

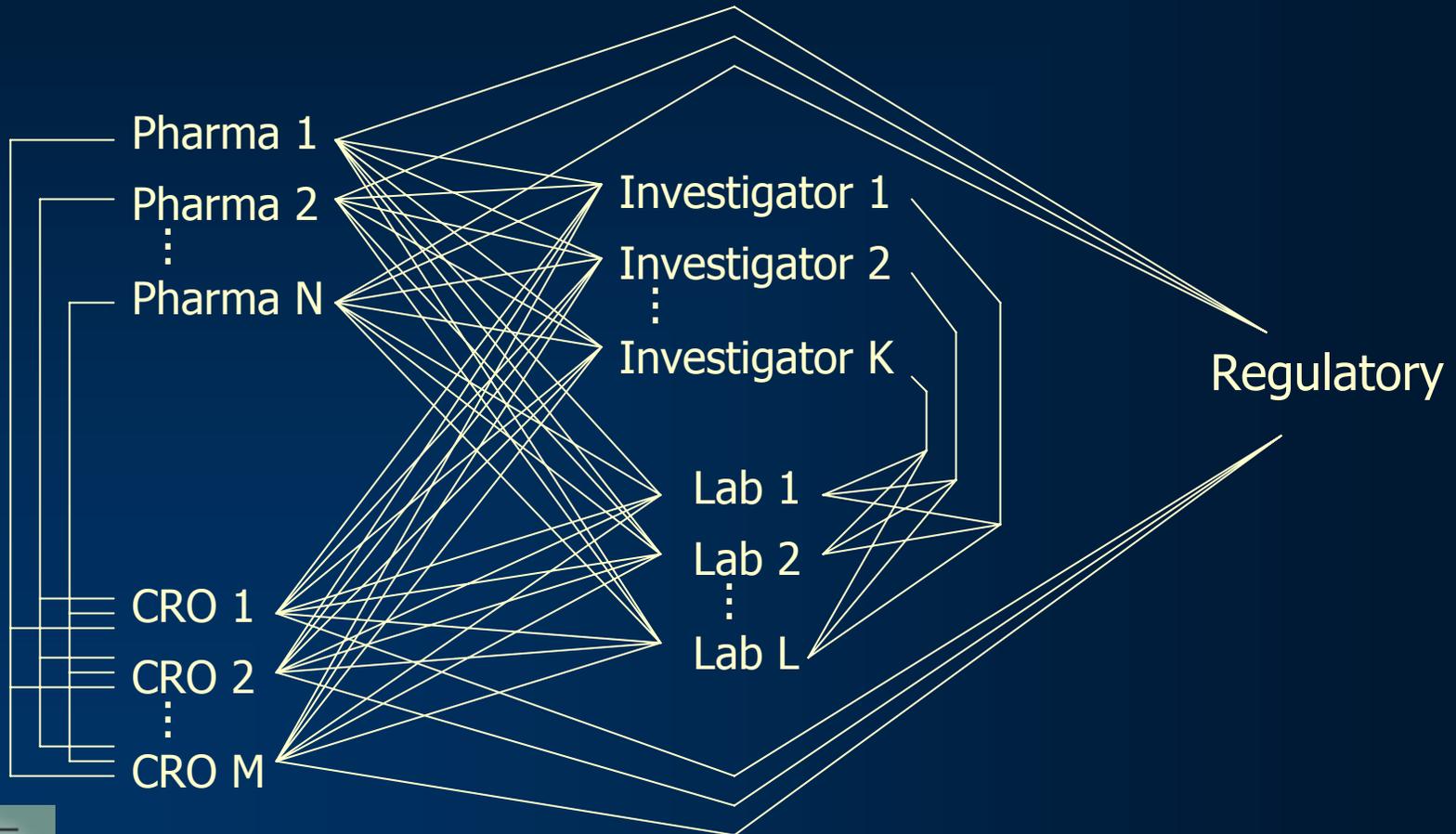


# CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM (CDISC)



# *Why do we need clinical data interchange standards?*

# Current State: Costly and Time-consuming





# CDISC Value: Cost of Clinical Data Interchange in Clinical Trials

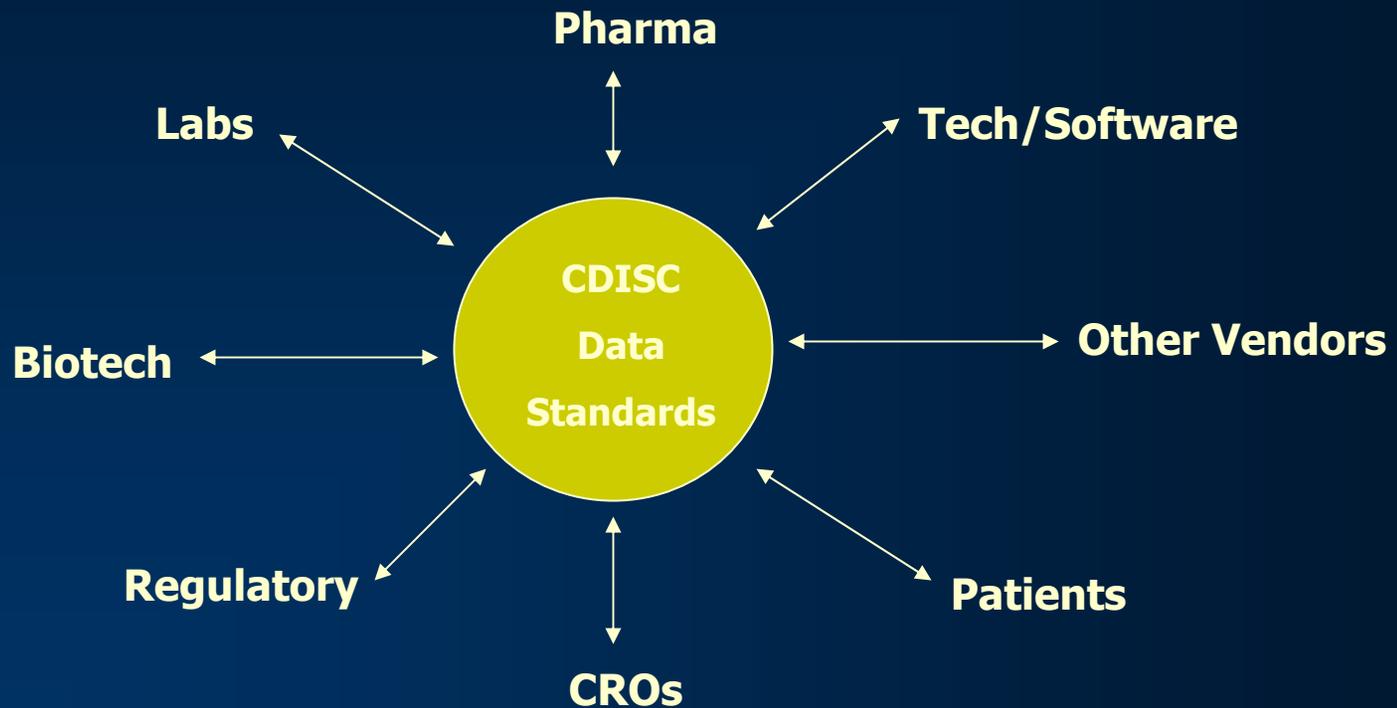
- ~7,000-8,000 clinical studies/year\*
- ~ 30 % outsourced and 5-10% EDC
- Estimated cost of \$35,000 for EDC transfers, \$25,000 for CRO data transfers, and \$10,000 for lab data transfers
- **Conservative Annual Cost to the Industry:**  
**156 million U.S. dollars (~19 Billion Yen)**

NOTE: The costs incurred with development partners or merged companies sharing data and the cost of preparing data for eSubmissions are not addressed in this set of calculations, nor are other costs included such as those for training, planning or equipment.

