CDISC Update

Pierre-Yves Lastic, PhD
Chairman of the Board

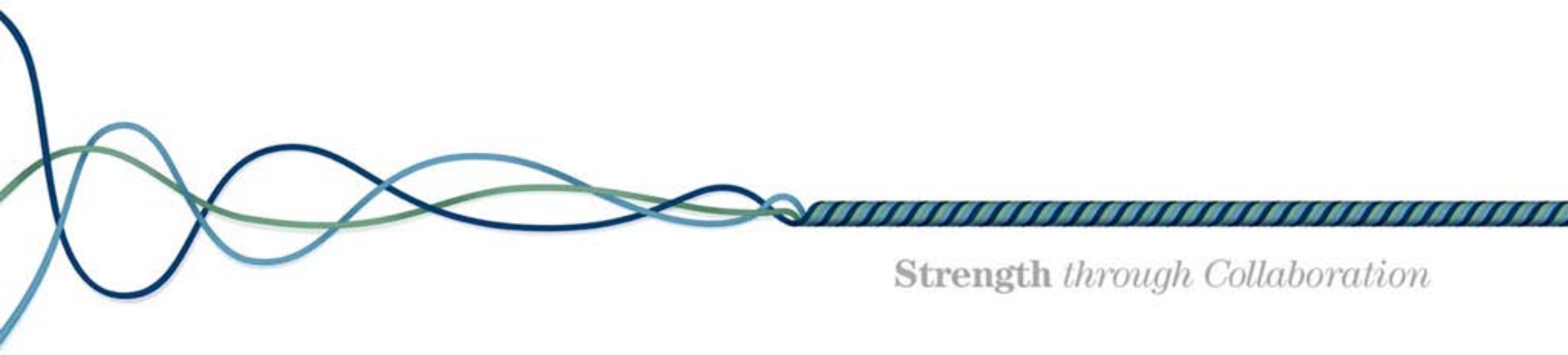
French-speaking User Group meeting
Brussels, 22 May 2014

Strength *through Collaboration*

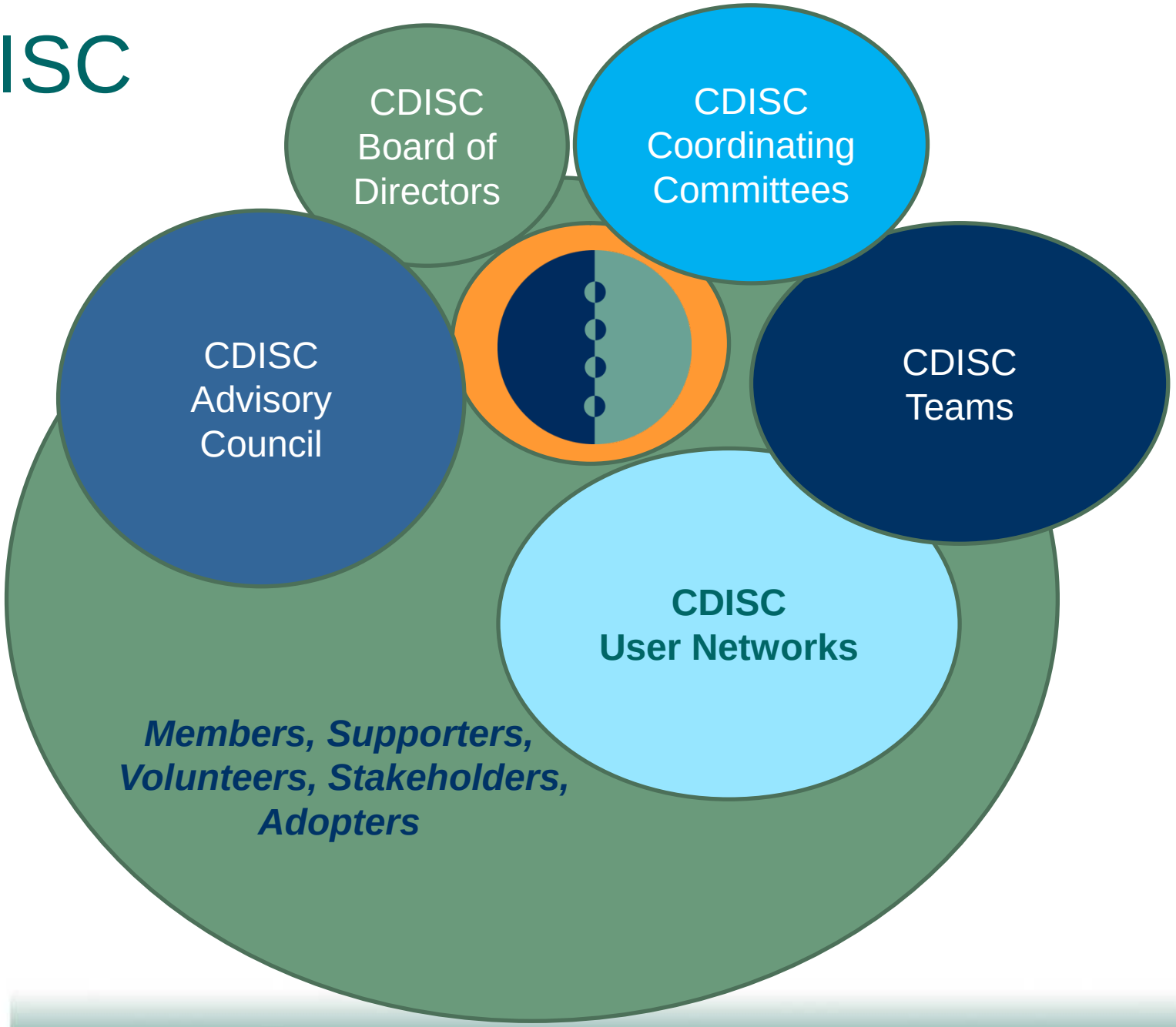
CDISC Update – May 2014

- CDISC
  - People
  - Products
- Regulatory Submissions
- Therapeutic Area Standards
- SHARE
- Conclusions

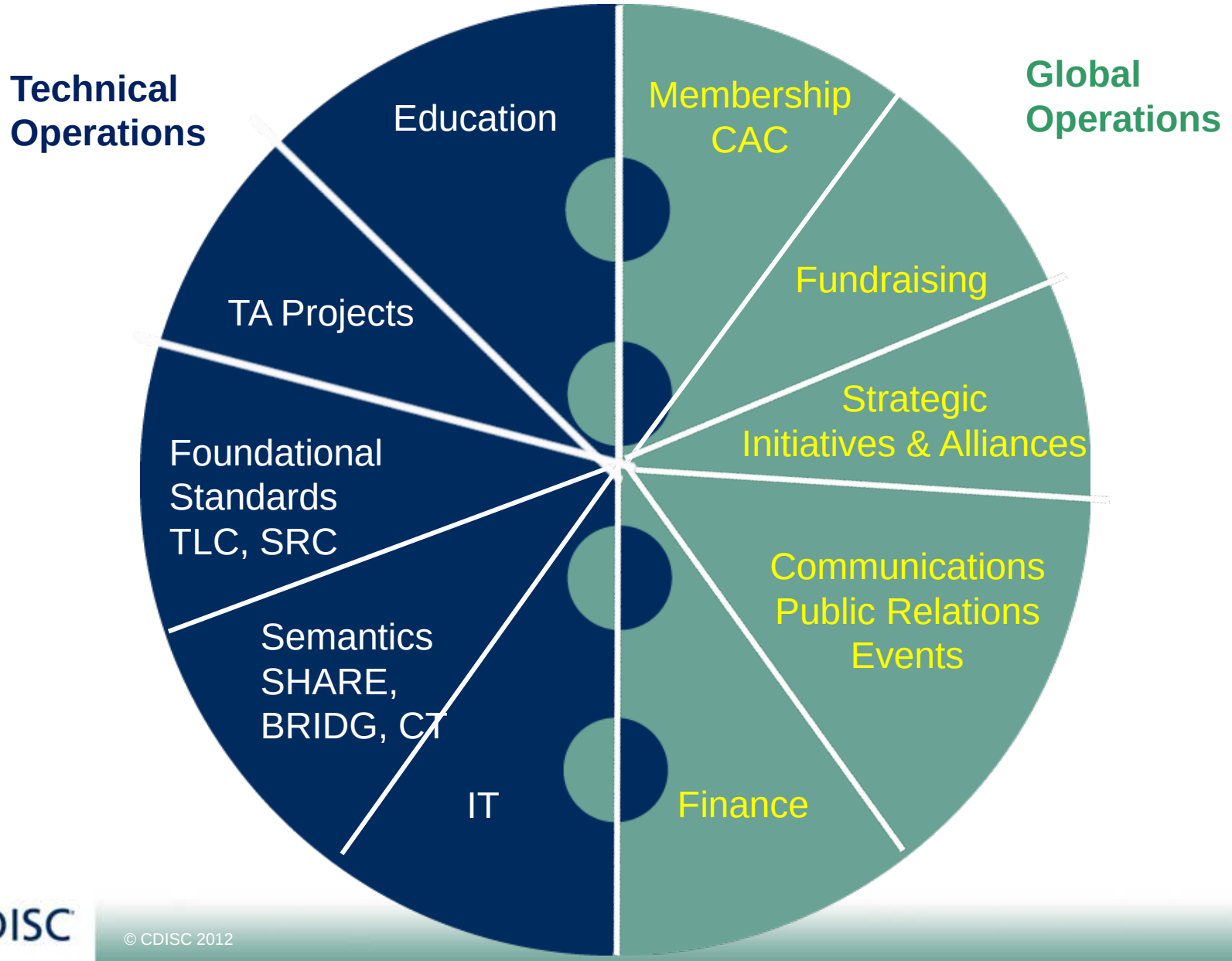
CDISC People:
A Growing Community
A Growing Team



