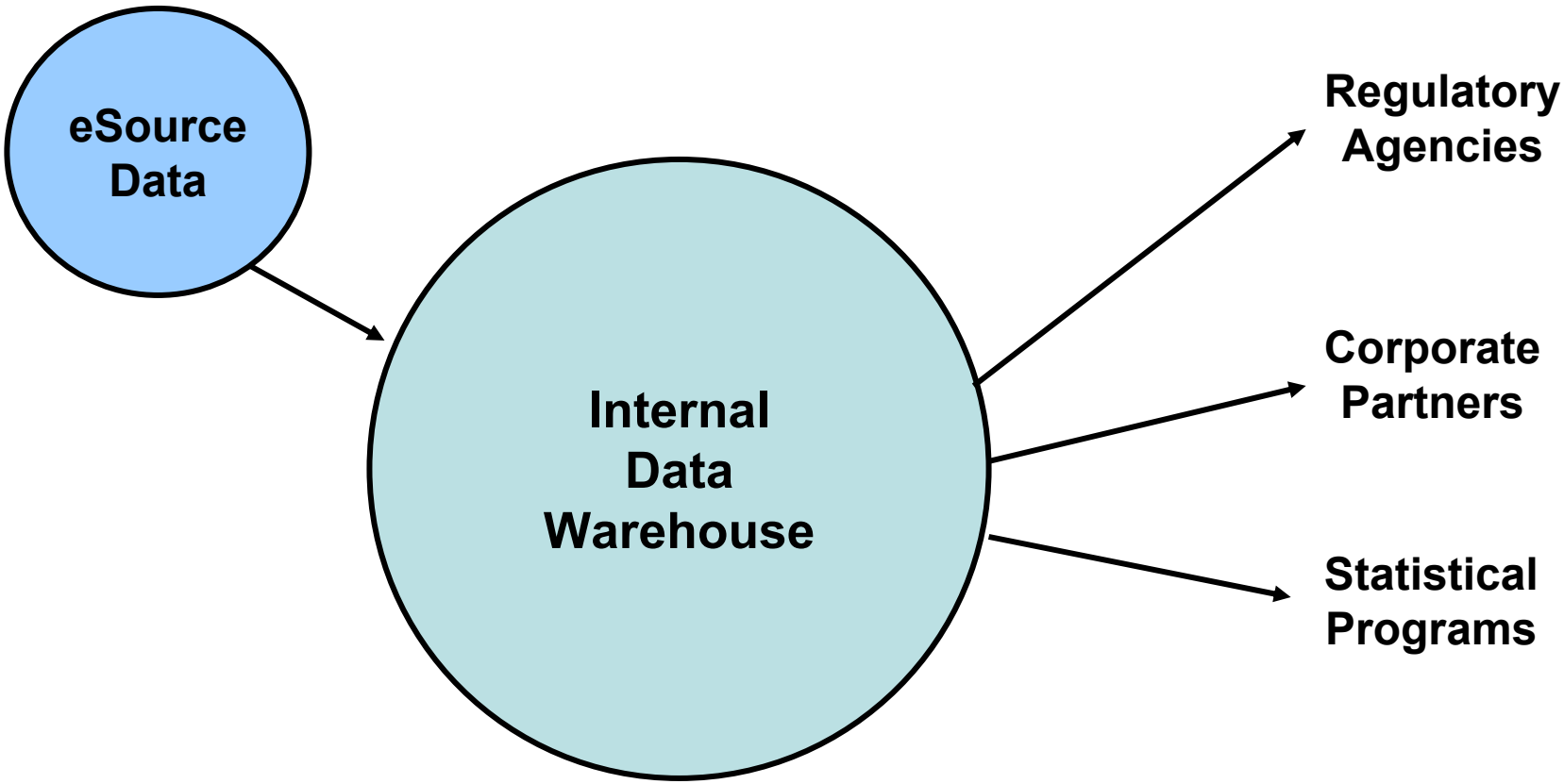
Why Are Standards Important?
Before Standards



After CDISC Standards



Looking into the future



…what other options exist?

Benefits of Standards – Regulatory View

Before SDTM

- Domains = Yes
- Standard Domain Names = No
- Standard Structure = No
- Standard Variables = No
- Standard Variable Names = No
- Standard Terms = No

After SDTM

- Domains = Yes
- Standard Domain Names = Yes
- Standard Structure = Yes
- Standard Variables = Yes
- Standard Variable Names = Yes
- Standard Terms = not yet, but coming

Benefits of Standards – Regulatory View

"The importance of a standard for the exchange of clinical trial data cannot be overstated. FDA reviewers spend far too much valuable time simply reorganizing large amounts of data submitted in varying formats. Having the data presented in a standard structure will improve FDA's ability to evaluate the data and help speed new discoveries to the public." *-Lester Crawford, Former Commissioner, FDA*