CDISC White Paper on Website

\* CenterWatch (v.7, issue 11)

# Desired State



# Benefits of Standardization in our Industry



- Reduce time and cost associated with clinical trials for drug development
- Facilitate business processes among biopharmaceutical companies, CROs, EDC vendors, clinical laboratories
- Facilitate reviews of regulatory submissions
- Increase familiarity with common data elements, reducing training requirements
- Improve data quality



# *What is CDISC, and what is the history?*

# History of CDISC



- Conceived and initiated in 1997 as an open, multidisciplinary volunteer organization
- Invited to be a DIA Special Interest Committee 1998
- Incorporated as non-profit organization in February 2000, with funding from Corporate Sponsors (Pharmas, CROs, Vendors, others)
- >75 Corporate Sponsors, Corporate Members and Associate Members today

# Clinical Data Interchange Standards Consortium



*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 CDISC mission is to lead the development of global, vendor-neutral, platform-independent standards to improve data quality and accelerate product development in our industry.*



# CDISC Principles

- Support for the scientific nature of clinical research
- Facilitation of regulatory submissions reviews
- Platform-independence
- Global, multidisciplinary, cross-functional
- Maximum sharing of information and minimum duplication of efforts
- Development of educational programs
- Refrain from promoting any individual vendor or organization



# *What is the Organization of CDISC?*

# Clinical Data Interchange Standards Consortium

CDISC Board of Directors

Industry Advisory Board

•Strategy TF ; Governance TF

R3C Executive Committee (R3CXC) & Regional CDISC Coordinating Committee (R3C)

## CDISC Operations and Infrastructure (OIS)

Membership Task Force  
PR/Communications Task Force; CSF  
Support for Boards and Working Teams

Finances  
Glossary Group  
Testing and Processes

### Alliances

•HL7  
•DIA  
•SCDM, ACDM, NCDM,  
DMB, ARCS...

### Education and Training

#### CDISC Working Teams

ODM  
LAB

SDS  
ADaM

Regional CDISC Groups (rCG)

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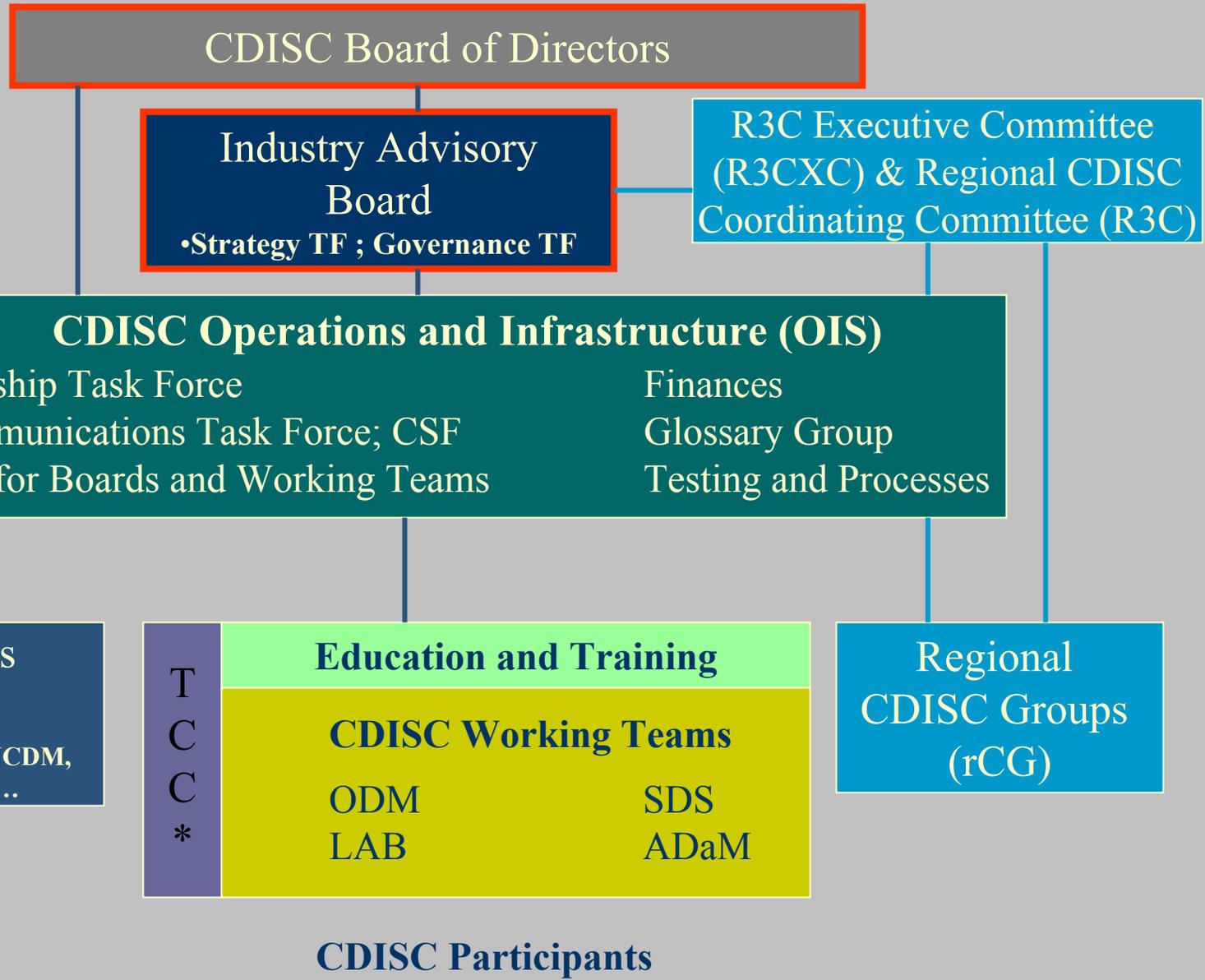
CDISC Participants