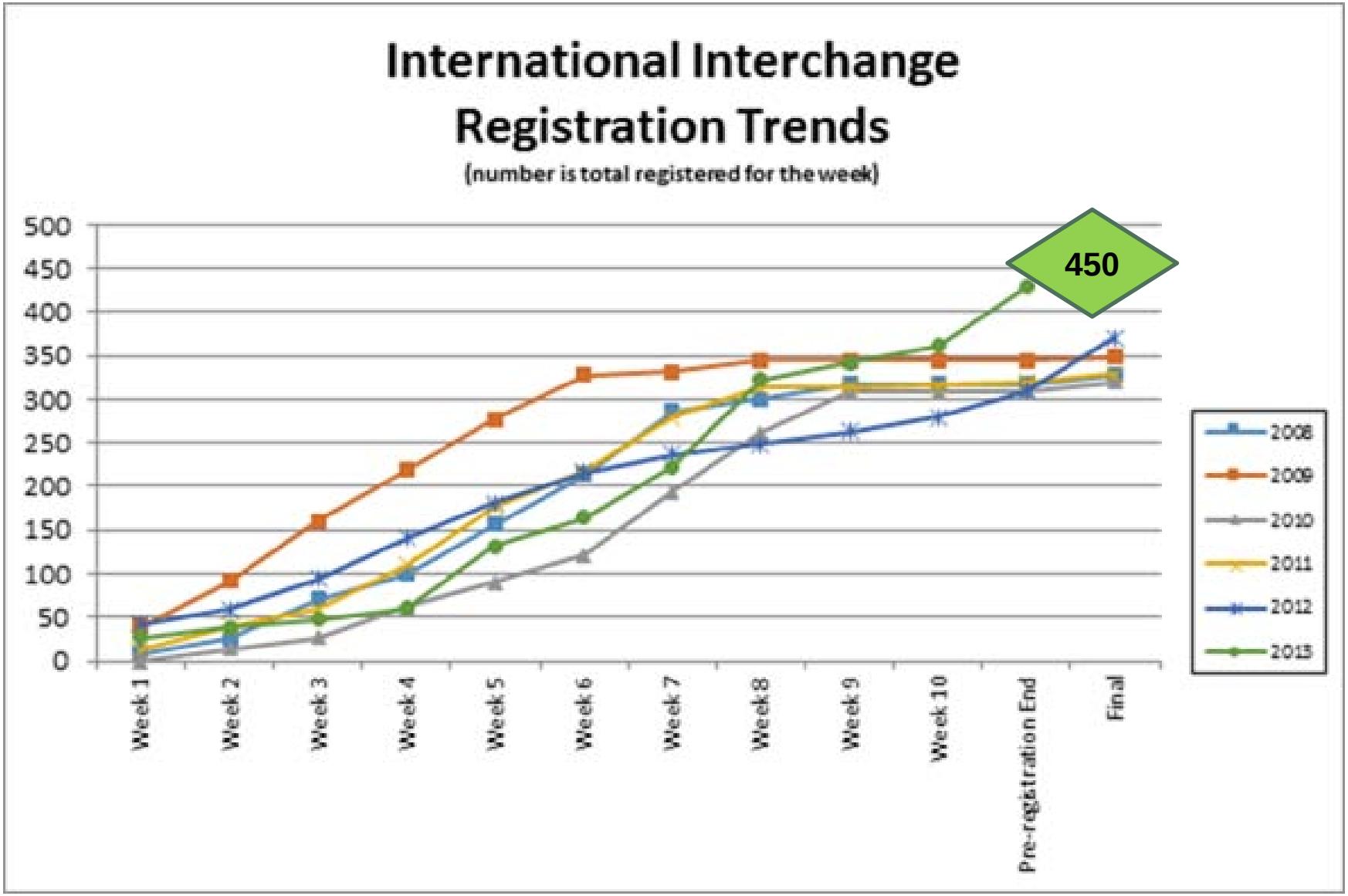
CDISC

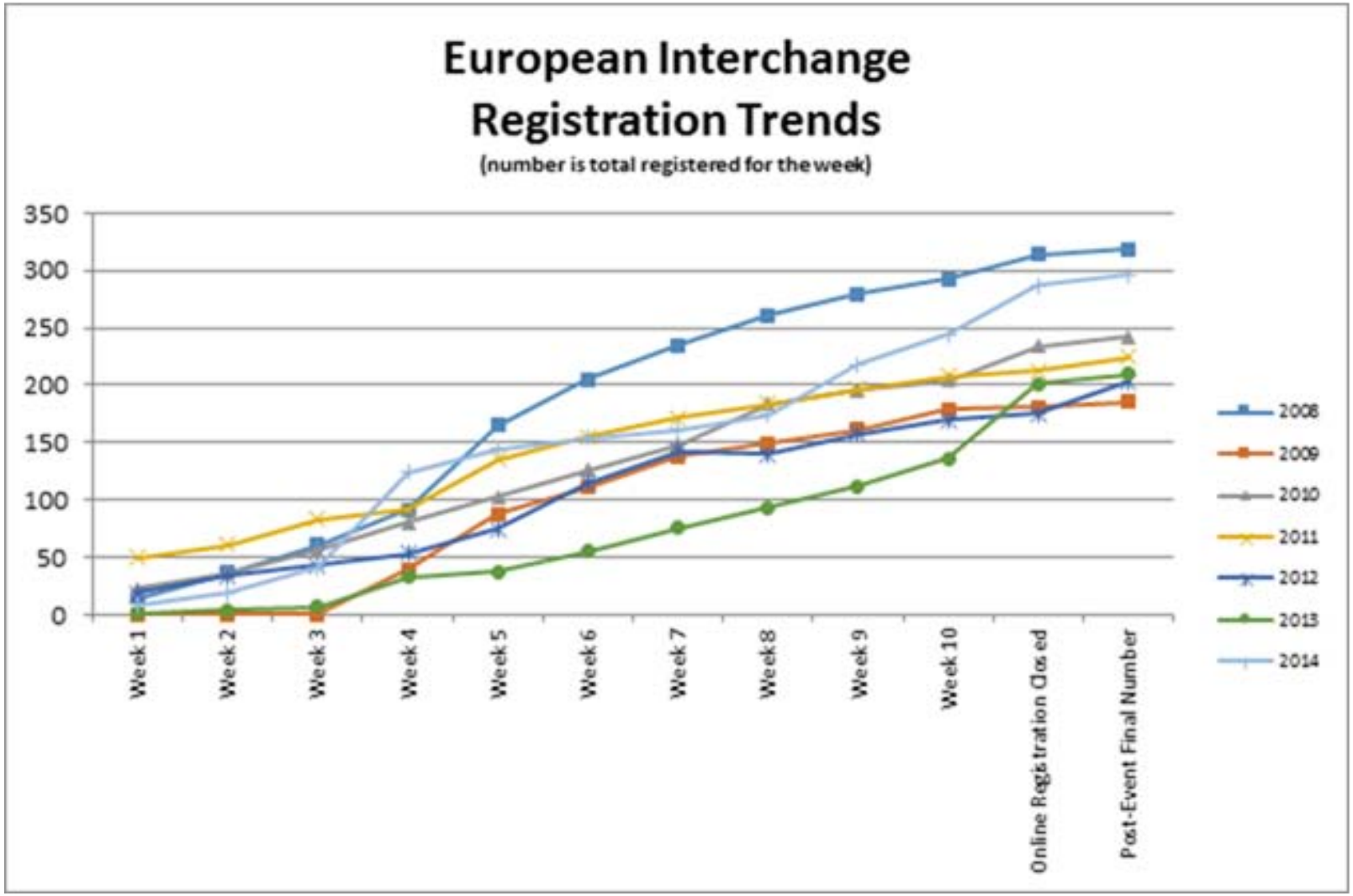

CDISC Board of Directors
CDISC Coordinating Committees
CDISC Advisory Council
CDISC Teams
CDISC User Networks
Members, Supporters, Volunteers, Stakeholders, Adopters

CDISC Operations



CDISC Around the World


International Interchange
Registration Trends
(number is total registered for the week)
450
500
450
400
350
300
250
200
150
100
50
0
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8
Week 9
Week 10
Pre-registration End
Final
2008
2009
2010
2011
2012
2013


European Interchange
Registration Trends
(number is total registered for the week)
350
300
250
200
150
100
50
0
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8
Week 9
Week 10
Online Registration Closed
Post-Event Final Number
2008
2009
2010
2011
2012
2013
2014

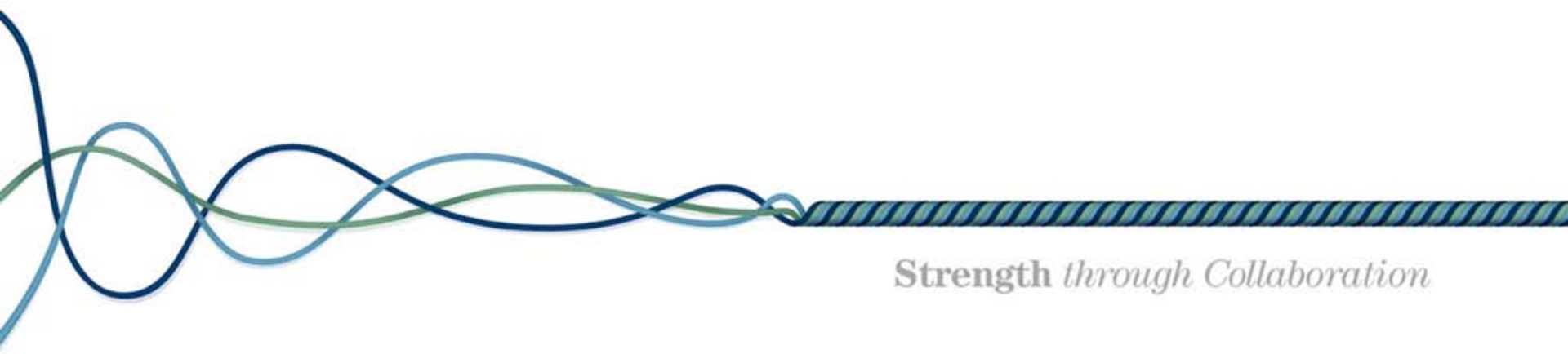
CDISC Communications

- **Website Upgrade** (www.cdisc.org)
- Tufts Survey – **PLEASE Respond**
- **Business Case** (Stage V) – In Review (Board, CAC, CFAST)
- YouTube Videos (e.g. SHARE)
- Press Releases and Announcements
- eNewsletter-New Format!
  Participate in the CONTEST