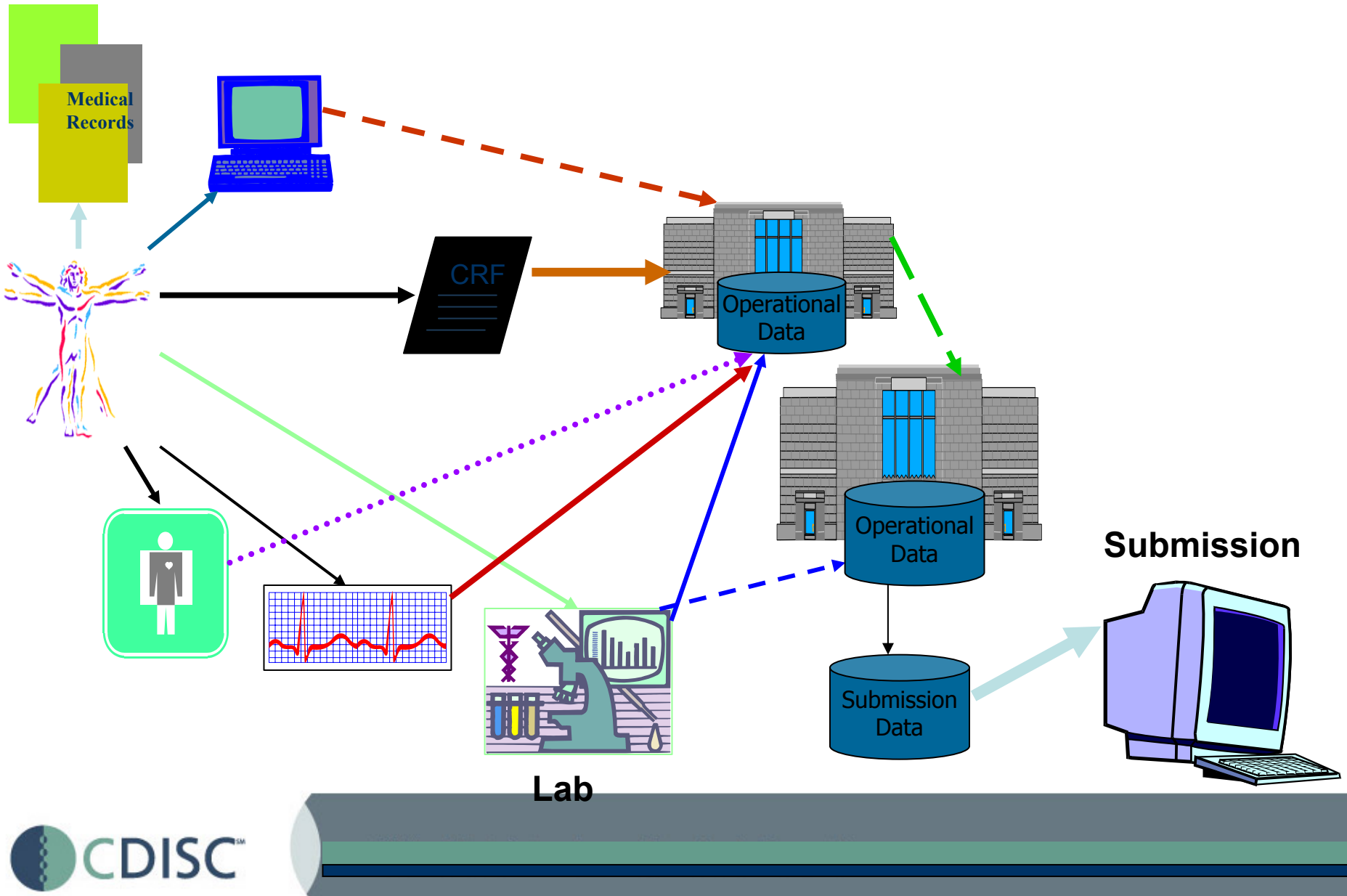

CD ISC

Clinical Data Interchange Standards Consortium: Original Mission Statement

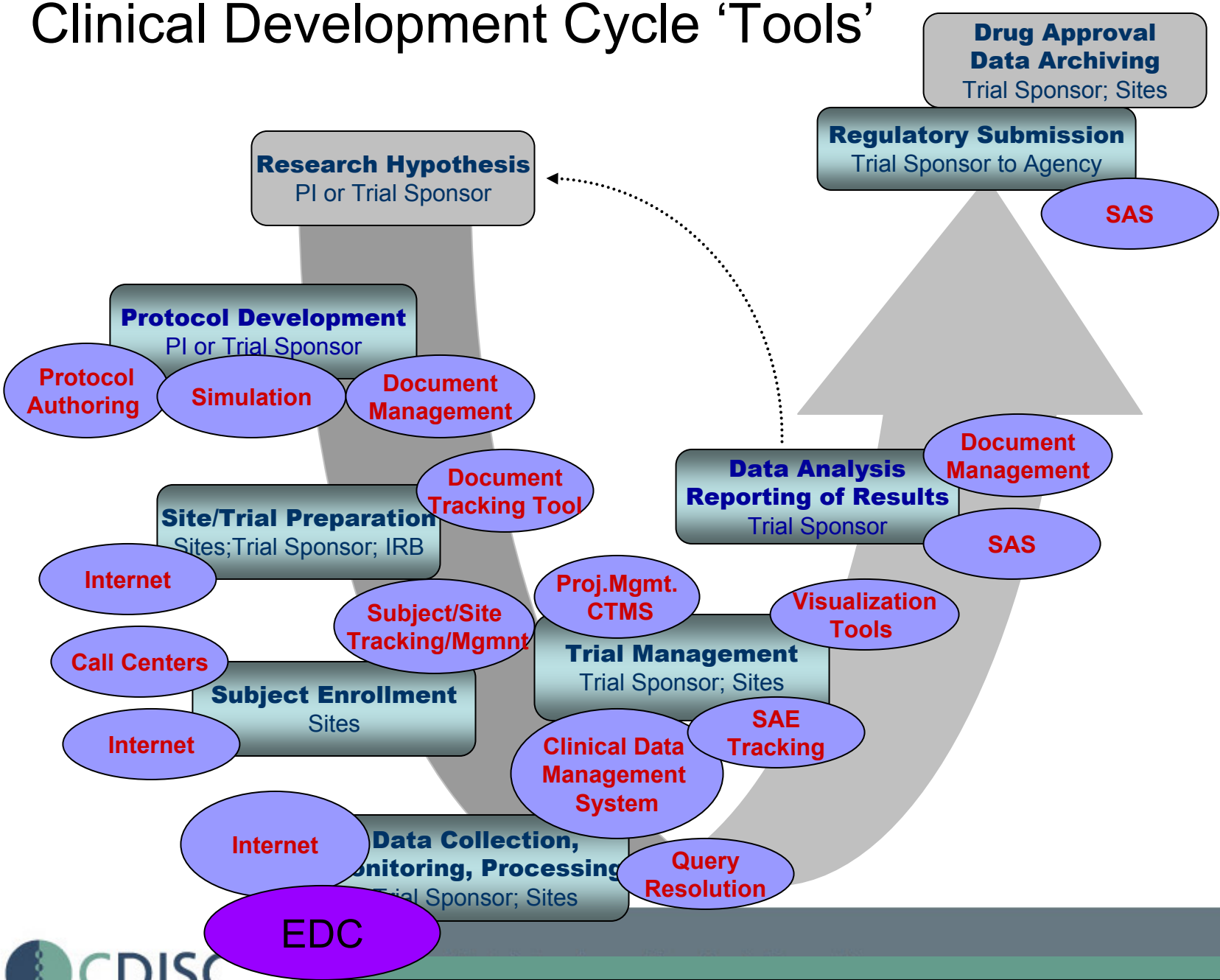
CDISC is an open, multidisciplinary, non-profit organization committed to the development of worldwide industry standards to support the electronic acquisition, exchange, submission and archiving of clinical trials data and metadata for medical and biopharmaceutical product development.