# CDISC Organization

- Collaborative, multidisciplinary environment
- Volunteer participants and team members are the basis of CDISC; anyone can participate
- Operations and Infrastructure group facilitates communication and provides support and processes
- Boards are responsible for governance and strategic direction

# Clinical Data Interchange Standards Consortium



CDISC Participants

\* Technical Coordinating Committee



# CDISC Board of Directors

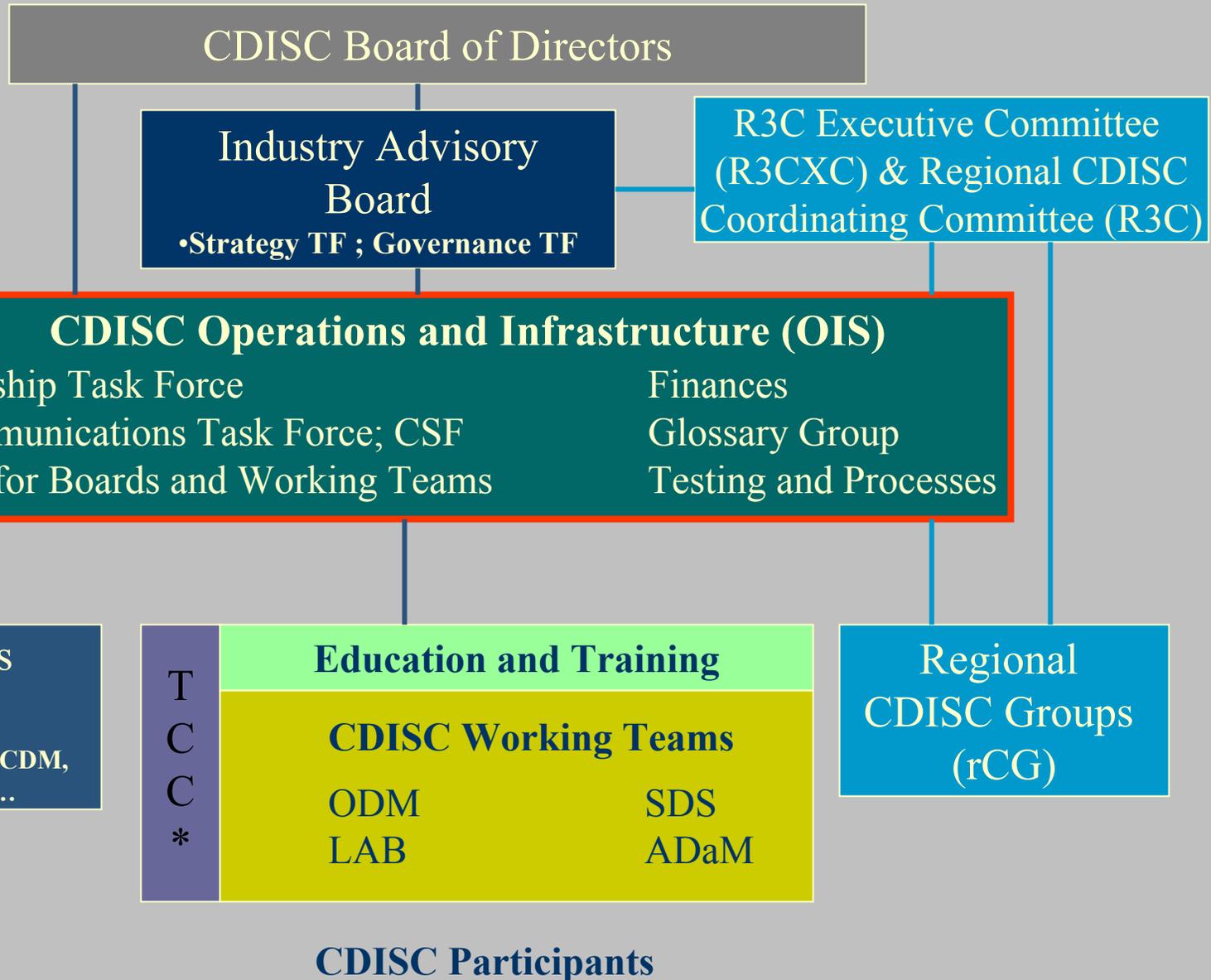
- **Responsibilities**
  - CDISC Bylaws and Governance
  - CDISC Strategic Direction
  - Oversee Financial Resource Management
  - Oversee Operations
- **Structure**
  - Nine Directors on the Board
  - Complementary expertise and skills
  - Annual election of three and three 'roll off'
  - Board selects two and IAB selects one

# Industry Advisory Board (IAB)



- One representative from each CDISC Corporate Sponsor
- IAB Chairperson: Elaine Job (Aventis);  
ex-officio member of the Board of Directors
- Meetings in person twice per year
- Provide strategic and financial advice to CDISC

# Clinical Data Interchange Standards Consortium



\* Technical Coordinating Committee

# CDISC Operations and Infrastructure



- Personnel (~2.5 FTE)
  - Rebecca Kush, Shirley Williams and Julie Evans
- Support for Modeling Teams, EDU and TCC
  - Identify Team Leaders, set up Conference calls, etc.
- Support for Boards and Finances
  - Implement Strategic Plan; budget and track finances
- Leadership and/or Coordination of Task Forces and other CDISC Support Activities
  - Testing and Processes
  - PR/Communications Task Force; CSF
  - Glossary Group
  - Membership Task Force

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### Education and Training

#### CDISC Working Teams

ODM

LAB

SDS

ADaM

Regional CDISC Groups (rCG)

CDISC Participants



# Alliances

- Alliance Principle
  - CDISC wishes to collaborate with other groups interested in standards development
  - CDISC does not wish to duplicate efforts
- FDA - has appointed Liaisons to CDISC
- Example: Version 2.0 of the SDS Model is compatible with the ICH E2B standard for adverse event reporting
- Current collaborations include data management organizations (SCDM, NCDM, ACDM, DMB, ARCS), Drug Information Association (DIA), Medical Writers Associations (AMWA, EMWA), NCI, HL7



# CDISC – HL7 Alliance

- January, 2001 – Associate Agreement between CDISC and Health Level 7 (HL7 - standards development organization for healthcare data interchange)
  - CDISC assists HL7 in re-instating HL7 Clinical Trials Special Interest Group (SIG)
- April, 2002 – HL7 Board approves new Regulated Clinical Research Information Management Technical Committee (RCRIM)
  - Co-leaders from HL7, CDISC, and FDA

# Benefits of an HL7–CDISC Alliance



- Capitalize on existing HL7 standards efforts and experience base
- Leverage HL7 ANSI and ISO accreditation
- HHS acknowledgement of HL7 as Standards Development Organization
- Expand value and influence of clinical trials standards efforts through harmonization
- CDISC brings domain expertise in clinical trial standards
- Opportunity to bring healthcare together with clinical research and clinical trials