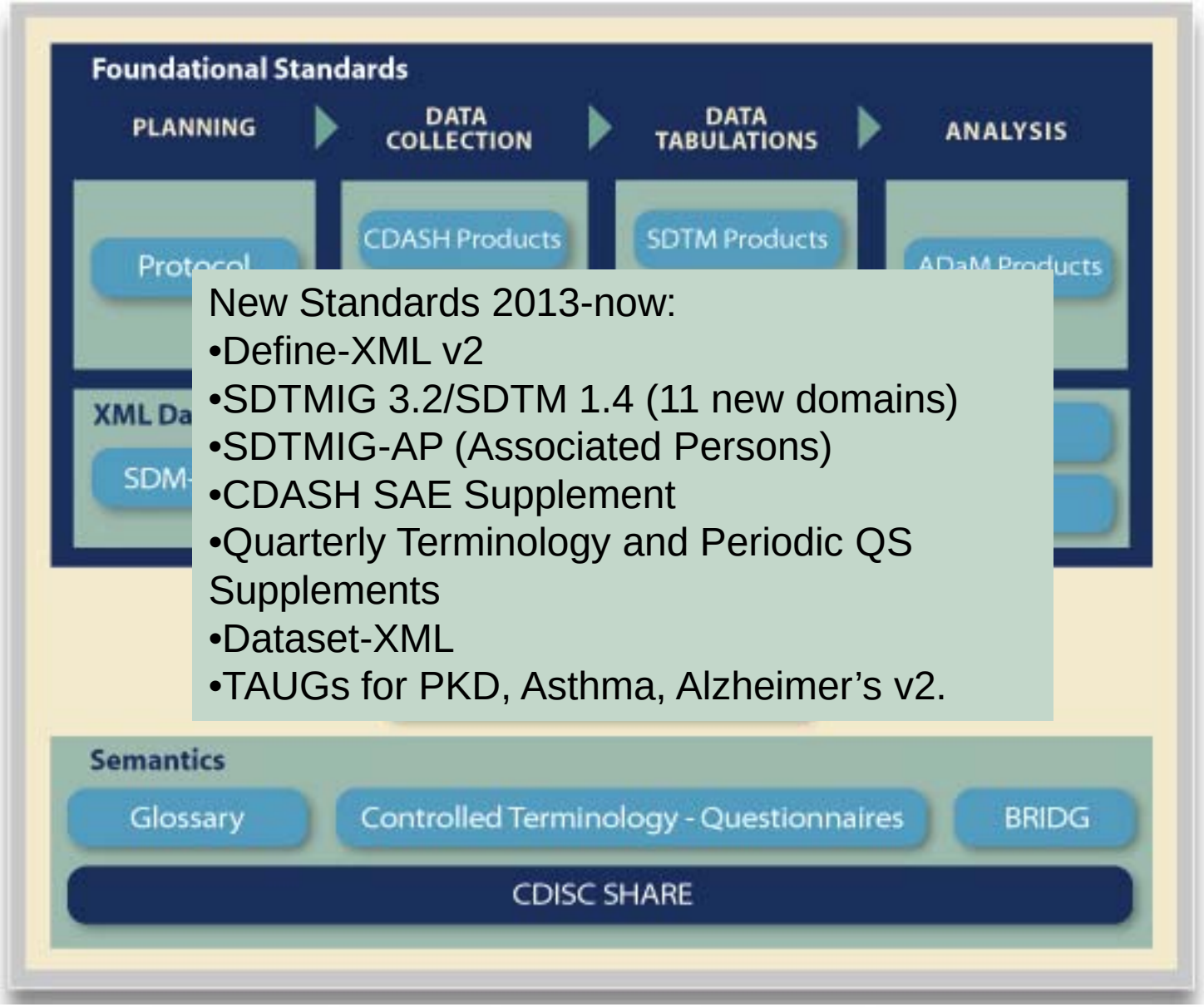
CDISC 2013 Annual Report Published in May !

Sign up online to our e-mail list!

