EHR4CR
A joint undertaking between Academia & Industry

Innovative Medicines Initiative

CDISC®
Setting the Global Standard for Medical Research

SANOFI

CDISC: Standards for Clinical Research and Healthcare Data re-Use

CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

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TMF Jahreskongress 2012
Kiel, Germany
29 March 2012

Overview

- Introduction to CDISC
  - What is CDISC
  - Overview of the core standards
  - Other initiatives
- Electronic source data (eSource) and the Use of Healthcare Data for Clinical Research
- Case Study: the IMI EHR4CR project

CDISC

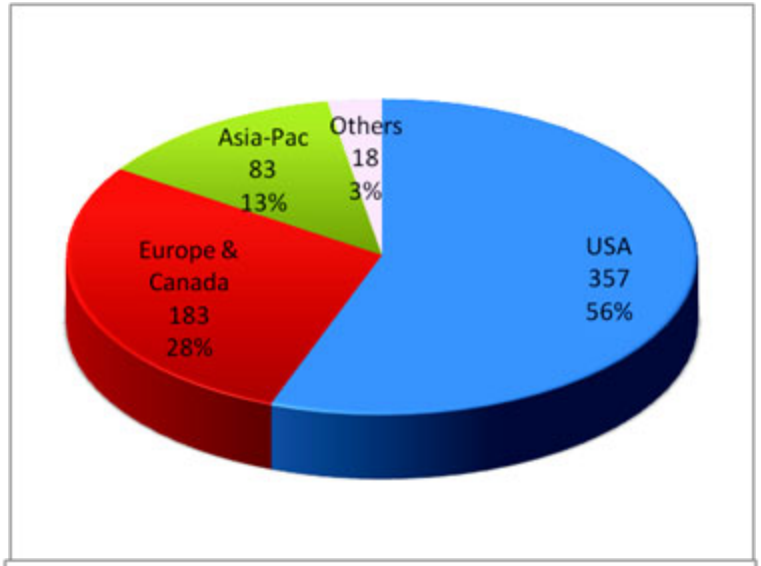
- **Global, open, multi-disciplinary, vendor-neutral non-profit standards developing organization (SDO)**
  - Founded in 1997; incorporated in 2000
  - >300 organizational members (academia, biopharma, service and technology providers, etc)
  - Liaison A Status with ISO TC 215
  - Charter agreement with HL7 since 2001
  - Member/Leader of Joint Initiative Council (JIC) for Global Harmonization of Standards
  - Member of ANSI-led ISO TAG
  - Active Coordinating Committees
    - Europe, Japan, China, Korea
  - Standards downloaded in over 65 countries