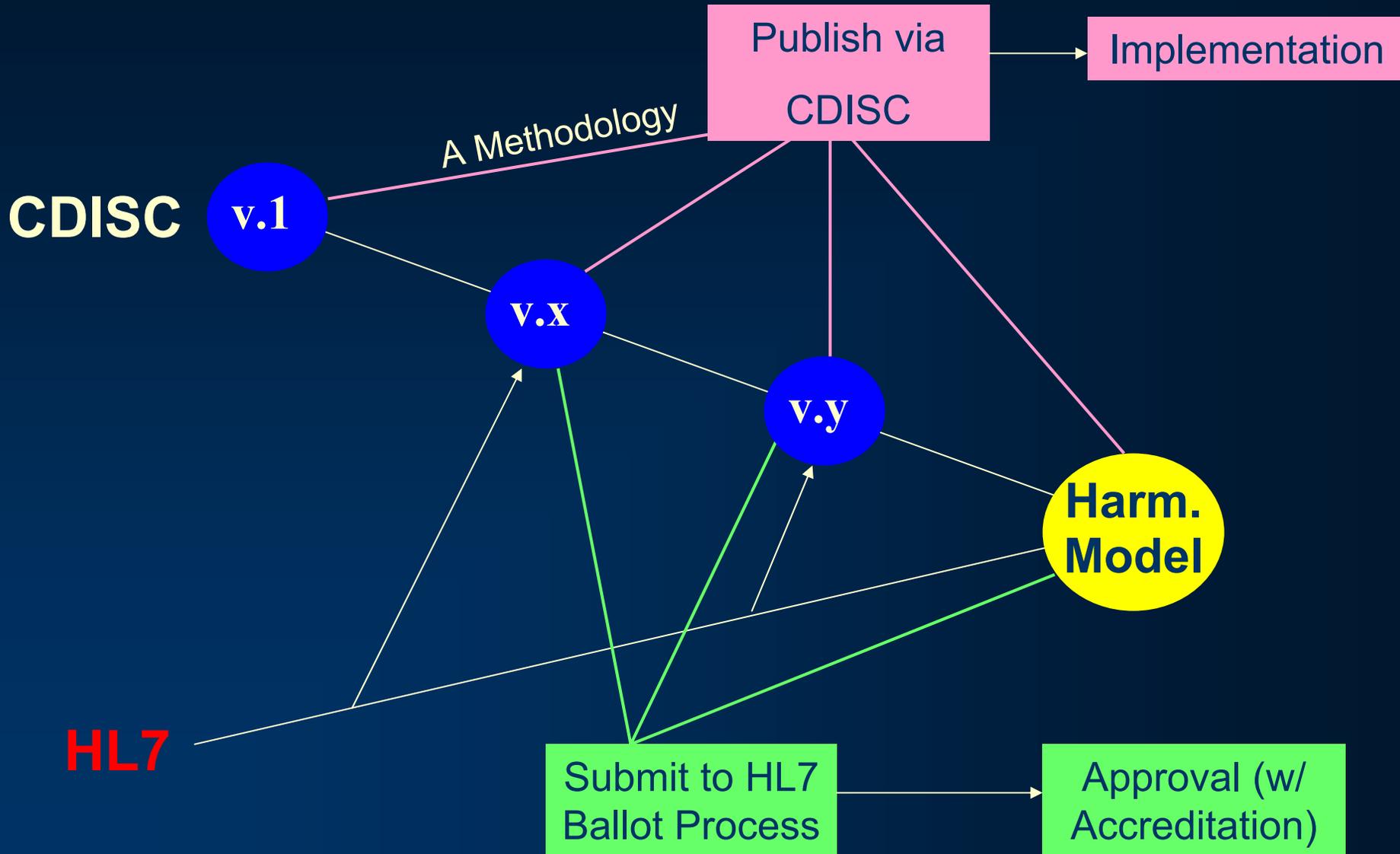
# HL7 RCRIM Technical Committee Projects



- Standard Clinical Trial Domains (e.g. ECG, AE, Demographics, Labs)
- Safety Surveillance Standards
- Medication Information (Labeling) Standards
- Submission Documents
- Protocol Representation (Elements)

[Collaborative efforts among HL7, FDA, CDISC, NIH, CDC and DIA]

# Harmonization Approach



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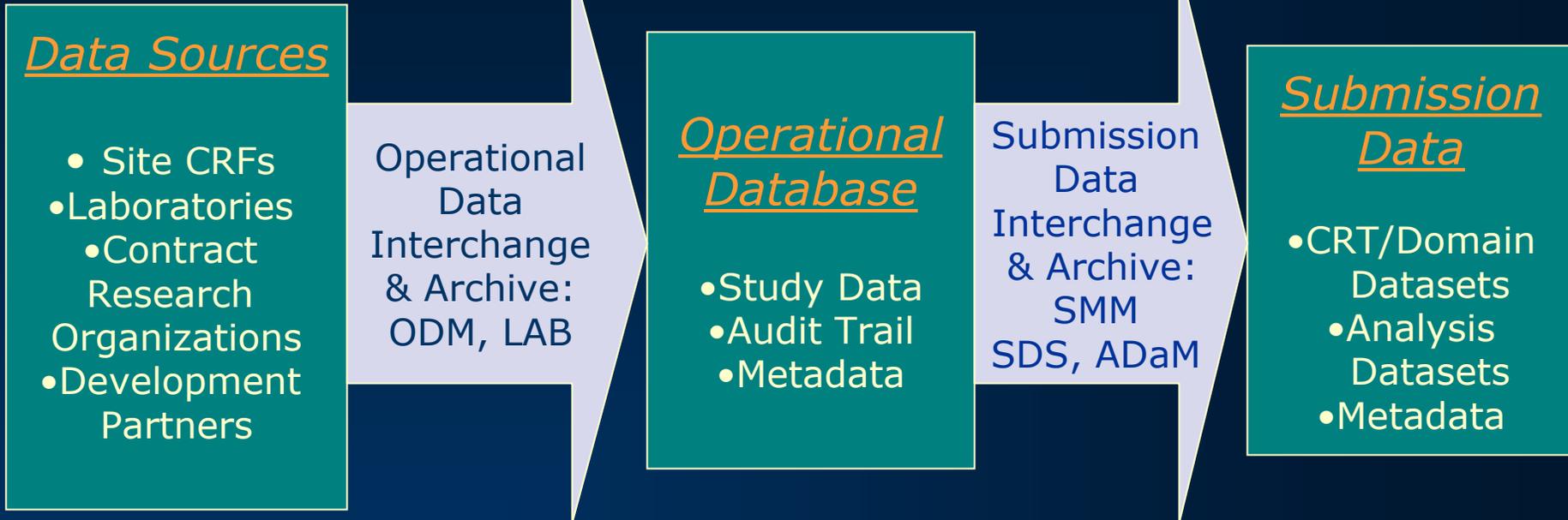
CDISC Participants