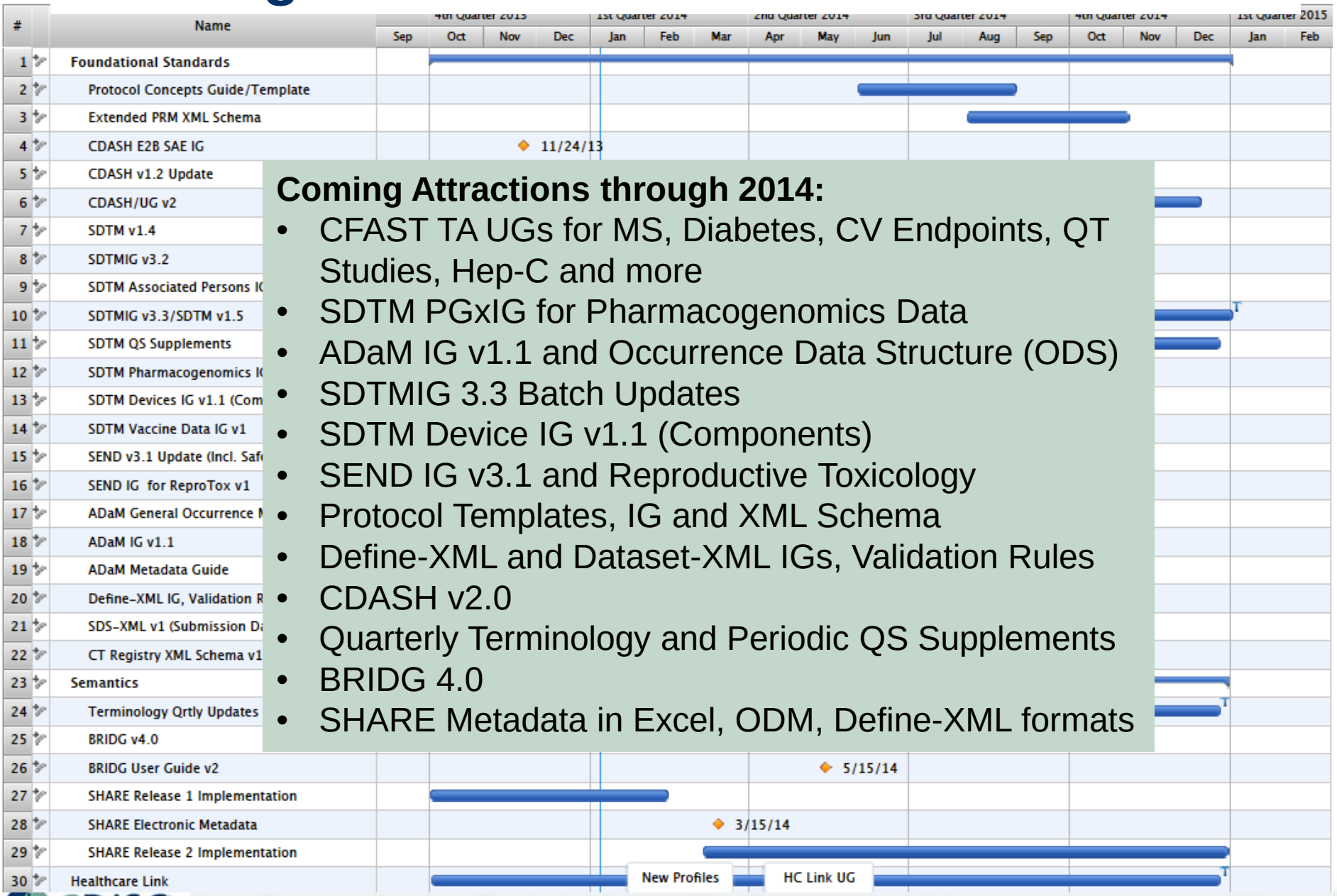
CDISC Products



Looking Back: Products Since 2013



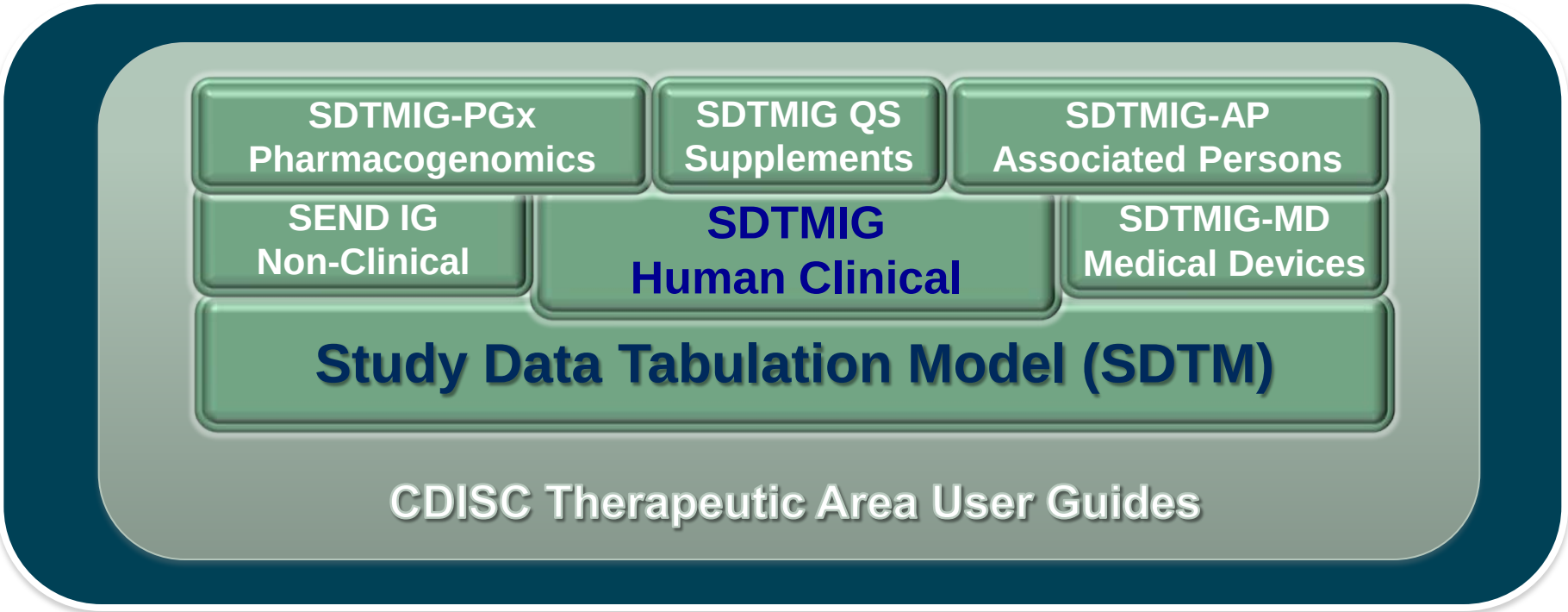
Looking Forward: Products Soon to Come



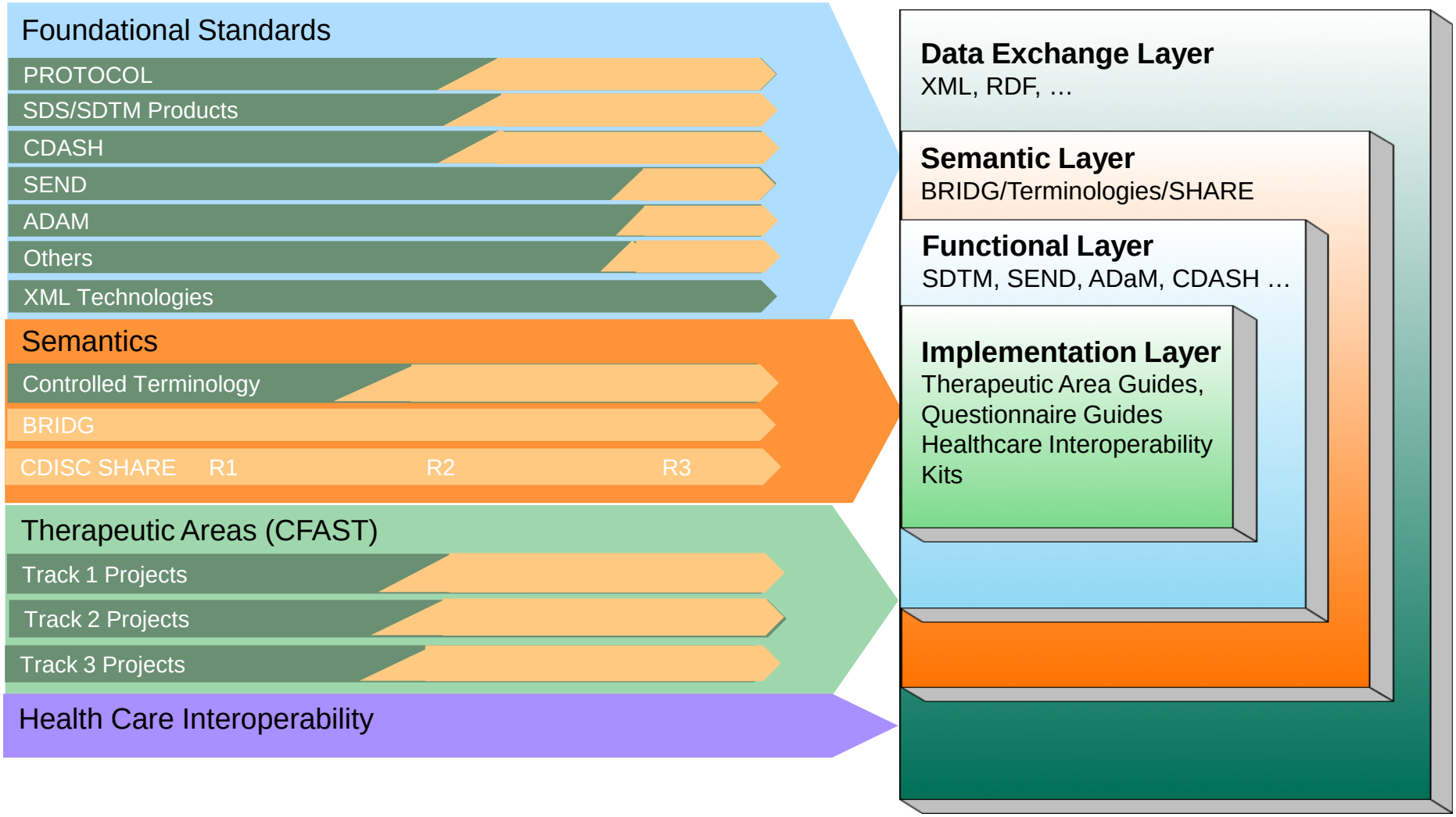
Coming Attractions through 2014:

- CFAST TA UGs for MS, Diabetes, CV Endpoints, QT Studies, Hep-C and more
- SDTM PGxIG for Pharmacogenomics Data
- ADaM IG v1.1 and Occurrence Data Structure (ODS)
- SDTMIG 3.3 Batch Updates
- SDTM Device IG v1.1 (Components)
- SEND IG v3.1 and Reproductive Toxicology
- Protocol Templates, IG and XML Schema
- Define-XML and Dataset-XML IGs, Validation Rules
- CDASH v2.0
- Quarterly Terminology and Periodic QS Supplements
- BRIDG 4.0
- SHARE Metadata in Excel, ODM, Define-XML formats

Governing the SDTM Product Family

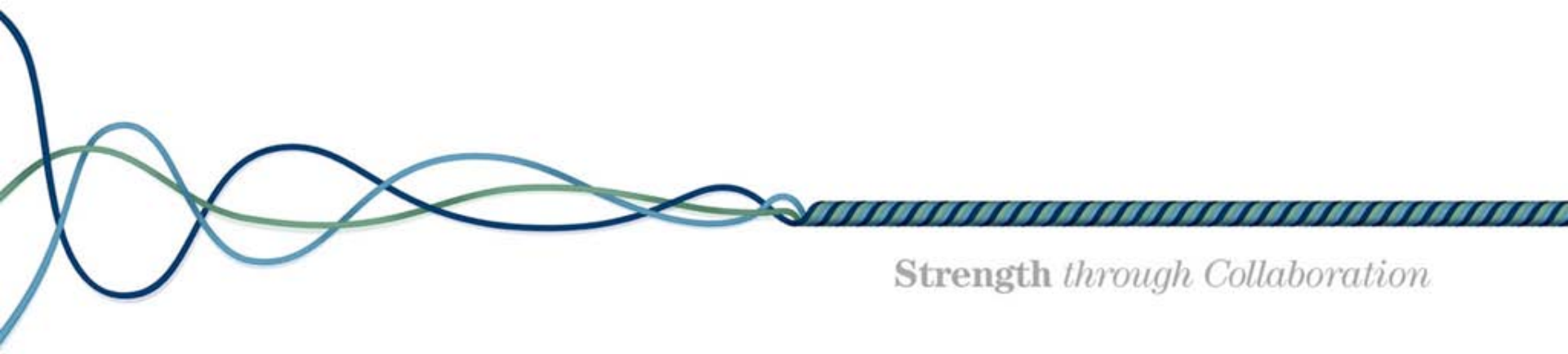


CDISC Technical Roadmap - 2014



The Roadmap depicts evolution from siloed standards to an integrated stack based on BRIDG and SHARE

Regulatory Submissions



For Industry

Home › For Industry › Data Standards › Study Data Standards

Data Standards

- **Study Data Standards**
  - **Study Data Standards for Regulatory Submissions**
  - Janus Clinical Trials Repository (CTR) Project
  - Standard for Exchange of Non-Clinical Data
  - Study Design Standard
  - Study Participation Standard
  - Subject Data Standard

Study Data Standards for Regulatory Submissions

Position Statement

FDA recognizes the investment made by sponsors over the past decade to develop the expertise and infrastructure to utilize Clinical Data Interchange Standards Consortium (CDISC)[1] standards for study data. The submission of standardized study data enhances a reviewer's ability to more fully understand and characterize the efficacy and safety of a medical product.

The Prescription Drug User Fee Act (PDUFA V)[2] Performance Goals state that FDA will develop guidance for industry on the use of CDISC data standards for the electronic submission of study data in applications. In the near future, FDA will publish guidance that will require study data in conformance to CDISC standards.[3]

FDA envisions a semantically interoperable and sustainable submission environment that serves both regulated clinical research and health care. To this end, FDA will continue to research and evaluate, with its stakeholders, potential new approaches to current and emerging data standards. FDA does not foresee the replacement of CDISC standards for study data and will not implement new approaches without public input on the cost and utility of those approaches.

September 13, 2013

http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/ucm368613.htm

PDUFA V Goals Section XII

- Clinical Terminology Standards: Using a public process that allows for stakeholder input, **FDA shall develop standardized clinical data terminology through open standards organizations (i.e., CDISC) …**
  - … FDA shall publish a proposed project plan for distinct **therapeutic indications** … for stakeholder review and comment by June 30, 2013
- … periodically publish final guidance specifying the completed data standards, formats, and terminologies that sponsors **must use** to submit data in applications.

Source: Ron Fitzmartin, FDA CDER, Office of Strategic Programs

FDA Goal

Standardize efficacy data elements in 57 therapeutic areas by 2017

- PDUFA V approved by US Congress and signed by President of the United States
- FDA intends to require submission using these standards by 2017

Priority Disease/Domain Areas for Data Standardization

Tier 1		
Acne	Pain*	Schizophrenia
Alzheimer's Disease*	Parkinson's Disease*	Solid organ transplantation
Anti-diabetic agents*	Prevention of pregnancy	Treatment of Hepatitis C*
Crohn's Disease	Psoriasis	Treatment of postmenopausal osteoporosis
Infections of skin and/or subcutaneous tissue	QT Studies	Tuberculosis*
Oncology: time to efficacy event other than overall survival*	Rheumatoid arthritis	Urinary tract infections
Tier 2		
Addiction	Gastroesophageal reflux disease	Pneumonia
Anticonvulsants	Influenza	Prevention of HIV
Asthma	Irritable bowel syndrome	Treatment of HIV
Bipolar Disorder	Lipid-altering drug groups	Treatment of overactive bladder
Clostridium difficile colitis	Major depressive disorder	Treatment of vasomotor symptoms due to menopause
Diabetic nephropathy	Objective tumor response*	Ulcerative colitis
Tier 3		
Actinic keratoses	Decompensated CHF	Tinea pedis
Aerosolized antimicrobals for cystic fibrosis	Diagnostic radiopharmaceuticals	Tramatic brain injury
Atrial fibrillation	General Anxiety Disorder	Treatment of cough
Attention Deficit Hyperactivity Disorder	Helicobacter pylori ulcer disease	Treatment of erectile dysfunction
Bacterial vaginosis	Infectious diseases of the abdomen	Treatment of hepatitis B
Chemotherapy-induced	MRI contrast agents	

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm269946.htm

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 24 June 2013
2 EMA/240810/2013
3 Executive Director

4 Publication and access to clinical-trial data

242 Wherever technically possible, analysable, de-identified raw CT data shall be made available for
243 downloading in the format in which they have been analysed by the applicant, submitted and
244 evaluated. For the time being, this can be according to CDISC (Clinical Data Interchange Standards
245 Consortium) or other appropriate standard. In future, CDISC shall be the required standard, in line
246 with future guidance from the Agency. No conversion of formats is recommended, either by the
247 marketing-authorisation holder or the Agency.

EMA Policy Next Steps

- Draft Policy
  published 30 June 2013 
- Public Consultation
  closed 30 September 2013 
- EMA reviewing comments
- Final Policy expected 2014
- Implementation Plan in development

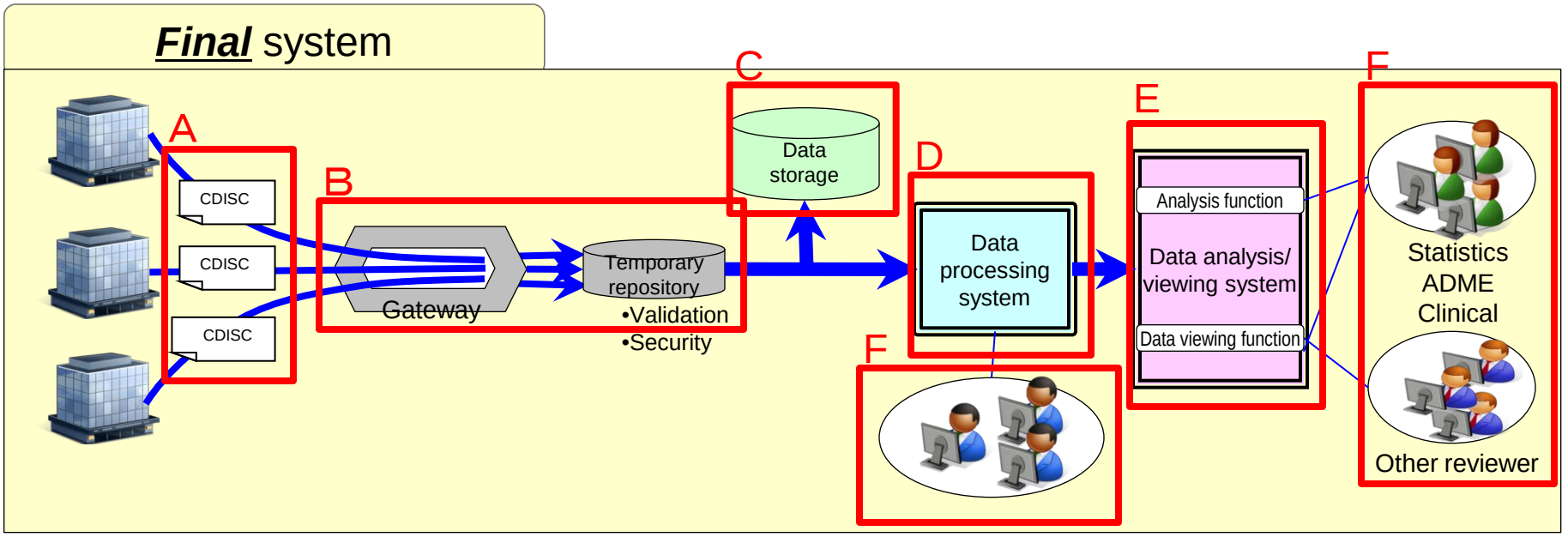
"PMDA plans to request patient level clinical trial data in electronic format which complies with CDISC standards."