The mission of CDISC is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.

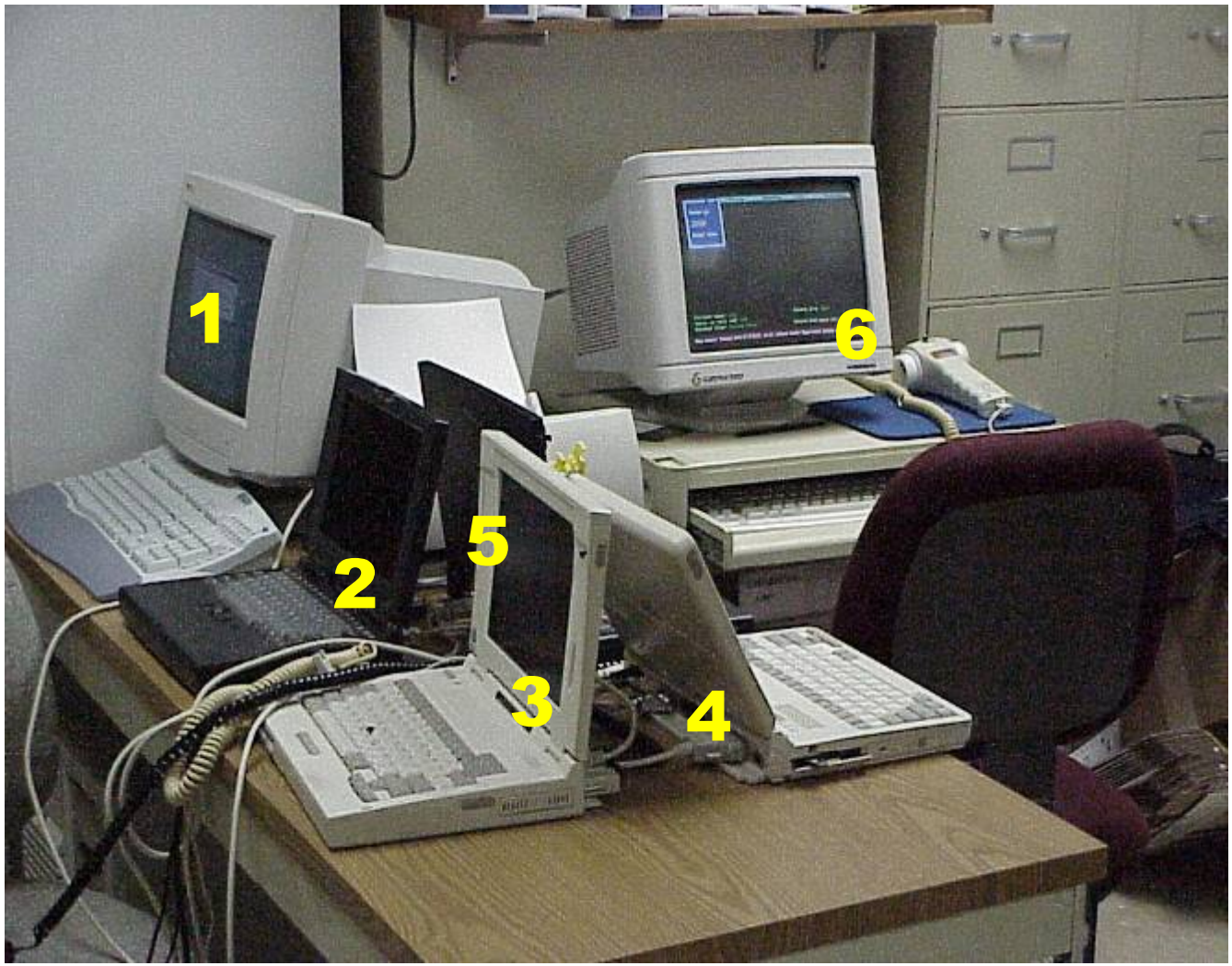
Current State of Clinical Data Transfer



Clinical Development Cycle 'Tools'