# Modeling Teams and TCC

- Four Modeling Teams and Leaders (Facilitators)
  - Operational Data Modeling Team (ODM) – Sally Cassells
  - Laboratory Data Standards Team (LAB) – Susan Bassion
  - Submissions Data Standards Team (SDS) – Wayne Kubick
  - Analysis Dataset Modeling Team (ADaM) – Dave Christiansen
- Technical Coordinating Committee – Wayne Kubick
  - Function is to harmonize standards development and associated activities across CDISC
  - Comprised of Team Leaders and alternates; representatives from Operations, Testing and Processes, and Education, and a Board Liaison

# Scope of CDISC Models



ODM = Operational Data Model  
LAB = Laboratory Data Model

SMM = Submission Metadata Model  
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# *CDISC Standards Development*

# CDISC Approach



- Multidisciplinary Teams ( $n = 7-12$ ) develop initial draft models ('strawmen')
- External review groups with expertise in area review and comment on draft models
- Broad open (public) review (via website)
- Testing at appropriate points throughout reviews
- Release/'Production' Version (1.0)
- Annual reviews and updates



# CDISC Approach

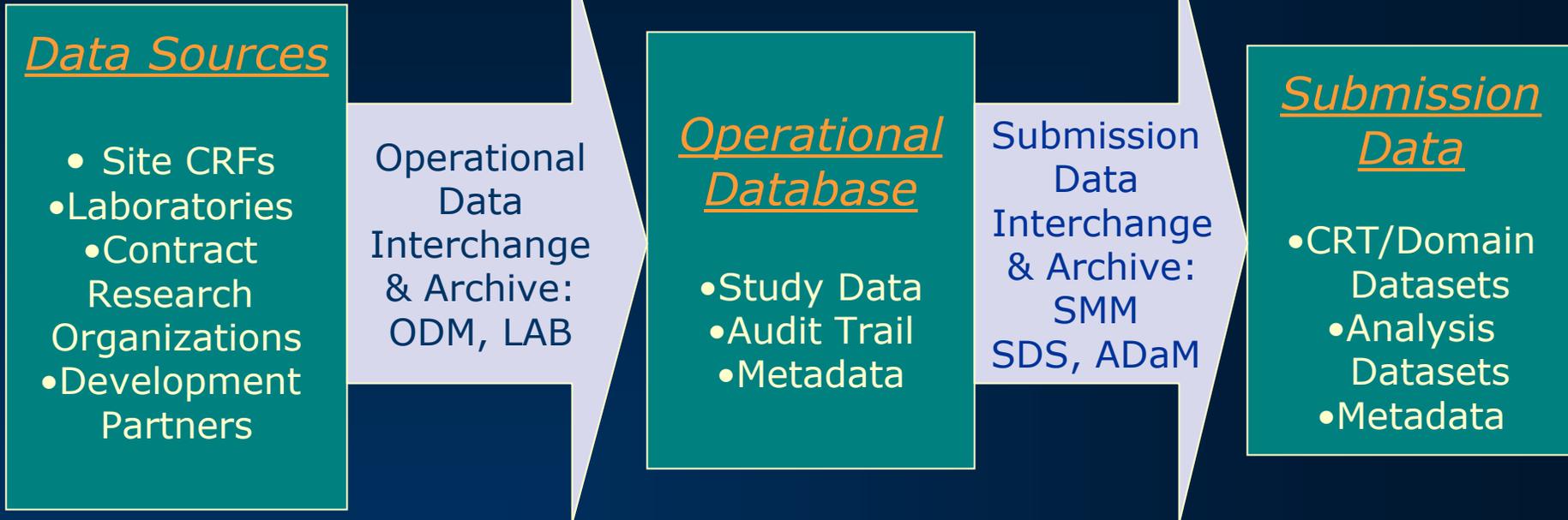
- The CDISC models are the products of contributions from numerous organizations, functional groups, and individuals; they do not have a sole source.
- Consensus building
  - Involves different disciplines within the industry
  - May involve ‘consolidating’ existing models
  - Involves collecting and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



# *CDISC*

## *Operational Data Model*

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# CDISC - ODM Goals



- Develop vendor independent models for **interchange** and **archive** of clinical **data** with **study metadata**
- Base models on **XML** technology

# ODM Evolution



- V0.8 Model
  - Derived in 1999 as a consolidated model based upon open sharing of models by two companies and a technical analysis of these models
  - Seven-member multidisciplinary team (two EDC vendors, two CDMS vendors, CRO, Biopharm and XML expert)

# ODM Evolution (cont'd)



- V1.0 Model
  - Team included additional representatives from leading EDC, technology and service providers
  - Enabled transfer of a single study
- V1.1 Model
  - Team expanded to include additional Pharma company and CRO representation
  - Supports multiple studies, labs, incremental transfers and other new features
  - Production Version released in May 2002