"PMDA plans to accept CDISC compliant data in new drug application for efficient and high quality new drug review. As a result, this may lead to standardization of study data and efficient drug development in Japan."

Yuki Ando
PMDA Senior Scientist for Biostatistics
CDISC International Interchange, 6 November 2013

PMDA has completed a pilot with CDISC standards. Results to be presented at the CDISC Europe Interchange April 2014.

Overview of utilization of electronic study data within PMDA (Dr. Taisuke Hojo, Senior Executive Director, PMDA)



Objective

- Improvement of regulatory review/ consultation quality
- Support to increase drug development efficiency

○ Factors involved in the "final system"

A) Study data in standardized format (***CDISC***)

B) Evaluation of electronically submitted data (Gateway + validation)

C) Storage of original data in one place (storage)

D) Data processing for easy analysis (data reduction system)

E) Analysis (data analysis/viewing system)

F) Effective use of the "final system" (trained experts)

Update on the Center of Drug Evaluations (CDE), China FDA (CFDA) and CDISC (C3C)

- 2012 -mid-2013 China CDISC Coordinating Committee 3C - CSTAR) validated translations of CDISC standards into Chinese and launched Traditional Chinese Medicine (TCM) Team
- June 2013 - Established **China Clinical Trial Data Standards Steering Committee**

(临床试验数据标准化工作指导组)

Co-led by C3C Chair with CFDA

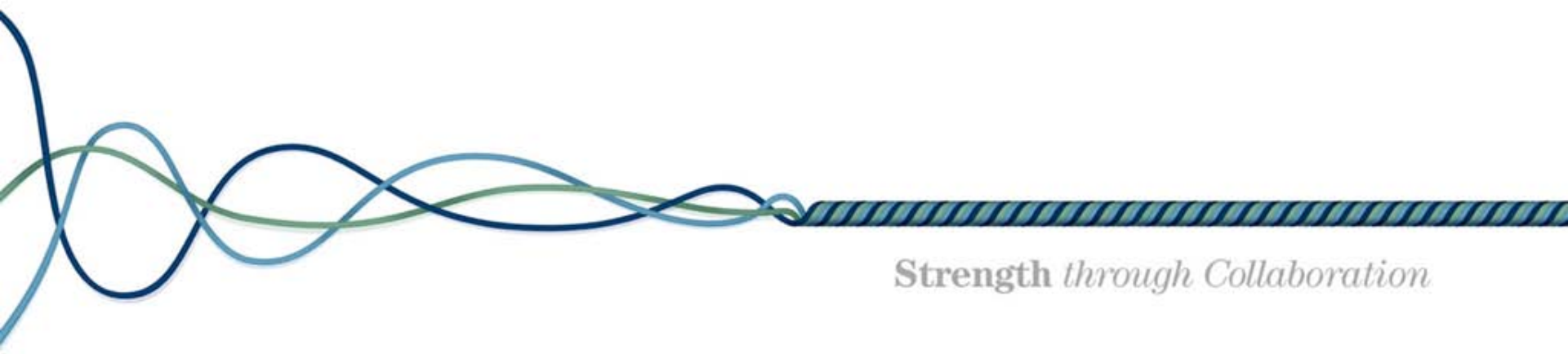
- July and August: Issued **China Clinical Data Plan (CCDP)**

and formed several working groups (**CTDS-WG**) around the CDISC Standards

- September through 2014: Pilot project (CDISC standards in Chinese)

Many thanks to Zibao Zhang, leader of C3C, and to the C3C teams.

Therapeutic Area Standards



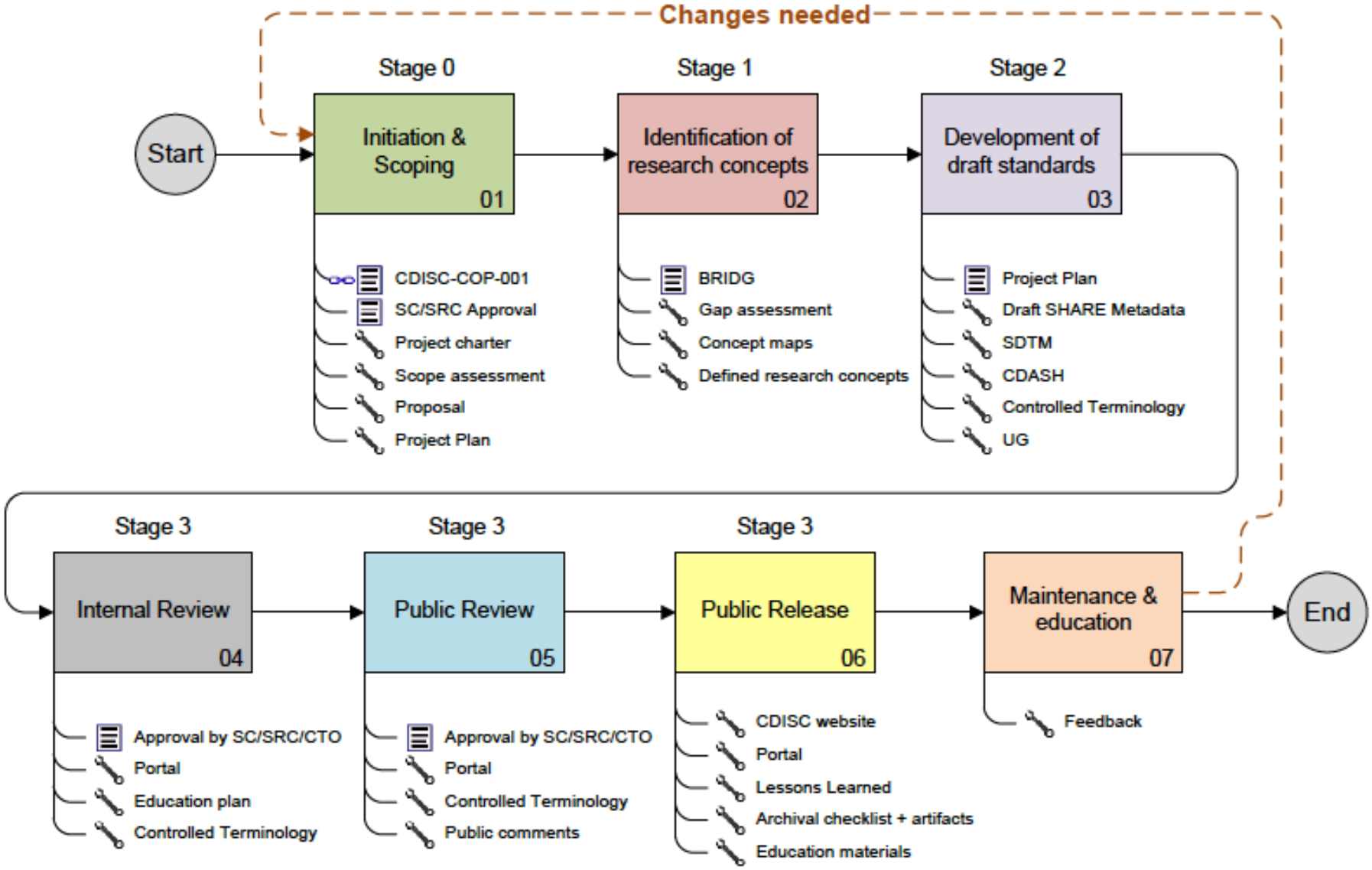
Launch of CFAST

Coalition For Accelerating Standards and Therapies

*CFAST is an **initiative** of CDISC and the Critical Path Institute to accelerate clinical research and medical product development by facilitating the creation and maintenance of data standards, tools, and methods for conducting research in therapeutic areas important to public health.*

(CDISC Constituents wanted ALL the standards developed.)

Standards Development Process



"Drug Makers Join Efforts in Research"

By ANDREW POLLACK, New York Times,

Published: September 19, 2012

"Ten of the world's largest pharmaceutical companies said on Wednesday that they would cooperate on research aimed at accelerating drug development, starting with streamlining clinical trials."

"TransCelerate said it would work with other organizations. At least two nonprofit organizations, each with pharmaceutical company participation, are already working on accelerating clinical trials and standardizing data. Just last week, those two organizations — ***the Clinical Data Interchange Standards Consortium and the Critical Path Institute — announced that they would form the Coalition for Accelerating Standards and Therapies***."