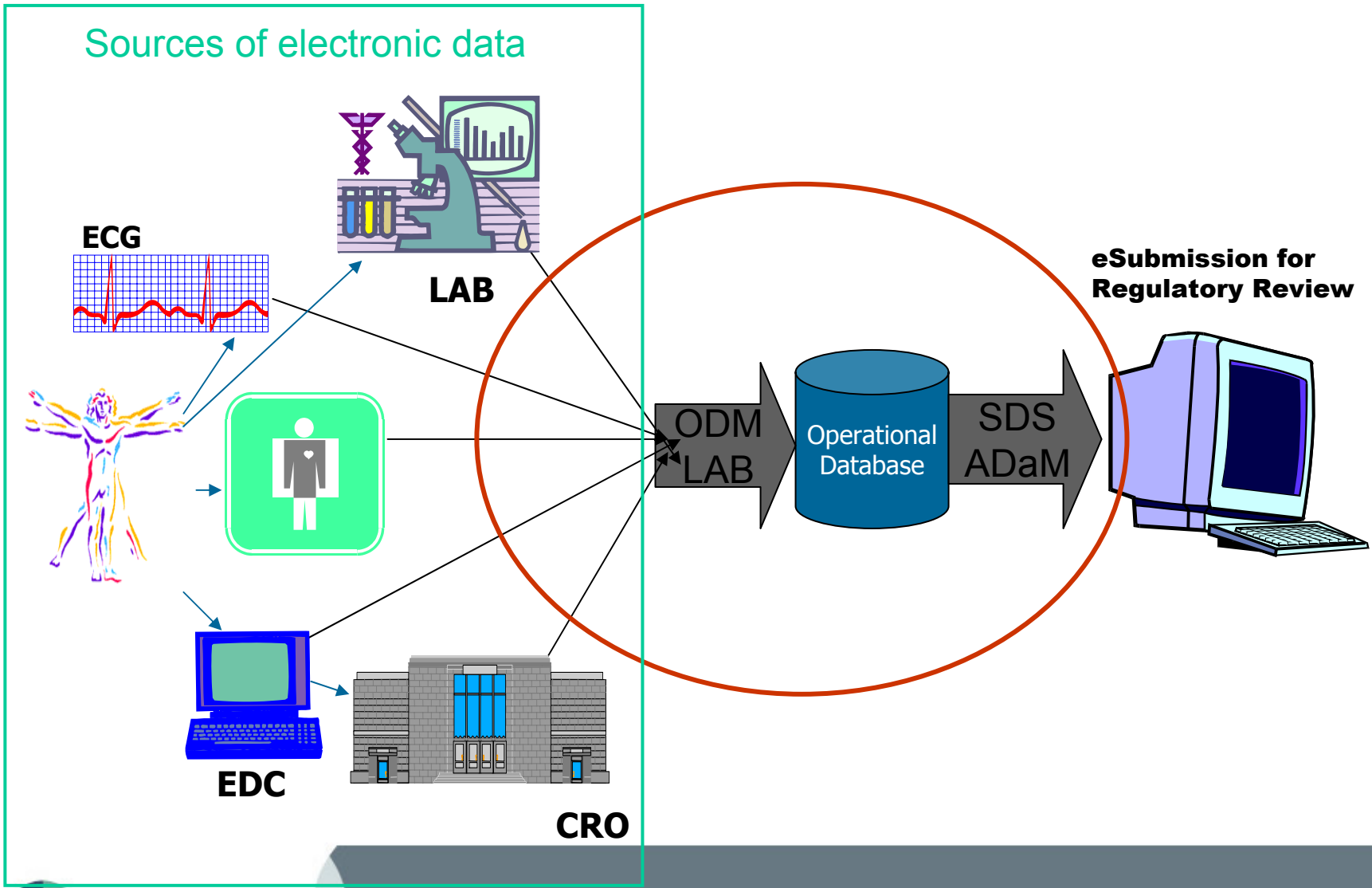


Clinical Back Office



EDC Without Standards, courtesy Charles Jaffe, MD, PhD

The Future: Standards to Facilitate Data Flow .from Source to Reviewers



CDISC

- Formed in 1997 as a volunteer group
- As of 2000, incorporated and funded as non-profit organization
- Now supported by >170 member companies:
  - pharmaceutical companies; biotech companies; CROs/service providers; technology providers
- CDISC Groups now growing in Japan, Europe, India
- Standards developed through consensus-based approach with public reviews; open standards

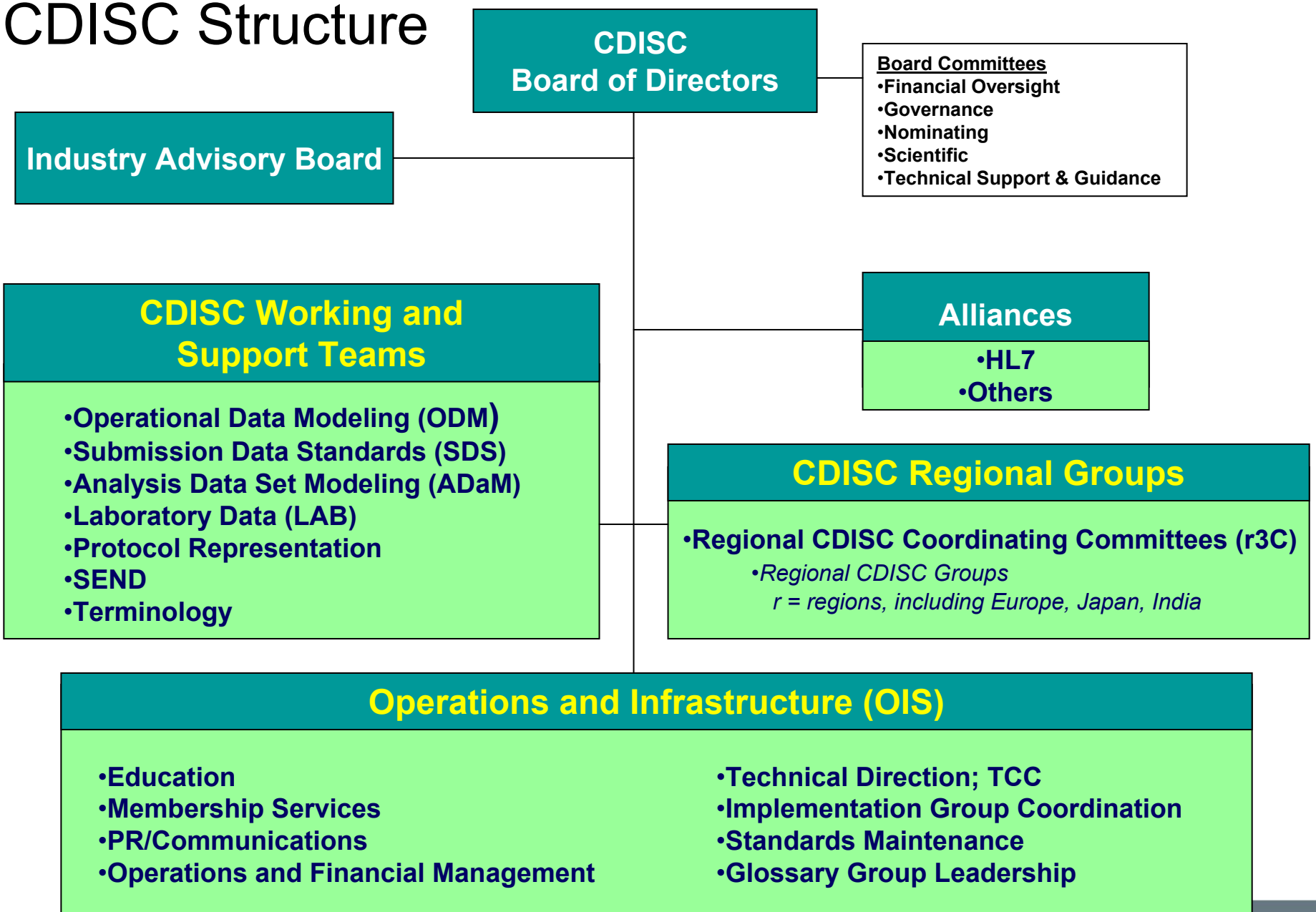
CDISC Principles

- Lead the development of **standard data models** that improve process efficiency while supporting the scientific nature of clinical research.
- Recognize the ultimate **goal of creating regulatory submissions** that allow for flexibility in scientific content and are easily interpreted, understood, and navigated by regulatory reviewers.
- Acknowledge that the data content, structure and quality of the standard data models are of paramount importance, **independent of implementation strategy and platform.**

CDISC Principles

- Maintain a **global, multidisciplinary, cross-functional** composition for CDISC and its working groups.
- Work with other professional groups to encourage that there is **maximum sharing of information and minimum duplication of efforts**.
- Provide **educational programs** on CDISC standards, models, values and benefits.
- Accomplish the CDISC goals and mission **without** promoting any individual vendor or organization.