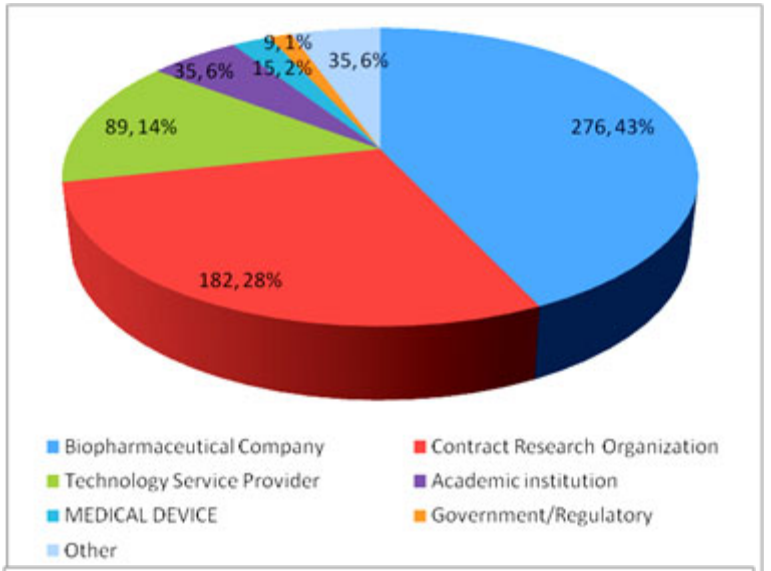
www.cdisc.org

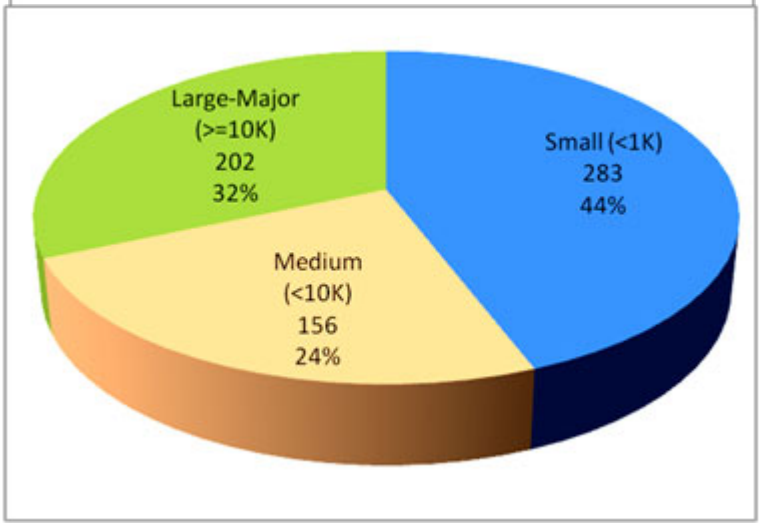
Established global industry standards to support the electronic acquisition, exchange, submission and archiving of data to streamline biomedical research (open via www.cdisc.org)

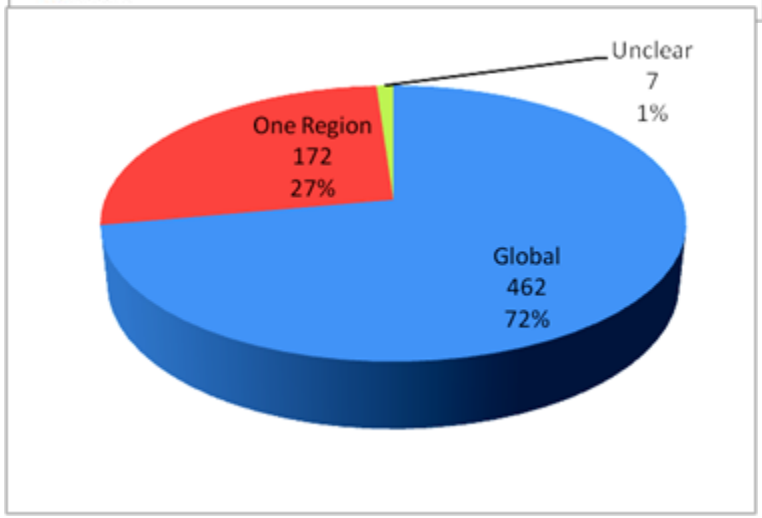
CDISC Develops Global Standards

Implementation Survey (March 2010) Participants Demographics









RTRN (Research Centers in Minority Institution Translational Research Network) – CRFNA