Therapeutic Area Standards Governance

CFAST SAC
Scientific Advisory Committee

- Provides Scientific Advice to TAPSC
- Identifies Risks and Opportunities
- Identifies/Engages Relevant Partners

CFAST TAPSC
Therapeutic Area Program Steering Committee

- Prioritizes/Approves Proposals
- Approves Projects & Charters
- Resources & Oversees Projects

CDISC TA Standards Project Teams

Project Leader +

Clinical leads (SMEs), BRIDG Modeler, Concept Creators, Terminologists, Metadata Analysts, Stats Consultants, Writers, Communications

CDISC Research Community

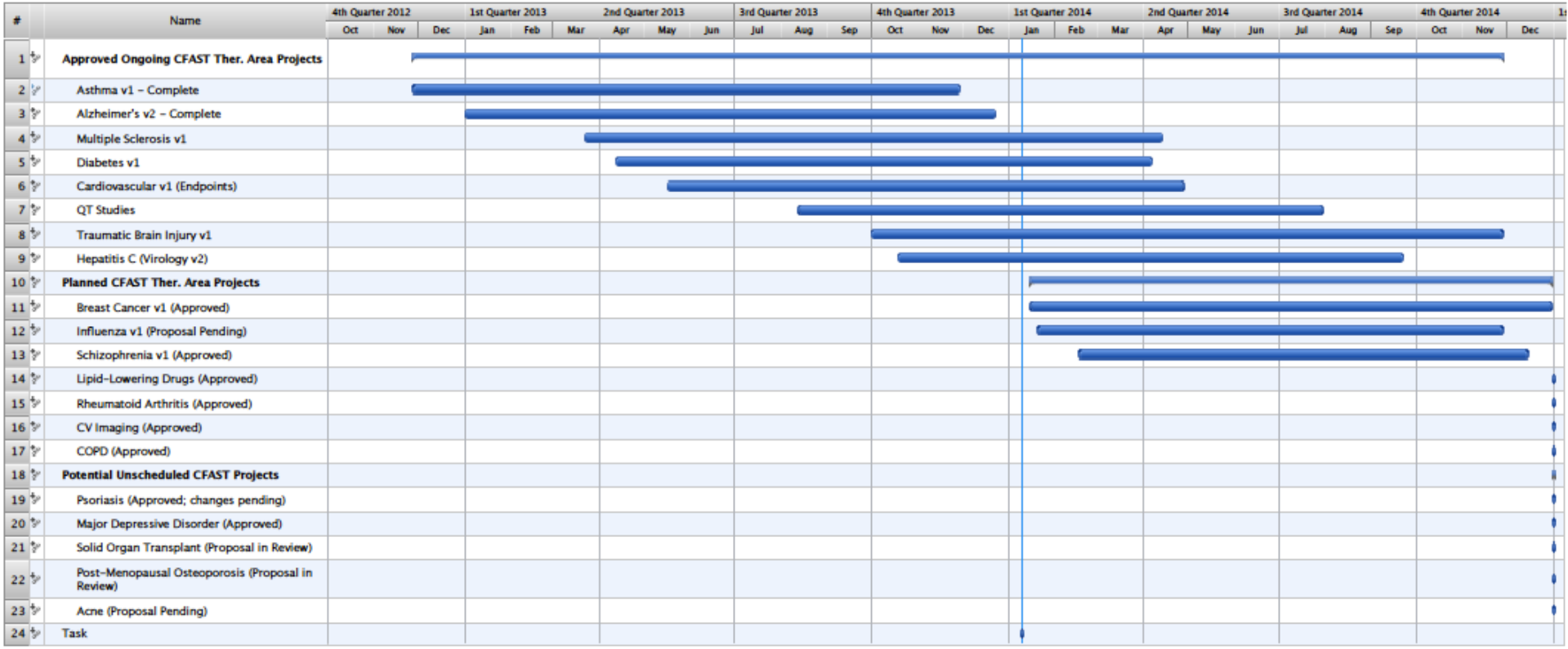
Ongoing Maintenance & Enhancement of Foundational CDISC Standards

CDISC Research Community

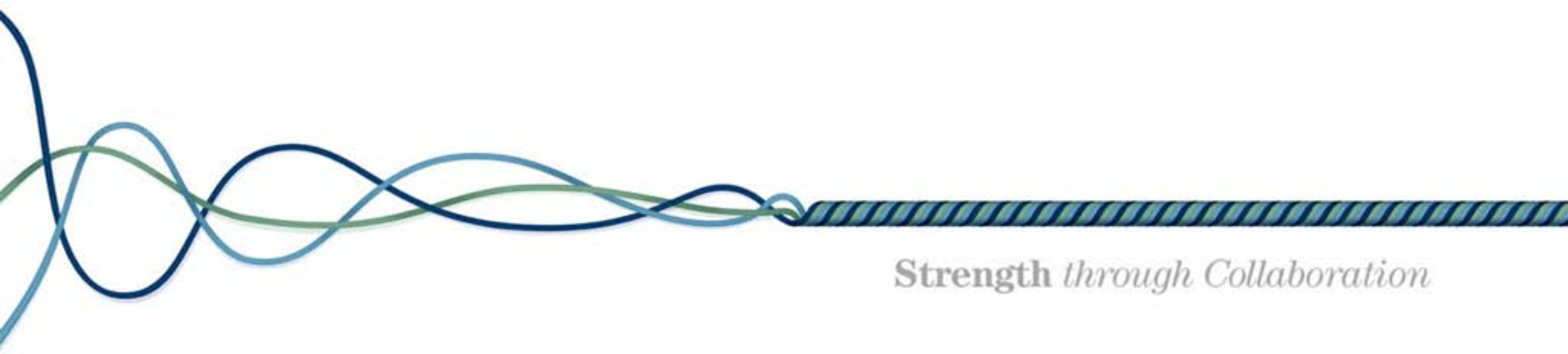
CDISC Therapeutic Area Standards

Released Standards	Work in Progress	Planned Standards
Alzheimer's Disease v1 & v2	Cardiovascular Endpoints v1	Breast Cancer v1
Asthma v1	Diabetes v1	COPD v1
Parkinson's Disease v1	Hepatitis-C v1	Rheumatoid Arthritis
Polycystic Kidney Disease v1	Influenza v1 (and Vaccine Standard v1)	Traumatic Brain Injury
Tuberculosis v1 (pulmonary)	Multiple Sclerosis v1	Tuberculosis v2 (pediatrics)
Virology v1	QT Studies v1	
	Schizophrenia v1	

Current CFAST Working Plan



CDISC SHARE



“Data are More Meaningful when SHARE’d”

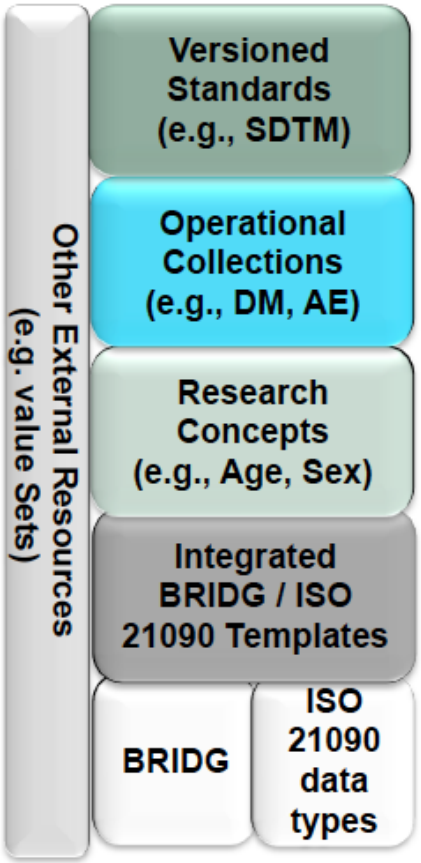
Shared Health and Research Electronic Library (SHARE)

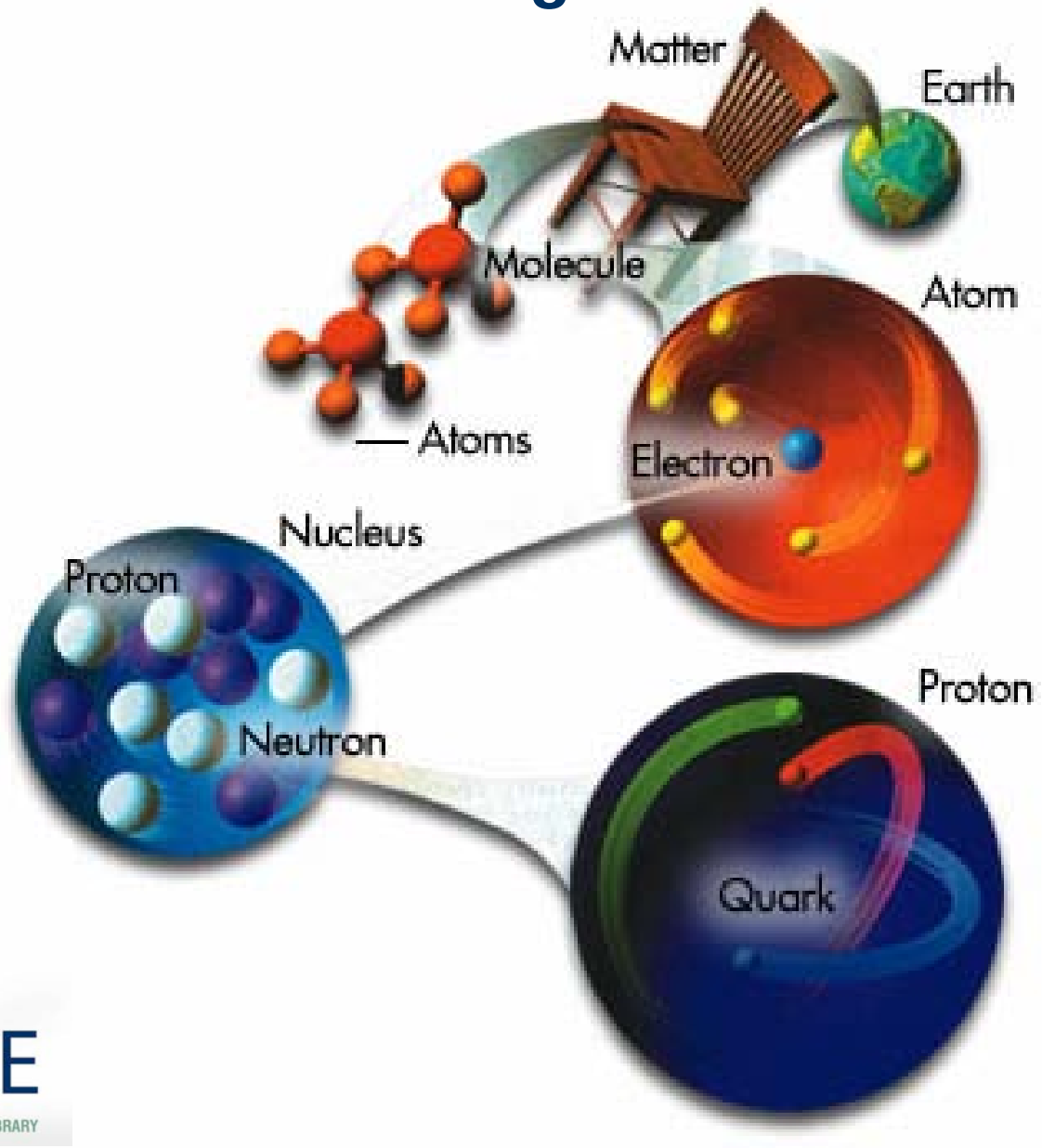
A global electronic repository for developing, integrating and accessing CDISC standards metadata in electronic format.

SHARE should dramatically improve the quality, reusability and integration across CDISC standards and controlled terminologies, and improve interoperability with healthcare.