CDISC Structure



Standards

- Definition of Standard: An object considered by an authority or by general consent as a basis of comparison; an approved model*
- Standard data models, metadata models, codes, terminology, content, technology .
- Definition of Model: A standard or example for imitation or comparison*

* The Random House Dictionary of the English Language, unabridged version

Data and Metadata: Definitions

- Data
  - representations of facts, concepts, or instructions in a manner suitable for communication, interpretation, or processing by humans or by automated means. [FDA] (Synonym: Information)
- Metadata
  - Data about data
- Metadata Elements
  - The metadata of a study describes the types of study events, forms, item groups, and items that are allowed in the study.

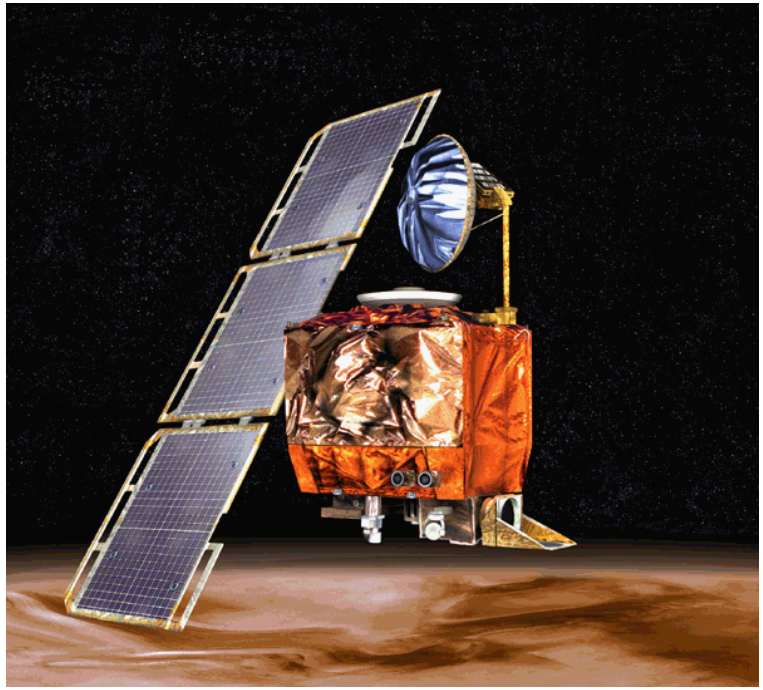
How Important is Metadata?

Event	Time	D	S	F
Begin	9/23/99 02:01:00	121,900,000	12,300	143.878
End	9/23/99 02:17:23		9,840	

Event	Time	D	S	F
Start	19990923 05:01:00	196,200,000	5.5	640
Finish	19990923 05:17:23		4.4	

Slide developed by David Christiansen, DrPH

In this case $125,000,000: Mars Climate Orbiter



Mars Orbit Insertion Burn	**M/D/Y HH:MM:SS PDT (Earth Receive Time, 10 min. 49 sec. Delay)**	**Distance (miles)**	**Speed (miles/hr)**	**Force (Pounds)**
Begin	9/23/99 02:01:00	121,900,000	12,300	143.878
End	9/23/99 02:17:23		9,840	
Mars Orbit Insertion Burn	**YYYYMMDD EDT (Earth Receive Time, 10 min. 49 sec. Delay)**	**Distance (km)**	**Speed (km/sec)**	**Force (Newtons)**
Start	19990923 05:01:00	196,200,000	5.5	640
Finish	19990923 05:17:23		4.4	