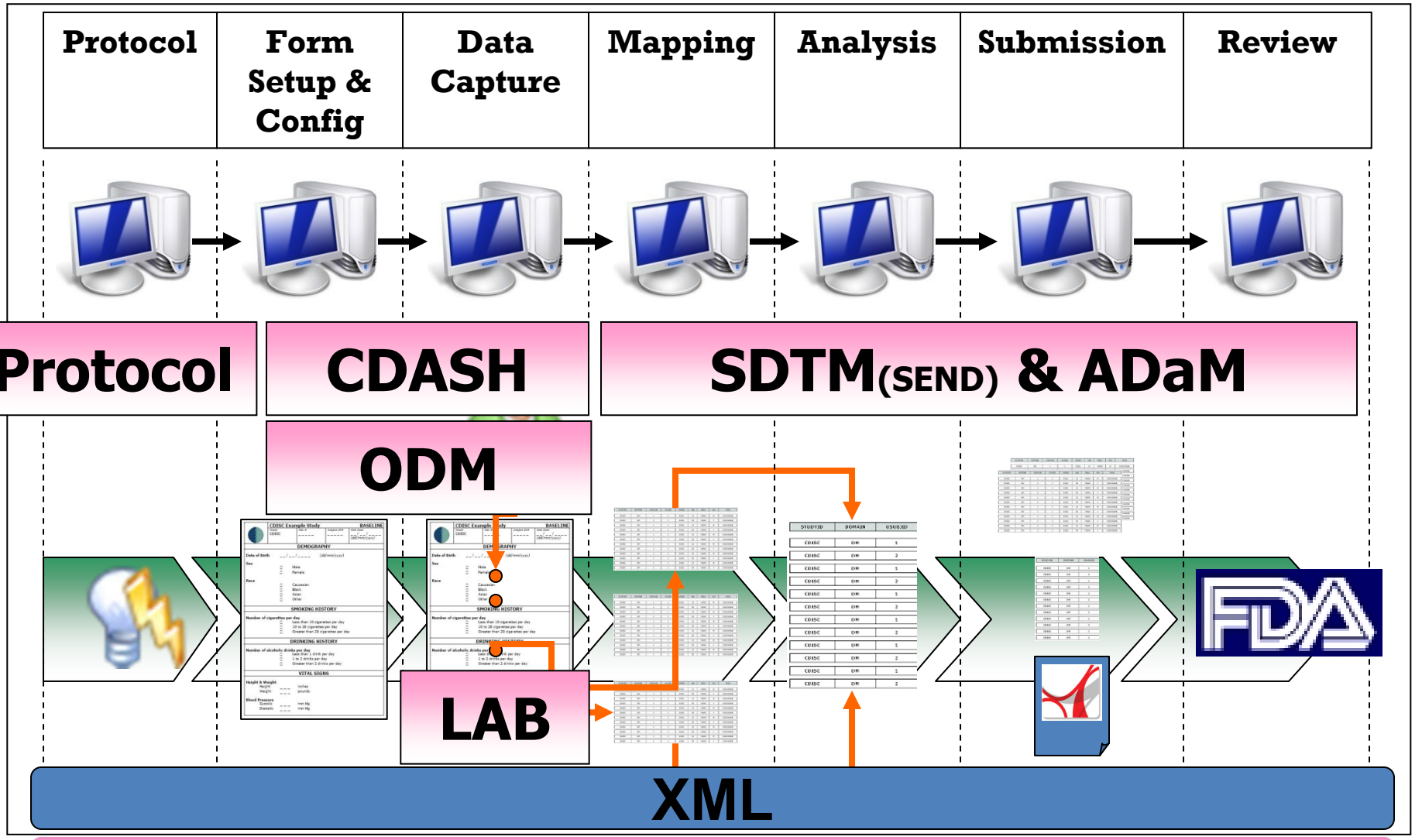
Joint Initiative Council - JIC

- Opportunity to harmonize healthcare and related standards across SDOs globally
  - SDOs 'opt in' on JIC-approved projects, as appropriate)
  - Comparison and alignment of processes and comments/balloting across SDOs
- JIC Projects now include:
  - **ICSR (ICH)**
  - **BRIDG (CDISC)**
  - **CTR (CDISC)**
  - **IDMP (ICH)**