SHARE is a requirement for standards-based automation, which is key to ROI from standards implementation

The Chemistry of Metadata Through SHARE

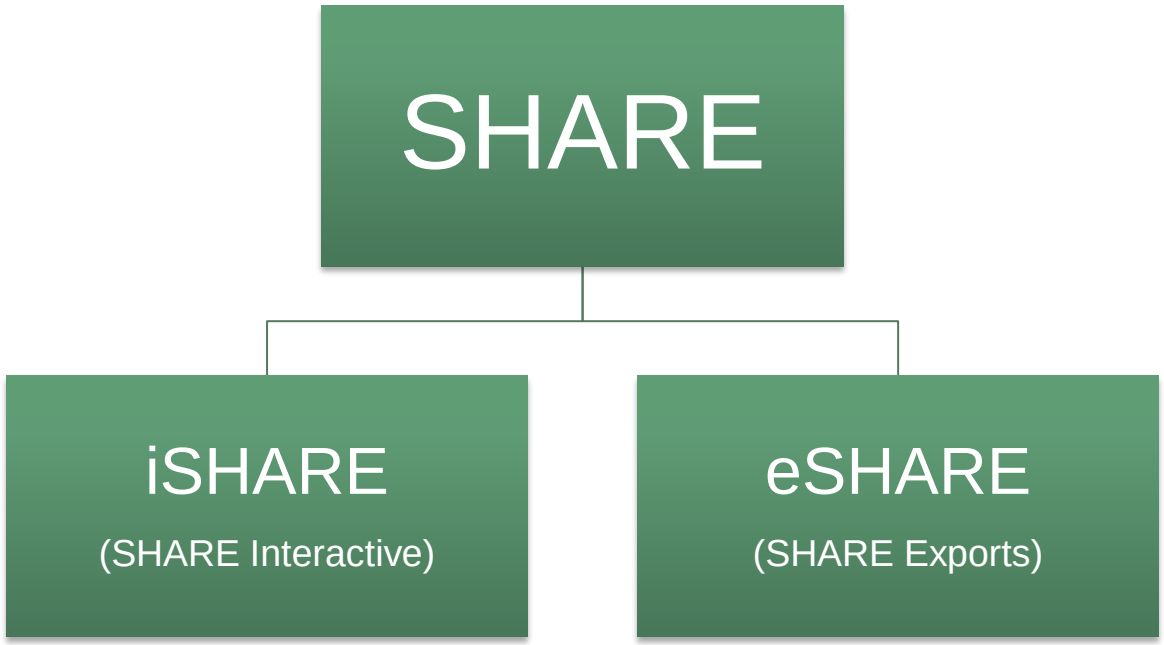




CDISC SHARE

SHARED HEALTH AND CLINICAL RESEARCH ELECTRONIC LIBRARY

User Perspectives of SHARE



Standards Development & Governance

Accessing Published Standards in a Machine-Readable Format

R1
Q1 2014

SHARE R1: Initial Capability

- First version of iSHARE
  - Implemented using SOA's Semantics Manager
  - Meta-model based on ISO11179, BRIDG and ISO21090/HL7 Datatypes
  - Cloud-based – hosted at Amazon
  - Exploring out-of-the-box functionality to develop, maintain and access CDISC standards.
- Load of Initial set of CDISC standards into SHARE
  - SDTM 1.2 (SDTMIG 3.1.2)
  - CDASH 1.1
  - BRIDG 3.2 and ISO21090
  - All CDISC Terminologies
  - New versions (e.g. SDTMIG 3.1.3, 3.2) now being added.

R1

Q1 2014

R1: Machine-Readable Standards and Basic Functions

- Export machine-readable standards
  - ODM v1.3.2
  - Define-XML v1.0 & v2.0
  - CSV / Tab delimited / Excel
- Version control & impact analysis
- Workflows (e.g. new requests, metadata governance)
- Reporting (e.g. governance metrics)

SHARE Near-Term Deployment Plan

- iSHARE used by SHARE Team and initial foundational standards team developers
- Develop champions that will help support the next wave of users

- eSHARE made available to initial content consumers
- Additional foundational standards developers trained in iSHARE

- Additional eSHARE deployment
- Prototype Development using Research Concepts
- Additional trained TA and foundational standards developers

Full deployment anticipated in 2016

License required to use iSHARE

eSHARE: Accessing SHARE Content

- Website for easy, one-stop download of SHARE machine-readable content
  - Metadata and Terminologies
- Export formats include:
  - ODM v1.3.2
  - Define-XML v1.0 & v2.0
  - CSV / Tab delimited / Excel
  - RDF/OWL (R2)
- Website for easy download of SHARE machine-readable content
- Initial pilot rollout to Platinum members in Q2 2014.

Agile Incremental Development Approach

- Each release will include incremental improvements in:
  - Expanded breadth of standards content
  - Standards quality & completeness
  - Relationships between metadata
  - Use of concepts to define standards and standards models
  - Ease of use refinements
  - New reports and metrics
  - Standards development and governance workflows
  - SHARE training and documentation
  - Reducing the reliance on spreadsheets and other document formats for standards development and governance
  - Efficiency in standards development and governance

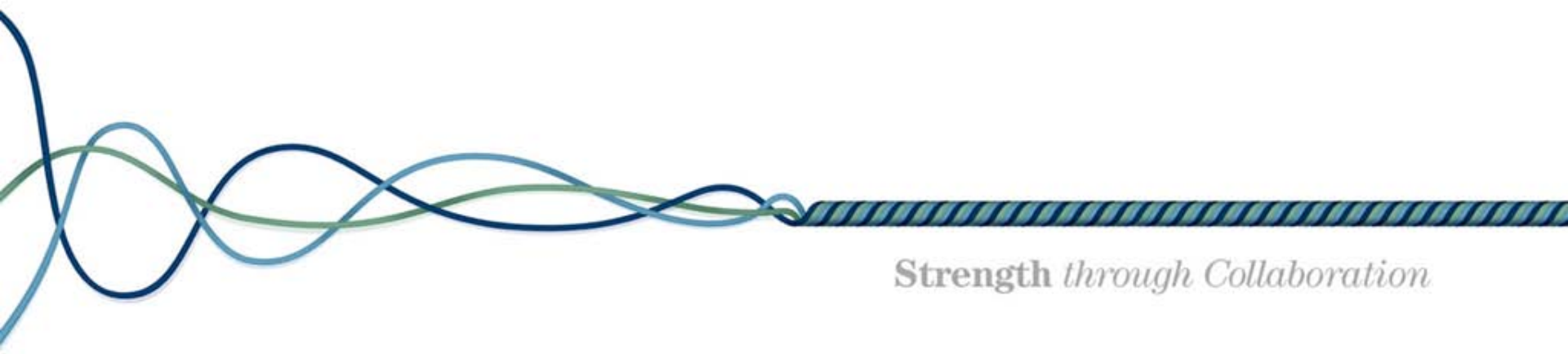
R2
Q4 2014

R2: SHARE Concept-based Standards

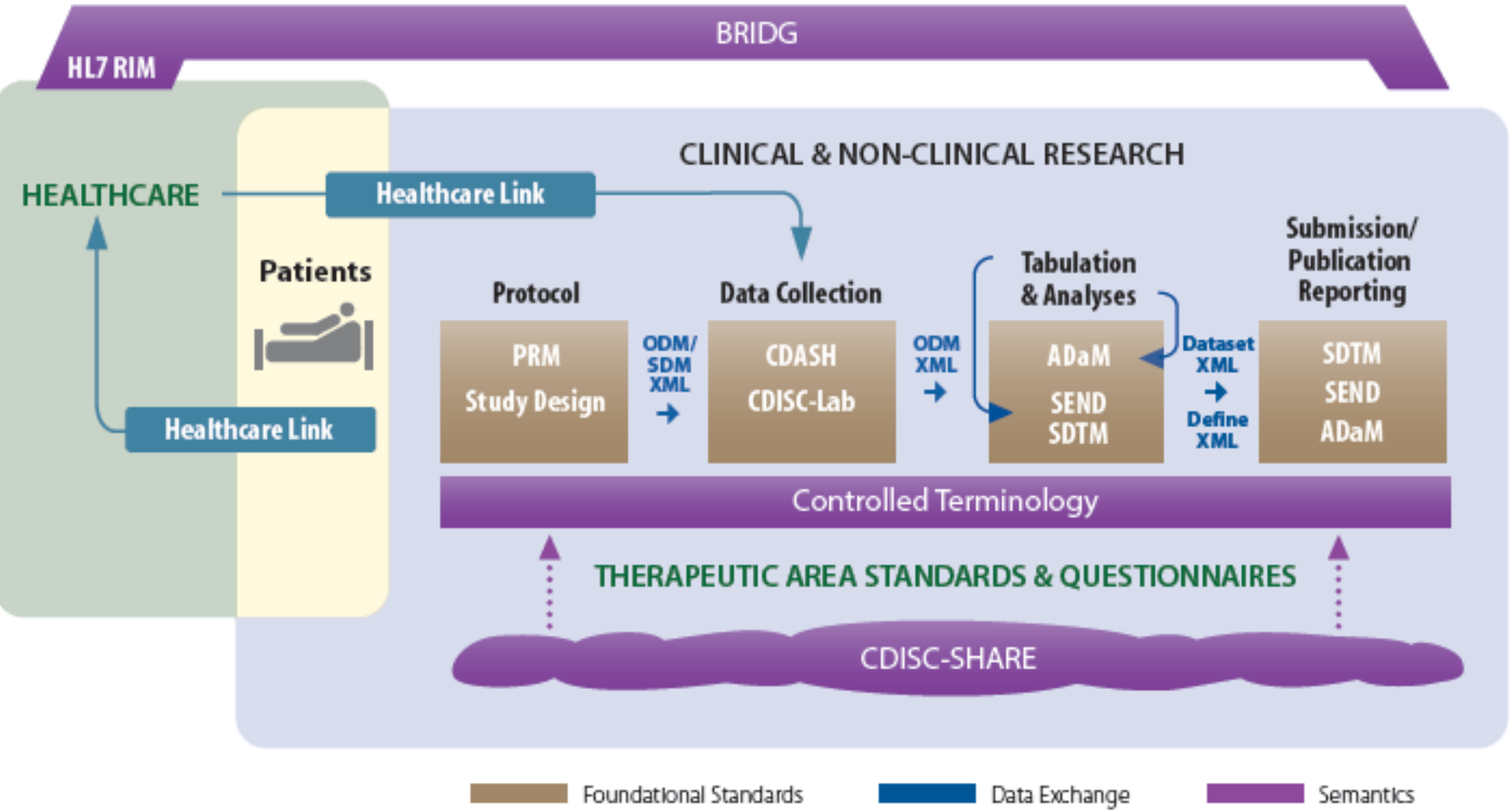
- Implementation of SHARE research concept model
  - Support for Therapeutic Area standards development
- Additional CDISC standards content (PRM, ADaM, SEND)
  - Single, trusted source for all CDISC data standards
- Expanded eSHARE content download site
  - Value Level Metadata content
- Improved Controlled Terminology process integration
- RDF/OWL export format
- Future releases will include:
  - Improved end-to-end standards integration
  - IG standards document generation
  - Support for other concept systems and increased interoperability.