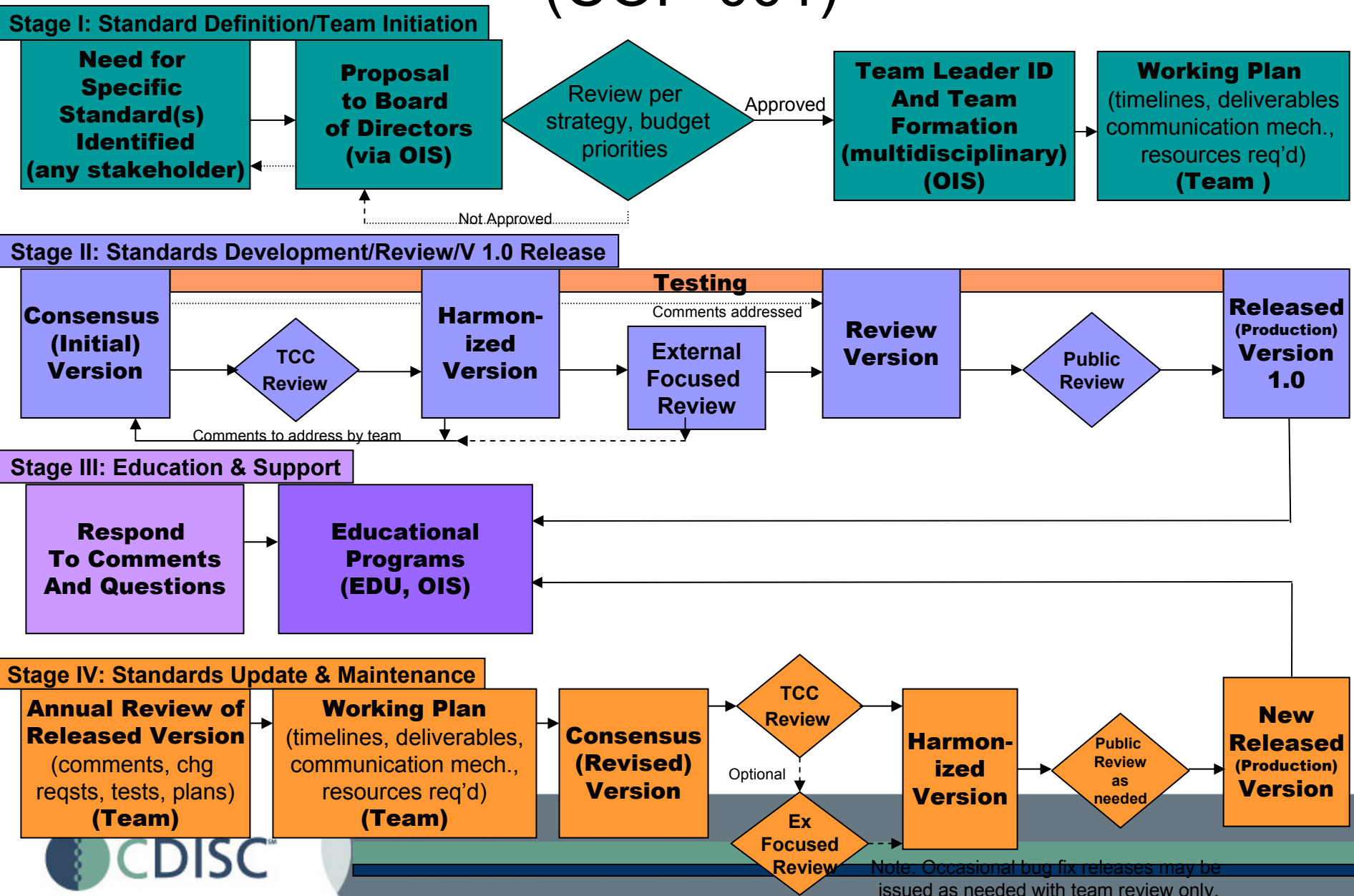
Data Interchange: Definition

- Data Interchange
  - the transfer of information between two or more parties. Data interchange is distinguished from data transfer in that the integrity of the contents of the data is maintained. [CDISC]
- CDISC Glossary is available on the website (www.cdisc.org) and in December resource issues of Applied Clinical Trials.

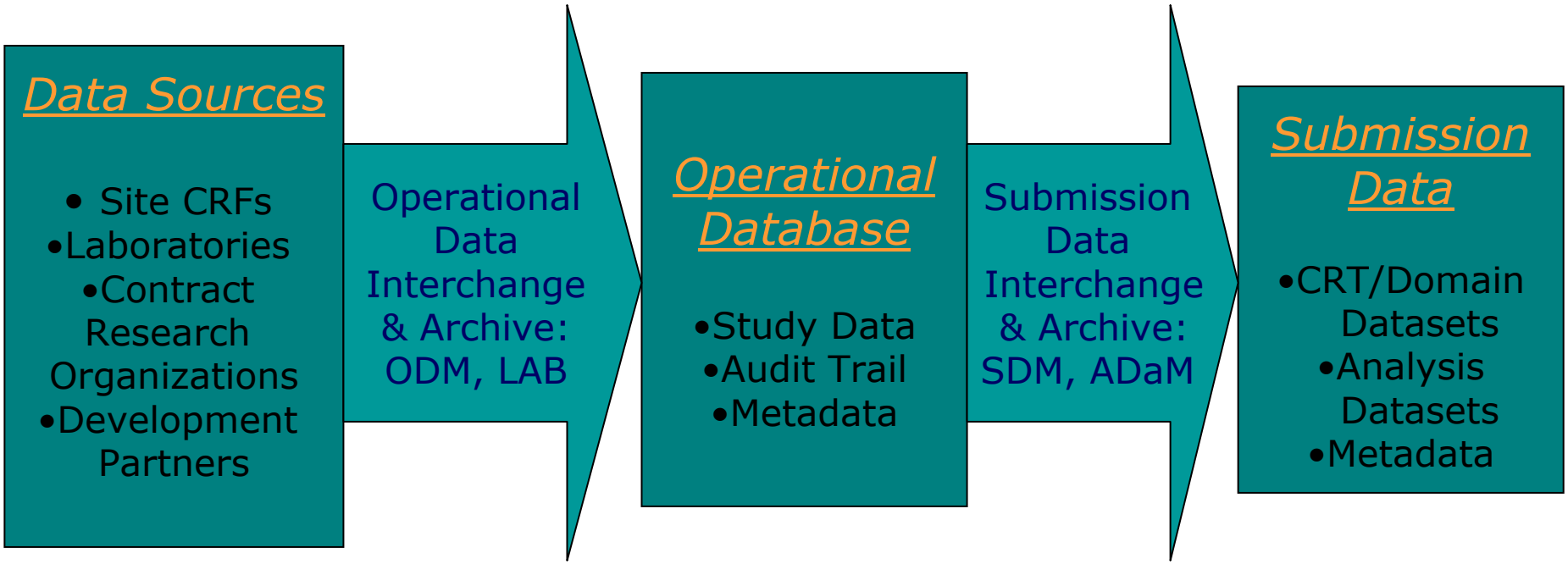
CDISC Approach

- The CDISC models are the products of contributions from numerous organizations, functional groups, and individuals; they do not have a sole source.
- Consensus building
  - Involves different disciplines within the industry
  - Involves ‘consolidating’ existing models, review comments and testing
  - Takes time, but results in widely accepted models

CDISC Standards Development Process (COP-001)