# Operational Data Modeling Team Accomplishments: Version 1.0 XML-based Data Model



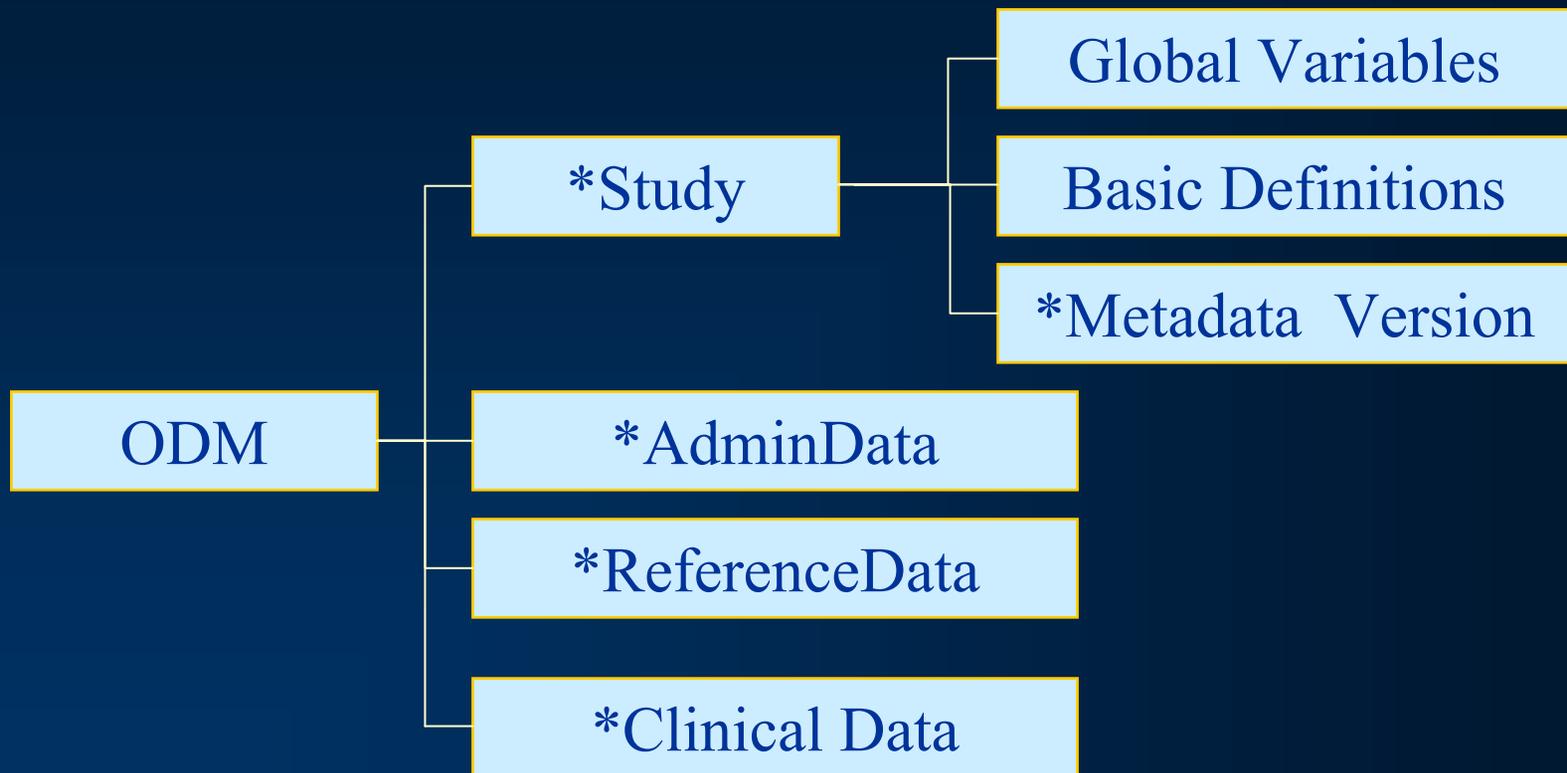
- Basic study description
- Support for electronic signature requirements
- Basic audit trail
- Presentation support for Archival purposes
- Support for 21 CFR Part 11 requirements & Guidance for Computers Used in Clinical Trials

# ODM Team Accomplishments: ODM Version 1.1 Enhancements



- Ability to handle changes to key values
- Expanded Transaction codes – support for record deletion
- Enhanced meta data elements to support more complex study event structures
- Support for multiple studies within a single transmission file
- Support for non-patient reference data (e.g. Lab Normal Ranges)
- Support for vendor extensions
- Increased compatibility with SDM model & patient profiles project
- Improved archiving support
- Removed support for flat data representation
- Bug fixes

# ODM V1.1 Overview



# Operational Data Modeling: Current Priorities



- Encourage support and adoption of the ODM model by industry
  - Documentation of testing and implementation scenarios
  - Support for educational programs
  - Increased support for different data interchange scenarios
- Support backward-compatible improvements
  - XML schema representation of ODM
  - Expanded protocol definition
  - Other new features using extensibility functionality
- Support XML representation of LAB model and HL7 harmonization.

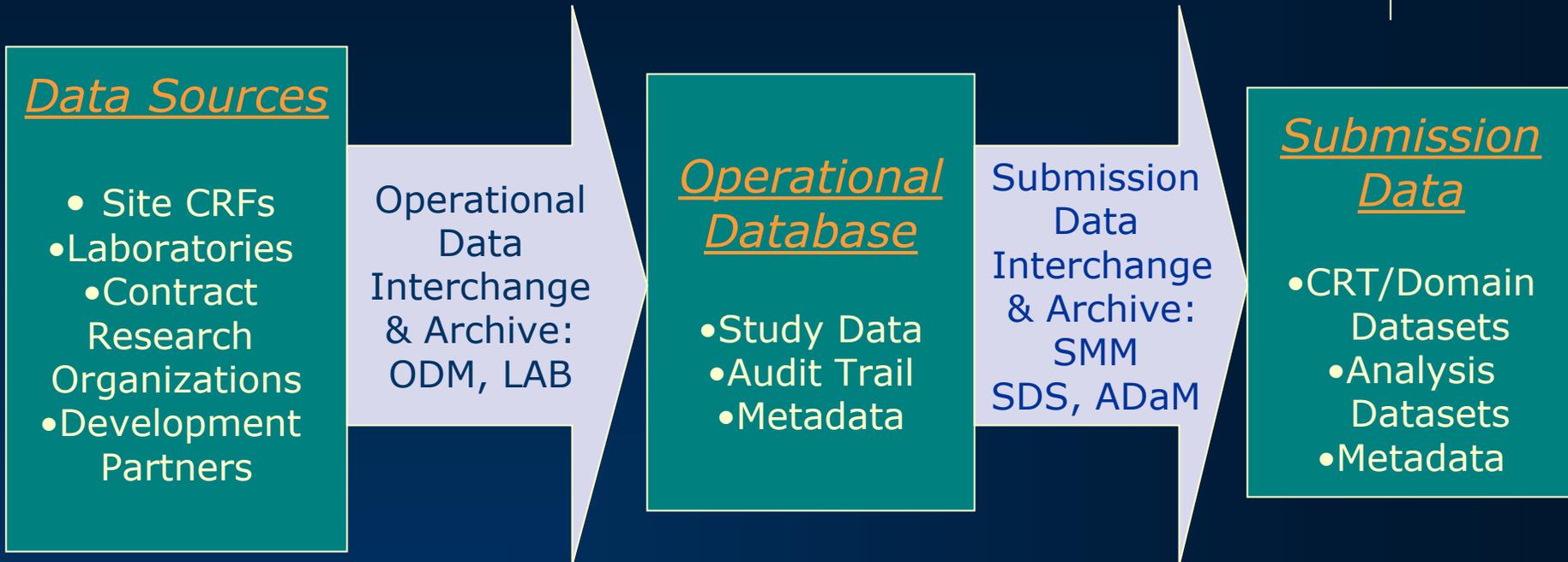


# *CDISC*

## *Submissions Data Model*



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# Submissions Data Standards Team Objectives



- Provide regulatory submission reviewers with clear descriptions of the usage, structure, contents & attributes of all submitted datasets and variables
- Allow reviewers to replicate most analyses, tables, graphs and listings with minimal or no transformations
- Enable reviewers to easily view and subset the data used to generate any analysis, table, graph or listing without complex programming



# SDS V. 2.0 Domain Models

- Demographics
- Disposition
- Exposure
- Labs (Chemistry, Hematology, Urinalysis)
- Physical Exam
- Medical History
- Concomitant Medications
- Adverse Events
- Vitals (Horizontal)
- Vitals (Vertical)
- ECG (Horizontal)
- ECG (Vertical)

# SDS Variable Metadata for Demographics

DEMO.xpt, Demographics, Version 2.0, October 22, 2001, One record per subject, CRT