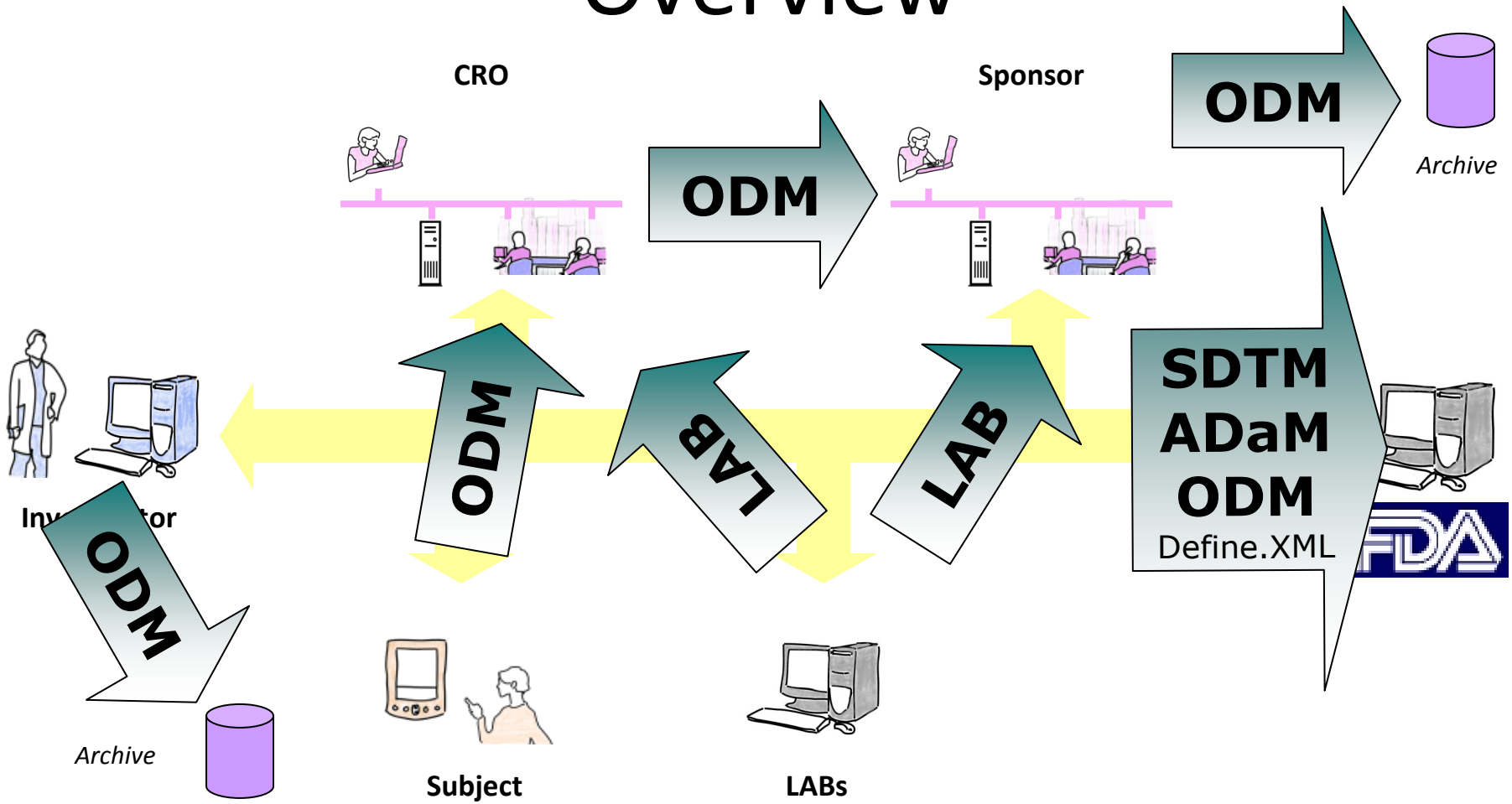
Strength through collaboration

Overview of CDISC core Standards

Clinical Information Flow
The CDISC Way

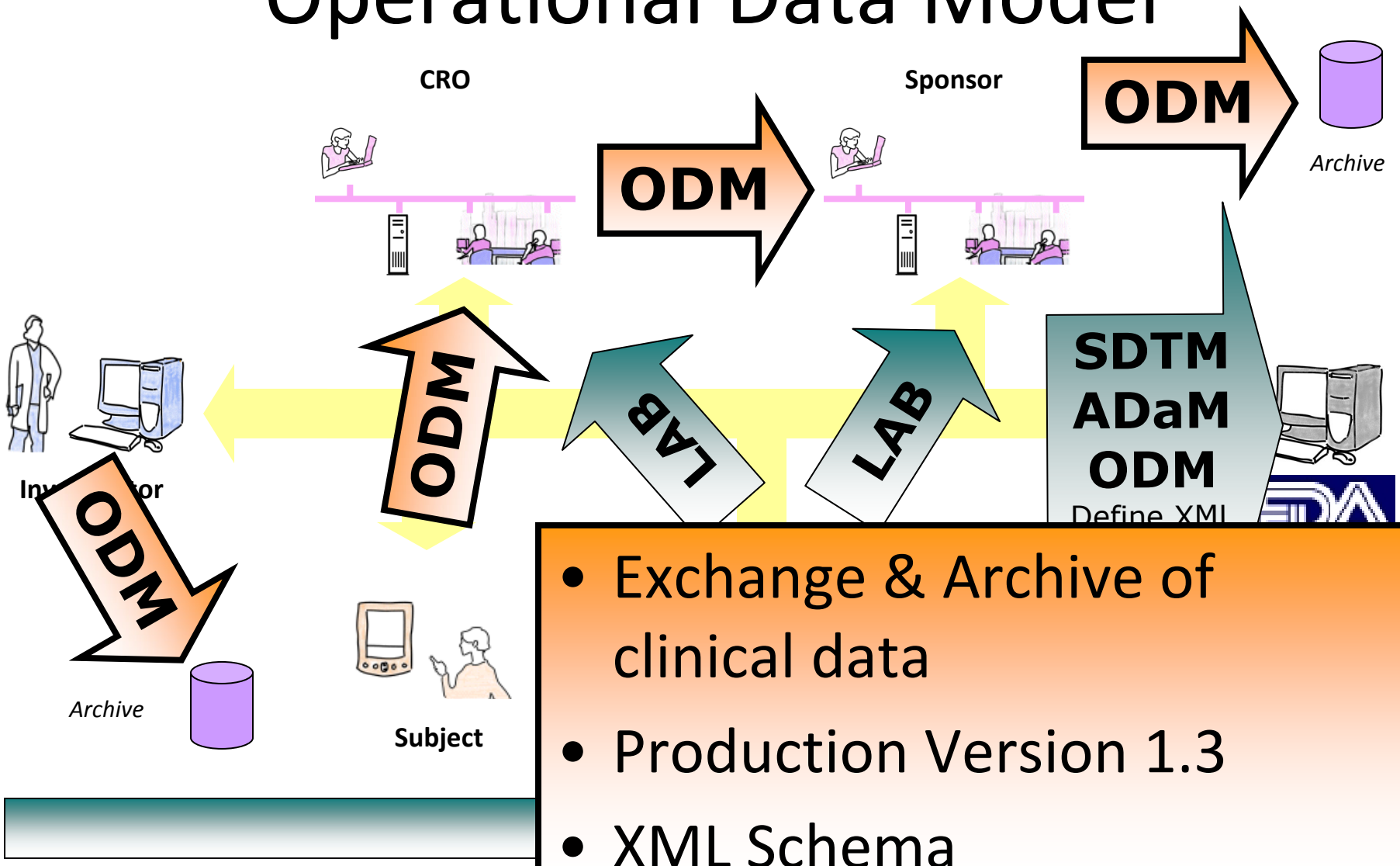


Overview



Protocol & BRIDG

Operational Data Model



- Exchange & Archive of clinical data