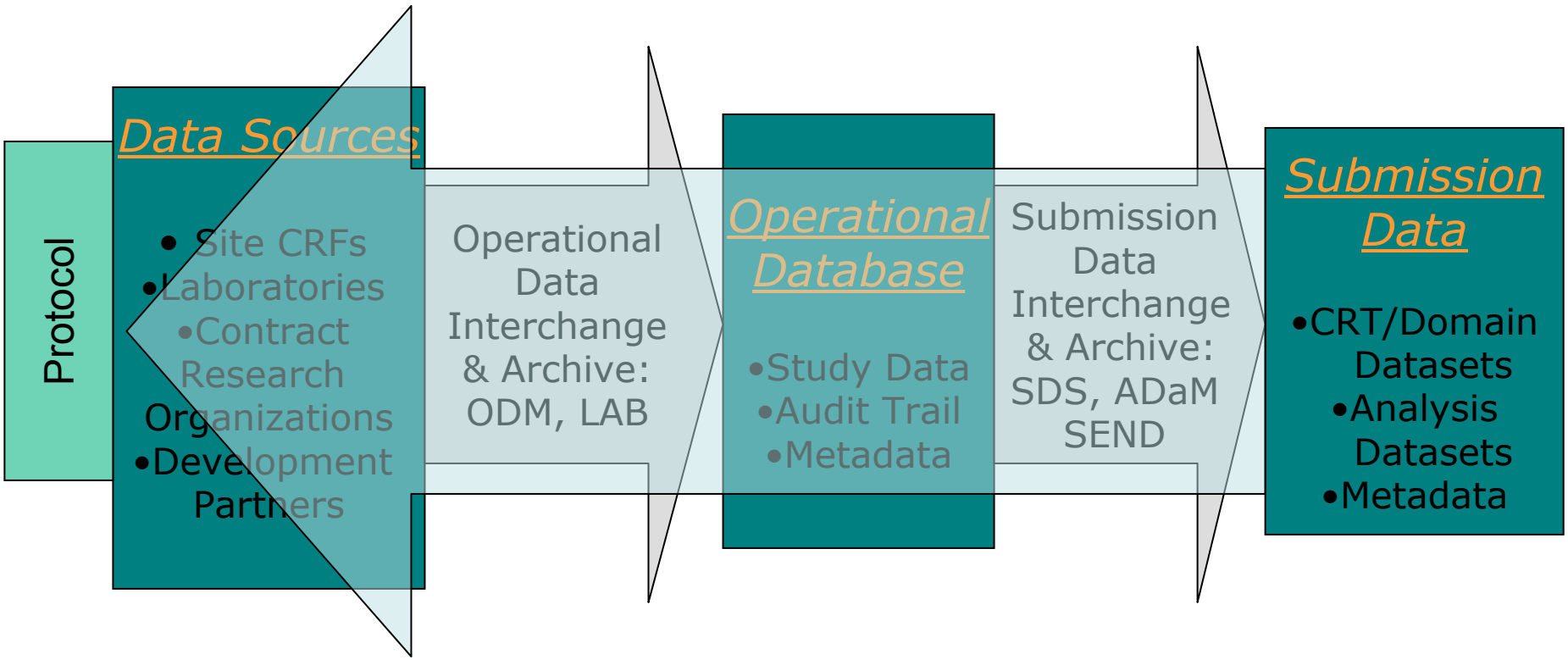
Scope of CDISC Models



ODM = Operational Data Model
LAB = Laboratory Data Model

SDM = Submission Data Model
ADaM = Analysis Data Models

Evolution of CDISC Standards: Started with the end in mind



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 Standards: Implementation (Production) Versions

Standard	Description	Implementation Release Version
Study Data Tabulation Model (SDTM), including SEND for non-clinical (animal) data	Content Model - regulatory submission of case report tabulations (CRT) and non-clinical (animal) data	July 2004
Operational Data Model (ODM)	XML-based Transport Standard – acquisition, exchange and archive	Mid-2001
Clinical Laboratory Model (LAB)	Content Model -exchange of laboratory data between labs and sponsors/CROs	Mid-2002
Analysis Dataset Model	Content Model - General Considerations Document and Examples of Datasets	Late 2004
Case Report Tabulation (CRT) Data Definition Specification (Define.xml)	Transport Standard -Describes how to create data description doc (metadata) for submission in ODM XML standard.	Late 2004
Structured Clinical Trial Protocol (SCTP)	Machine- and Human-readable model that enables exchange of protocol information amongst stakeholders.	In progress

FDA has endorsed the standards by including them as specifications in FDA Guidance.

FDA U.S. Food and Drug Administration — Department of Health and Human Services

FDA Home Page | Search FDA Site | FDA A-Z Index | Contact FDA

FDA News

FOR IMMEDIATE RELEASE
P04-73
July 21, 2004

Media Inquiries: 301-827-6242
Consumer Inquiries: 888-INFO-FDA

FDA Announces Standard Format That Drug Sponsors Can Use to Submit Human Drug Clinical Trial Data

The Food and Drug Administration (FDA) today announced a standard format, called the Study Data Tabulation Model (SDTM) developed by the Clinical Data Interchange Standards Consortium (CDISC), that sponsors of human drug clinical trials can use to submit data to the agency. It is expected that this step will lead to greater efficiencies in clinical research and FDA reviews of New Drug Applications (NDAs).

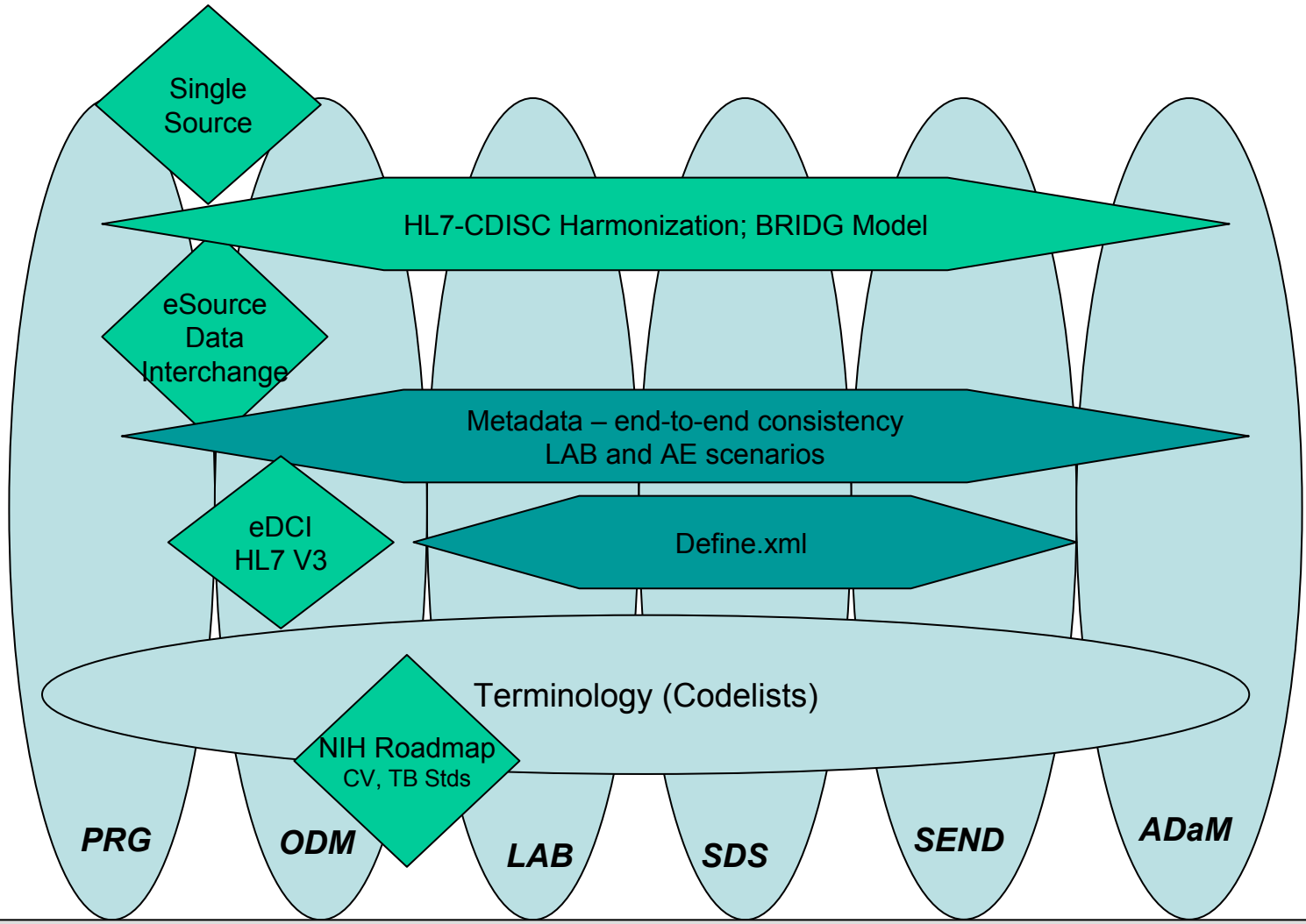
SDTM and define.xml: Specifications for FDA implementation of the ICH eCommon Technical Document.