Variable Name	Variable Label	Type	Decode/Format	Origin	Role	Sponsor Comments for FDA	CDISC Notes	CDISC Core Variable
STUDYID	Study ID	Char		Demog CRF Page	Selection		Uniquely identifies a study within a particular	Y
SITEID	Center or site ID	Char		Demog CRF Page	Selection		* Some sponsors may use an Investigator ID instead of or in addition to the SITEID.	At least one must be core in all files
INVID	Investigator ID	Char (or Num)		Demog CRF Page	Selection		* May be used instead of or in addition to the SITEID.	
INVNAME	Investigator name	Char		Demog CRF Page or Derived	Selection		* 1. May be used in addition to the SITEID or INVID. 2. Possibly linked from an external table.	N
USUBJID	Unique Subject ID	Char (or Num)		Sponsor Defined	Selection		1. Must be unique identifier across all trials. 2. Previously defined as PID.	Y
SUBJID	Subject ID	Char (or Num)		Demog CRF Page	Selection		Number captured on CRF to identify subject.	Y
AGE	Age in Years	Num		Demog CRF Page or Demog derived	Selection		Additional variables may be necessary for age collected in other units.	Y
SEX	Sex	Char	M. F	Demog CRF Page	Selection		CDISC recommends that all CRTs use M for male and F for female.	Y
RACE	Race	Char		Demog CRF Page	Selection		1. Example of decodes. Actual content of decode dependent upon company	Y

# Submission Domain Standards

## Team: Accomplishments



- Metadata Models for 12 Safety Domains in 1999FDA  
FDA eSubmissions Guidance
- Additional Domain Models in Progress
  - Substance use (tobacco, alcohol, drugs)
  - Study Summary (protocol attributes)
  - PK/PD Domains
  - Inclusion/Exclusion
- Other Activities
  - New generic domain models
  - Implementation guides
  - Reference data on investigators and visits

# CDISC SDS Test Case: FDA Patient Profile Pilot



- Described in USA Federal Register
  - Docket # 01N-0496
- Pilot includes 9 sponsors (8 SDS team members) who submitted electronic data and metadata based on CDISC SDS V2.0
- Facilitates FDA adoption of Patient Profiles tool and CDISC SDS Standards
  - PPV Roles can be mapped to SDS core variables
- Demonstrated value of standard domain formats
  - Identified similarities, gaps and ambiguities
- Pilot data has been evaluated; second phase pilot in planning (with additional data).

# Submission Domain Standards: Current Priorities

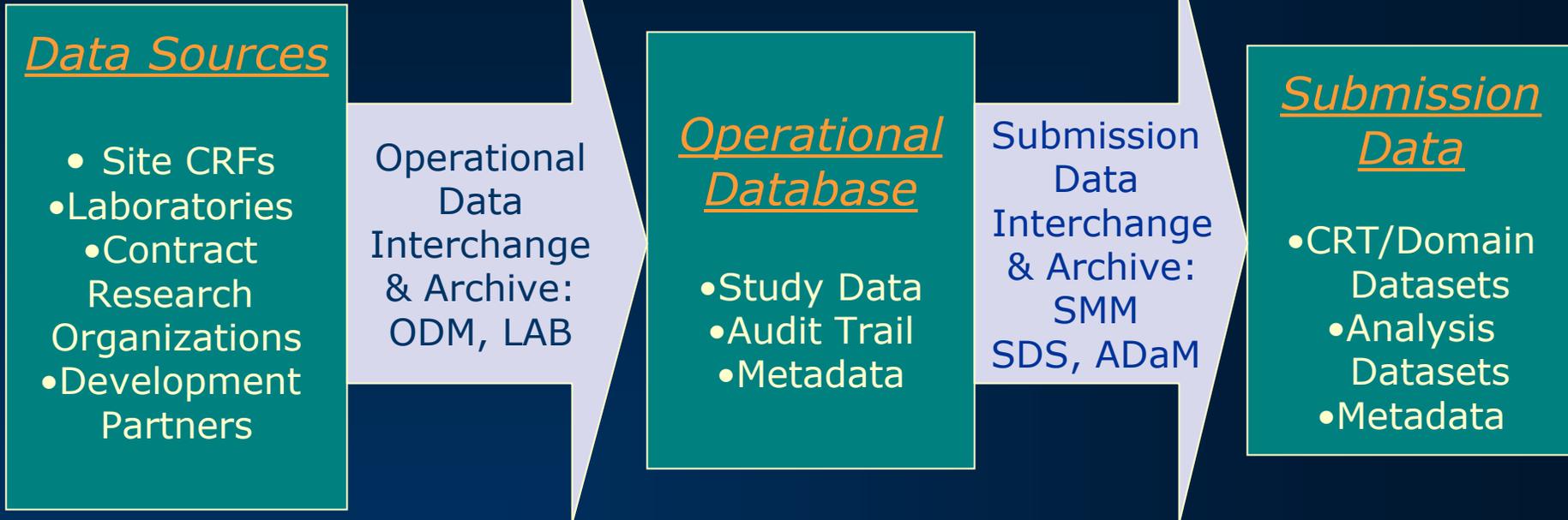


- **SDM Implementation Activities:**
  - Incorporation of industry and FDA Patient Profile Viewer pilot feedback
  - Increased Implementation documentation
  - Educational programs
- **New Features:**
  - Expansion of Submission metadata models
  - New domain models (e.g. PK/PD data, Inclusion/Exclusion)
  - Work with FDA on new generic domain models.



*Other CDISC Working  
Team Activities:  
LAB and ADaM*

# Scope of CDISC Models



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# CDISC LAB Team Approach

- Lab data interchange identified as highest priority for data interchange standards in CDISC Customer Requirements Survey
- Multidisciplinary team includes sponsors, CROs and labs (EU and US)
- Special use case of ODM general model
- Modified focus to define content model first vs. execution or transmission method

# CDISC LAB Team Progress



- Model specifications and requirements defined
- Content “Superset” developed, reviewed, revised, and tested
- LAB Content Model posted on CDISC Website for public comment by August 2002
- Comments currently being addressed; production version to be posted October 2002

# Laboratory Data Modeling Team: Accomplishments



- Version 1.0 now published as three pdf documents:
  - CDISC Laboratory Data Interchange Standard Review Version, June 6, 2002
  - CDISC Laboratory Data Interchange Standard Transmission Data Fields
  - CDISC Laboratory Data Interchange Standard References Range Transmission Data Fields