- Production Version 1.3
- XML Schema

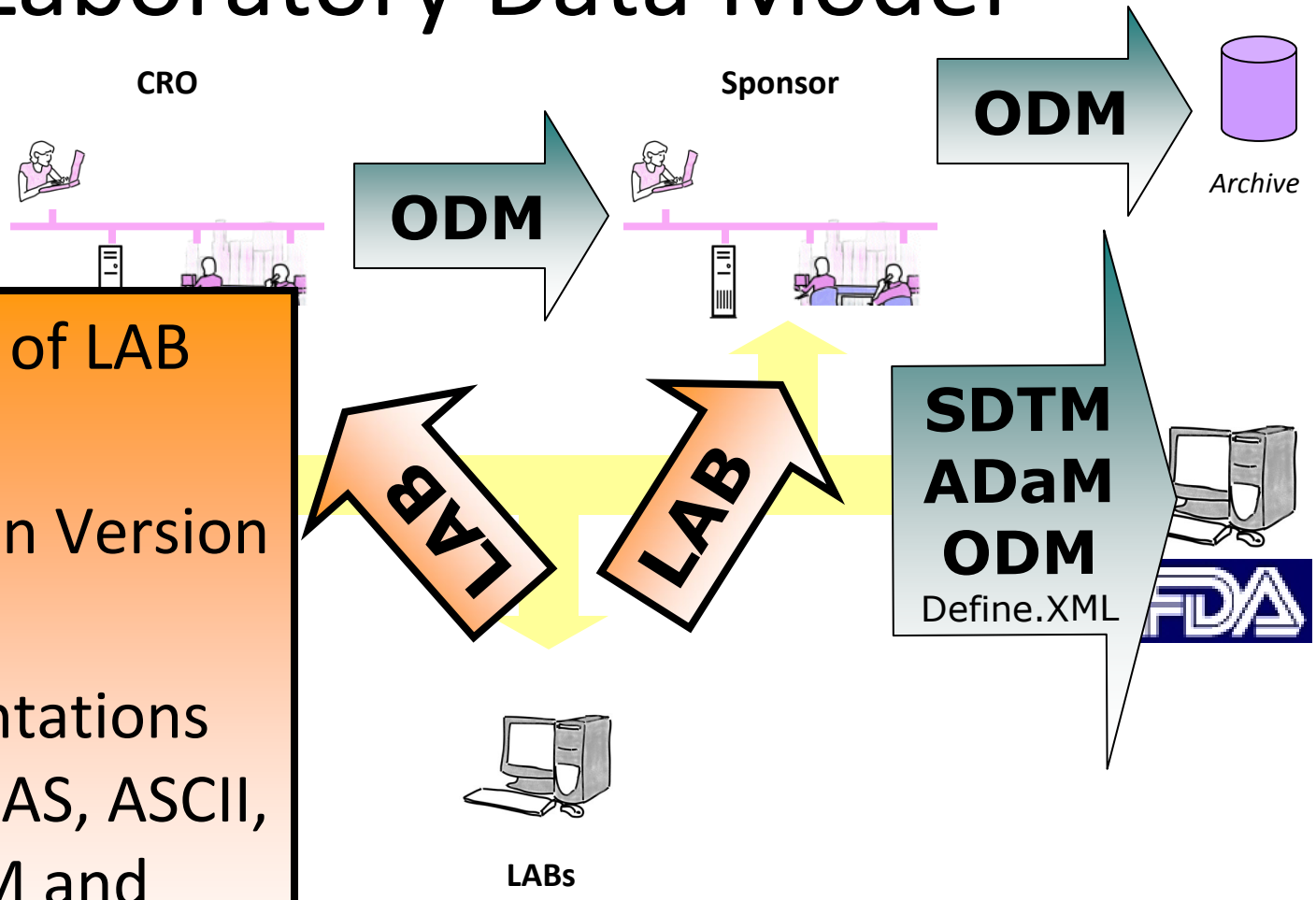
Original Use Cases

- Data Interchange – Transfer of information between two or more parties than maintains the integrity of the contents of the data.
- Data Archive – Long term storage of files that are no longer in active use

Other Use Cases

- Set up of systems
- Acquisition
  - eCRF
  - ePRO
  - EHR
- eSource
- Trial Registry
- Metadata Submission
  - Define.xml

Laboratory Data Model



- Exchange of LAB data
- Production Version 1.0.1
- Implementations through SAS, ASCII, XML/ODM and HL7 V3 RIM message