Speaking of health benefits/opportunities to be realized from making more effective use of IT .

- "I think that CDISC will be a big part of moving FDA onto an electronic information architecture where we can realize all of these opportunities. I think this will have a profound and positive impact on our drug review process, allowing us to design trials that can be less expensive and still tell us more about the risks and benefits of a new medical product. And I think that the most significant and perhaps enduring legacy to your efforts could be the very immediate and significant impact it has on improving the lives of patients."

-Mark McClellan, MD, PhD, FDA Commissioner, September 2003

CDISC Teams and Projects - 2005

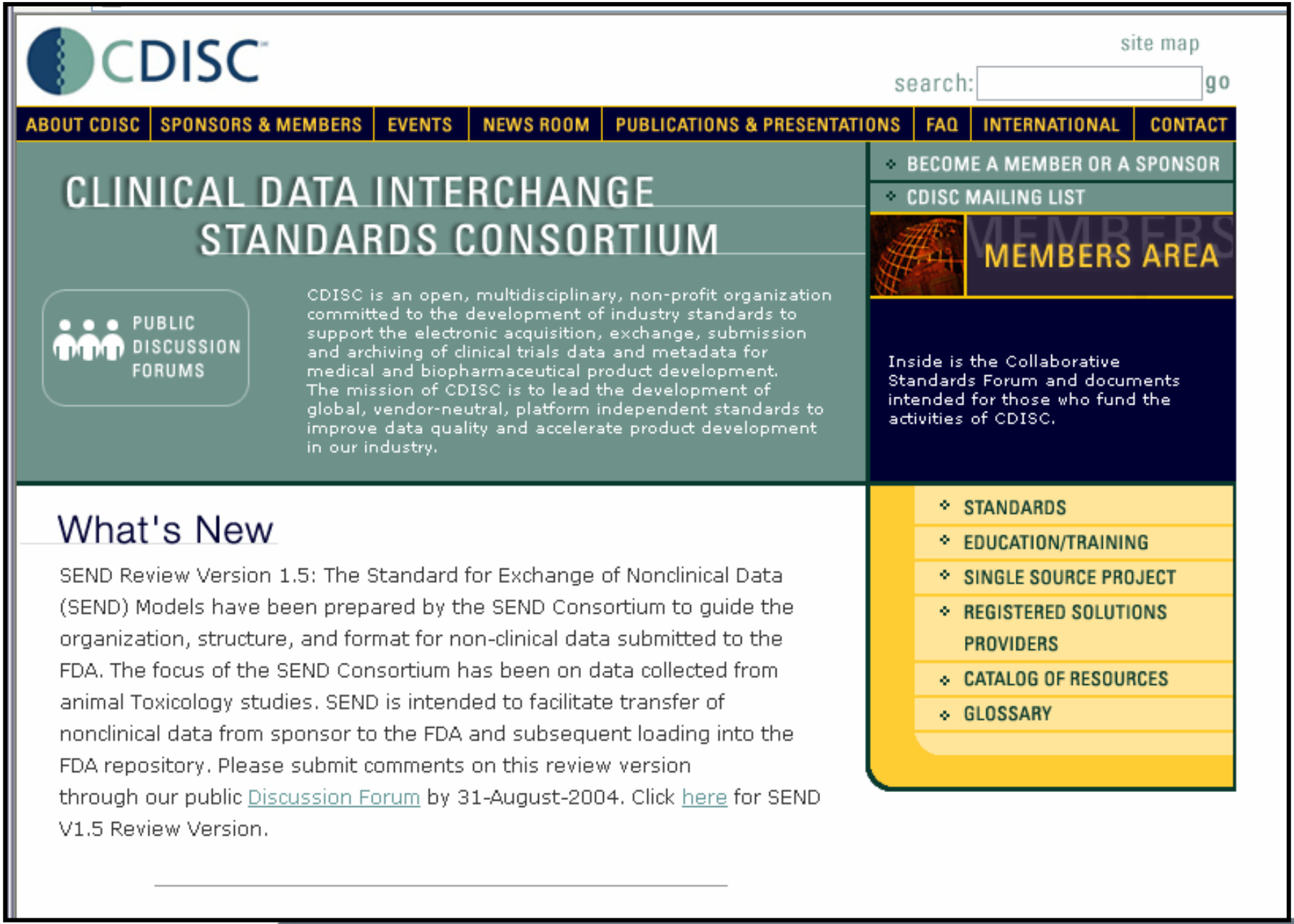


Maintenance, Member Relations, Education and Implementation Groups, Glossary

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
site map
search:
go
ABOUT CDISC
SPONSORS & MEMBERS
EVENTS
NEWS ROOM
PUBLICATIONS & PRESENTATIONS
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.
BECOME A MEMBER OR A SPONSOR
CDISC MAILING LIST
MEMBERS AREA
Inside is the Collaborative Standards Forum and documents intended for those who fund the activities of CDISC.
STANDARDS
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