Rx
2015-2016

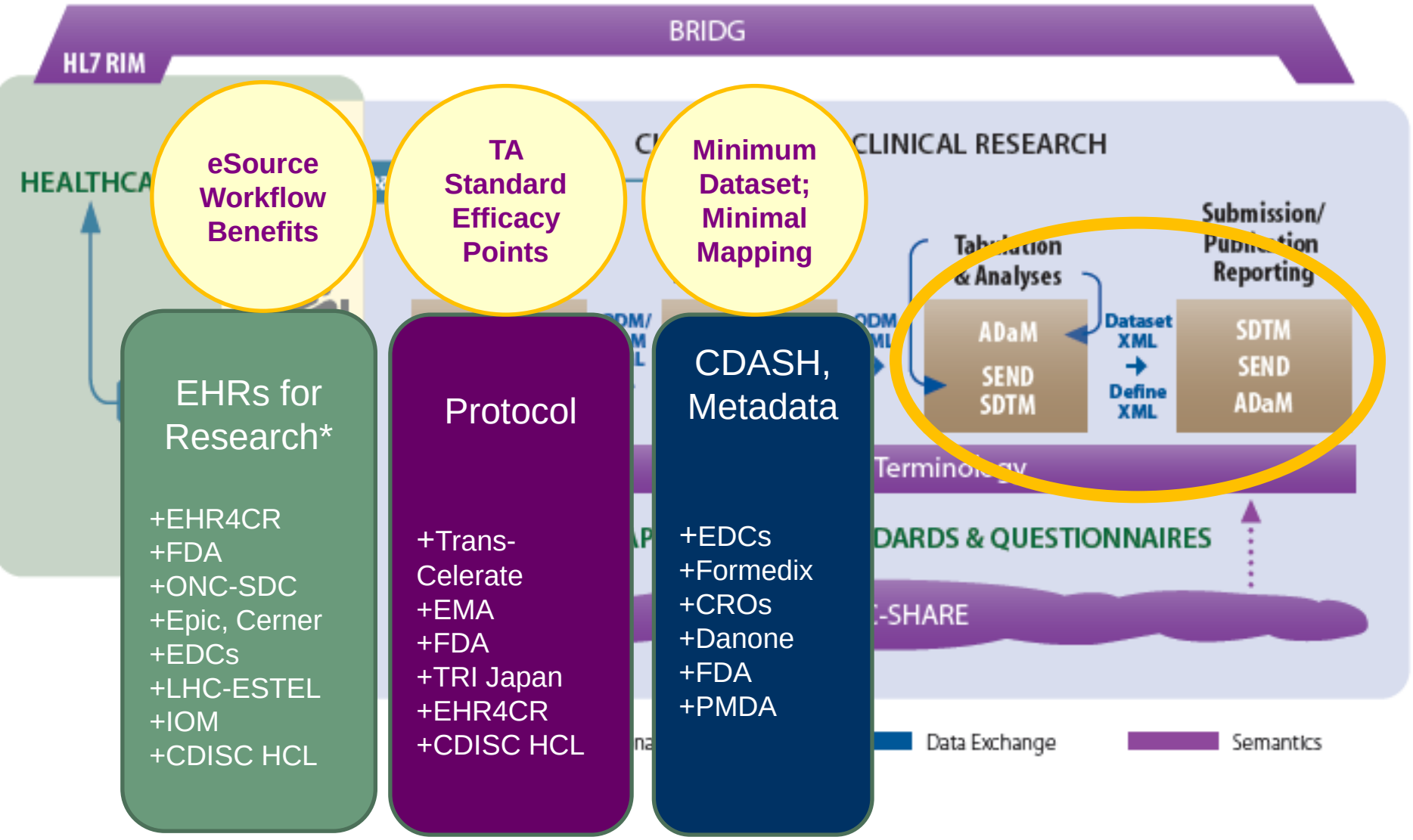
Conclusions



Achieving Interoperability



Achieving Interoperability



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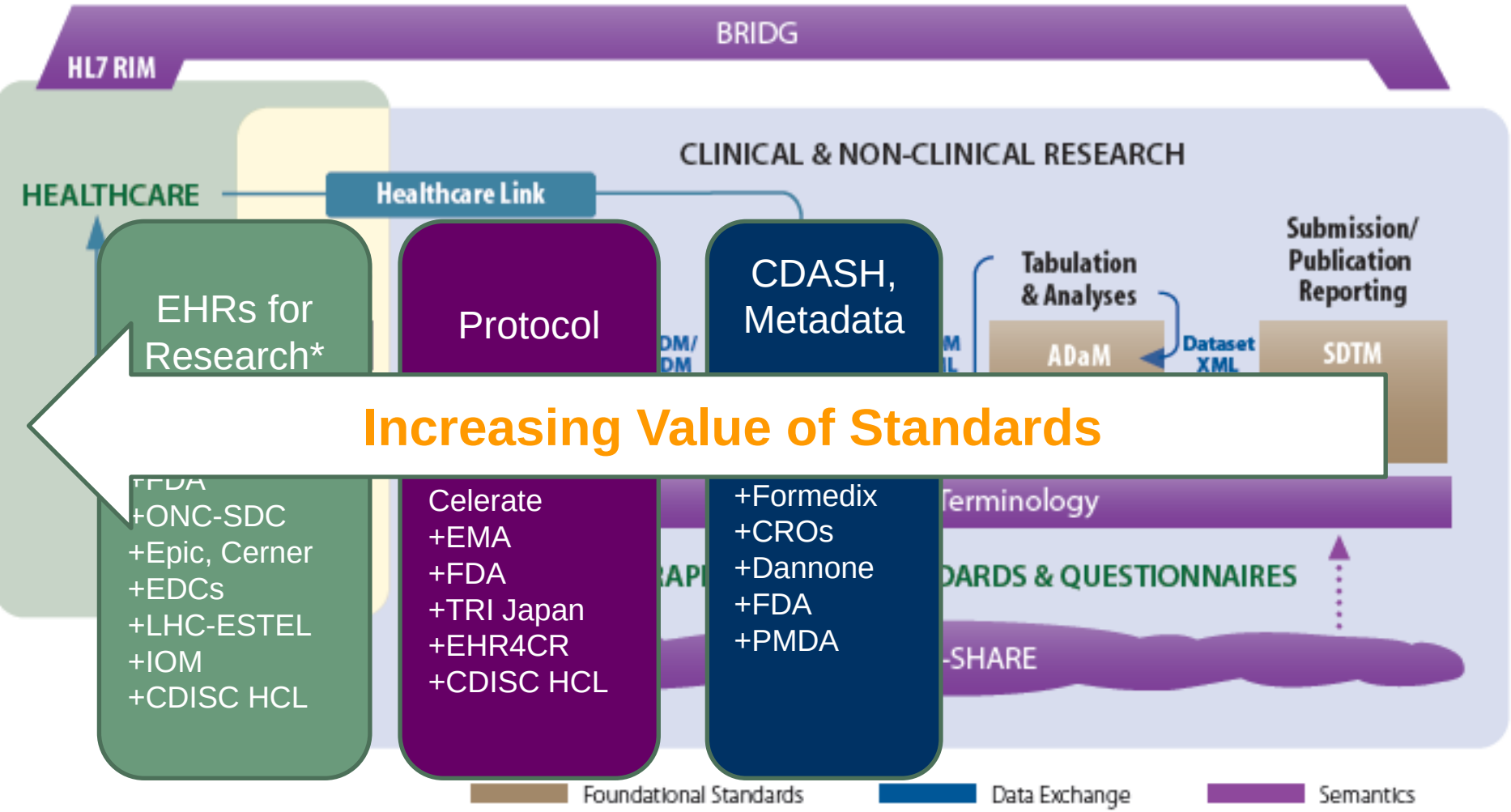
Achieving Interoperability



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The Research Landscape: Data Sharing

- **U.S. National Academies of Science Institute of Medicine (IOM): Committee to Report on Sharing of Data for Clinical Trials**
- **New England Journal of Medicine (NEJM): Series of Articles on Data Sharing**

- *Only ~ 45% of researchers share their data; 143 of 351 randomly selected papers complied with their data sharing policy*
- *Of 53 landmark basic science studies in oncology, Amgen could only reproduce results from 6.*

- *Data transparency, liquidity, liberation*
- *Data privacy, security, confidentiality*
- *Meta-analysis, data pooling and mining, clean vs. 'scruffy data, 'rogue data'*
- *Incentives/disincentives, especially for researchers*

CDISC Strategic Goals 2013-2015 (1)

1. **Continue to refine, support and provide education on existing foundational CDISC standards**, achieving significant progress in the use of CDISC standards to streamline research, build quality into the beginning of the research process and promoting scientifically sound data aggregation for the purposes of scientific investigation, comparative effectiveness and patient safety.

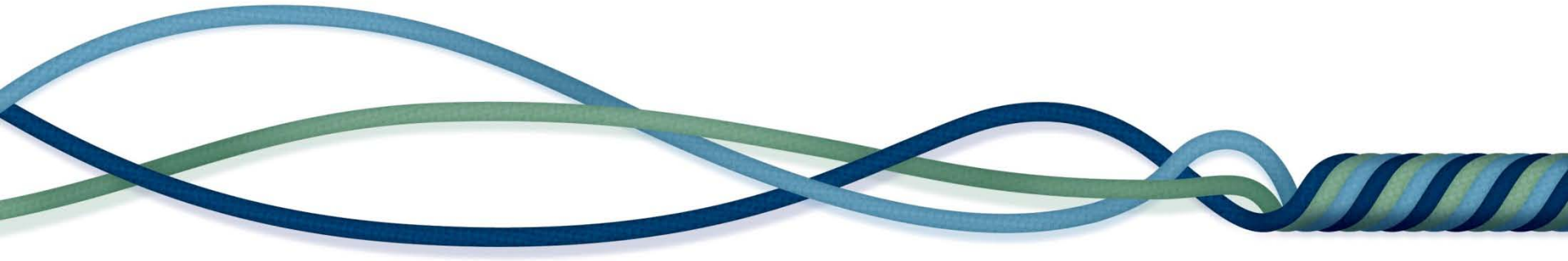
2. **Expedite the development and rollout of new therapeutic area standards** to ensure consistency in data capture and analysis related to efficacy in addition to patient safety.

3. **Achieve significant progress in enabling interoperability between clinical care and clinical research** and explore expansion from bench to bedside (translational research); accelerate the cycle through which healthcare informs research and research informs clinical decisions.

CDISC Strategic Goals 2013-2015 (2)

4. **Develop CDISC SHARE, a global, accessible, electronic library for CDISC content/semantics** that will enable precise and standardized data element definitions and richer metadata that can be reused within applications and across studies to improve biomedical research and its link with healthcare.

5. Leverage our global, non-profit/charitable, vendor neutral, independent status to forge **productive collaborations, to communicate well and to provide value to key stakeholder communities.**



Strength *through collaboration.*