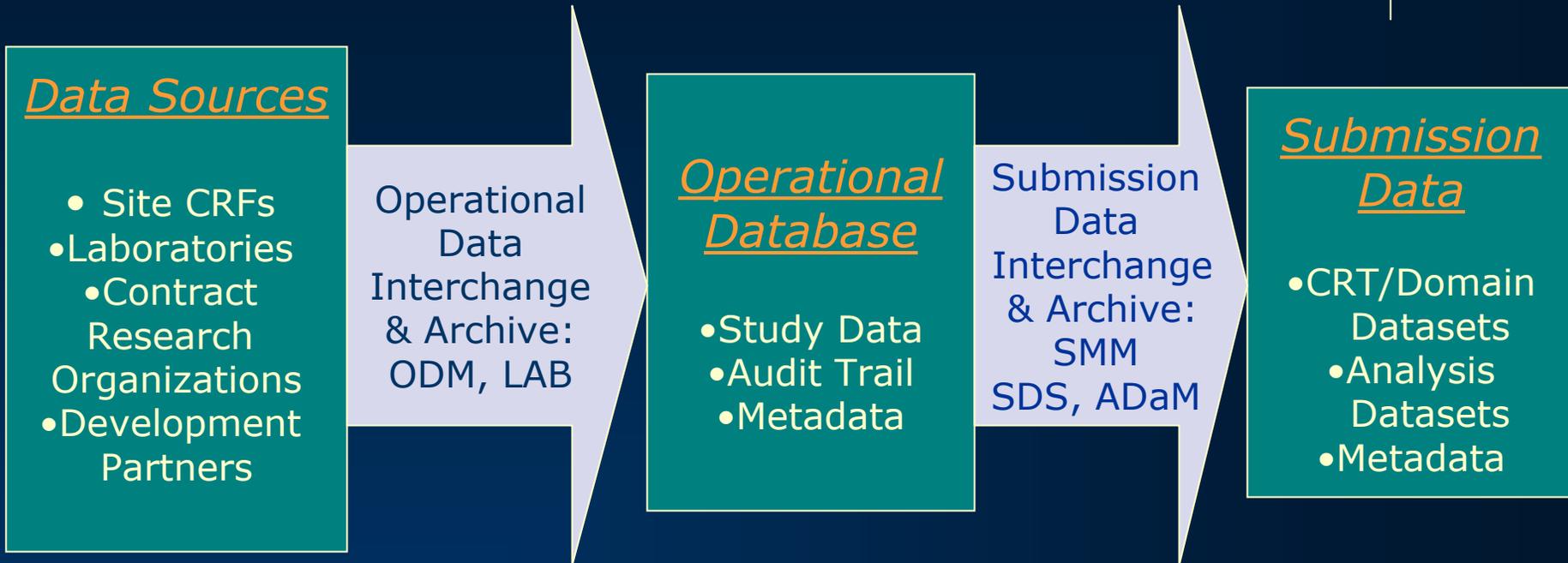
# Laboratory Data Modeling: Current Priorities



- Lab Model Implementation activities:
  - XML implementation of LAB model
  - Harmonization with HL7
  - Harmonization with ODM
  - Educational programs
  - Implementation case study plan
- New features:
  - Microbiology extension to LAB model
  - Genomics extension to LAB model



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# ADaM Data Model Approach



- Build on metadata CRT models developed for safety domains, adding attributes and examples specific to statistical analyses
- Use sample statistical results as guide for developing data set models
- Initially focus on primary and secondary efficacy variables.

# Analysis Dataset Modeling Team: Accomplishments



- Guidelines for the Selection of Dataset Structures
- Change from Baseline example of analysis dataset model
- Time to Event example of analysis dataset model
- Categorical Data Model (in review)

# Analysis Dataset Modeling: Current Priorities



- Implementation Activities
  - Educational programs
- New Features:
  - Complete Categorical Data Model
  - Develop dataset models in support of FDA Guidance on “Exposure-Response Relationships”
  - Develop other analysis dataset models



# *Other Current and Future Activities ...*

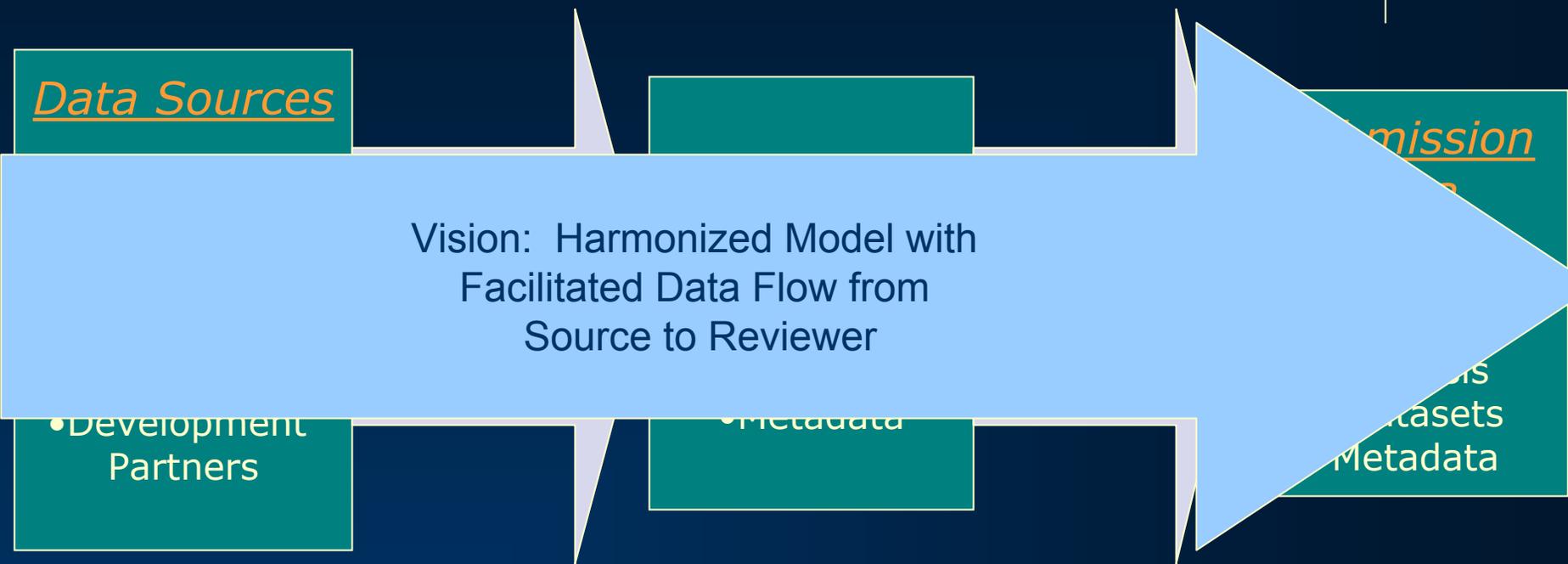


# CDISC Near-Term Objectives

- Develop additional standards as appropriate to support clinical trials
- Try new means for communications regarding standards and gaining feedback and momentum
- Continue to support, educate and increase use of CDISC operational models
- Continue to support needs of regulatory agencies for electronic submission of data
- Expand activities in Europe and Asia
- Increase collaboration with other standards organizations



# The Future of CDISC Models



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