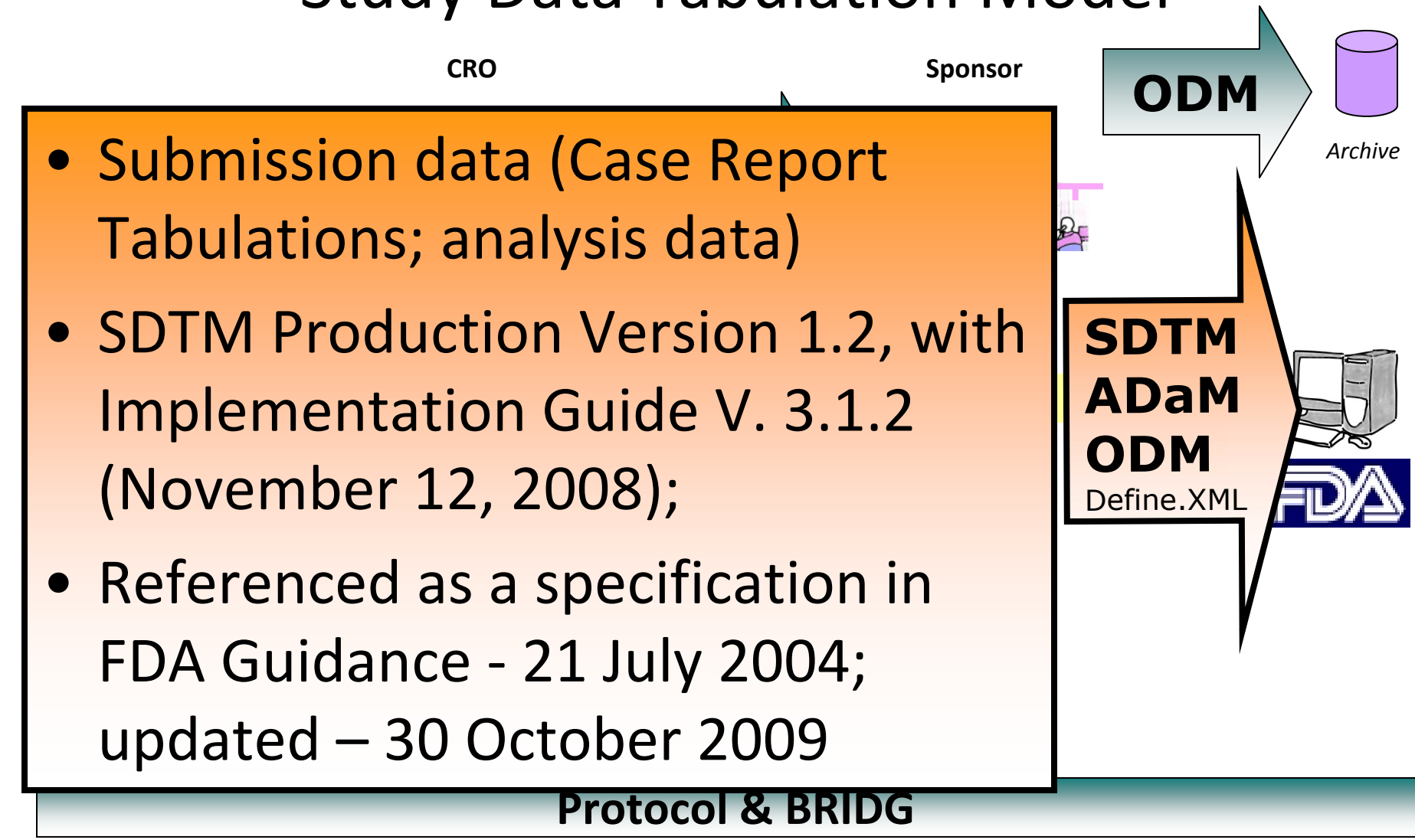
tocol & BRIDG

Use Case

- Support the bulk transfer of laboratory data

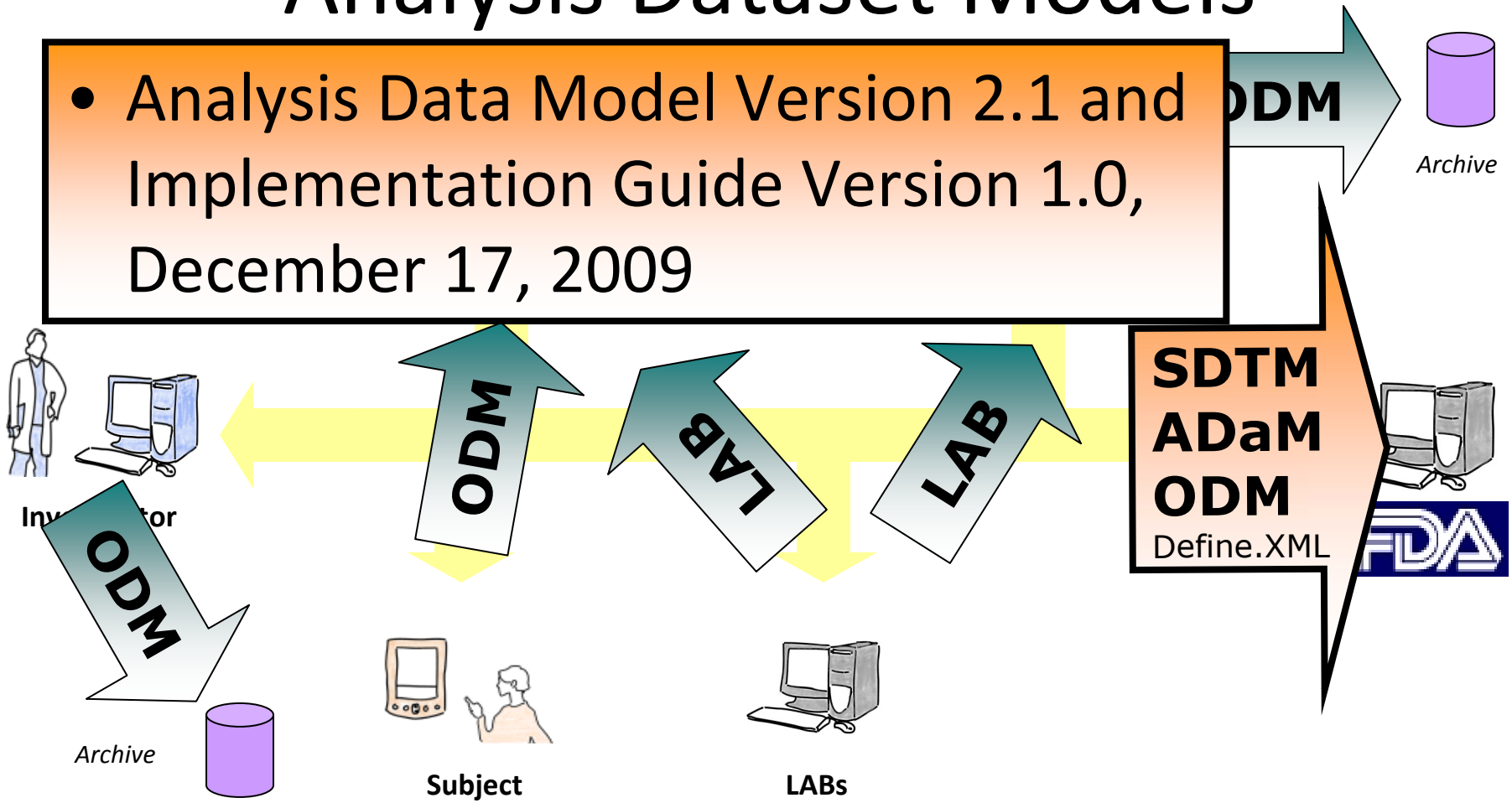
Study Data Tabulation Model

- Submission data (Case Report Tabulations; analysis data)
- SDTM Production Version 1.2, with Implementation Guide V. 3.1.2 (November 12, 2008);
- Referenced as a specification in FDA Guidance - 21 July 2004; updated – 30 October 2009



Analysis Dataset Models

- Analysis Data Model Version 2.1 and Implementation Guide Version 1.0, December 17, 2009



Protocol & BRIDG

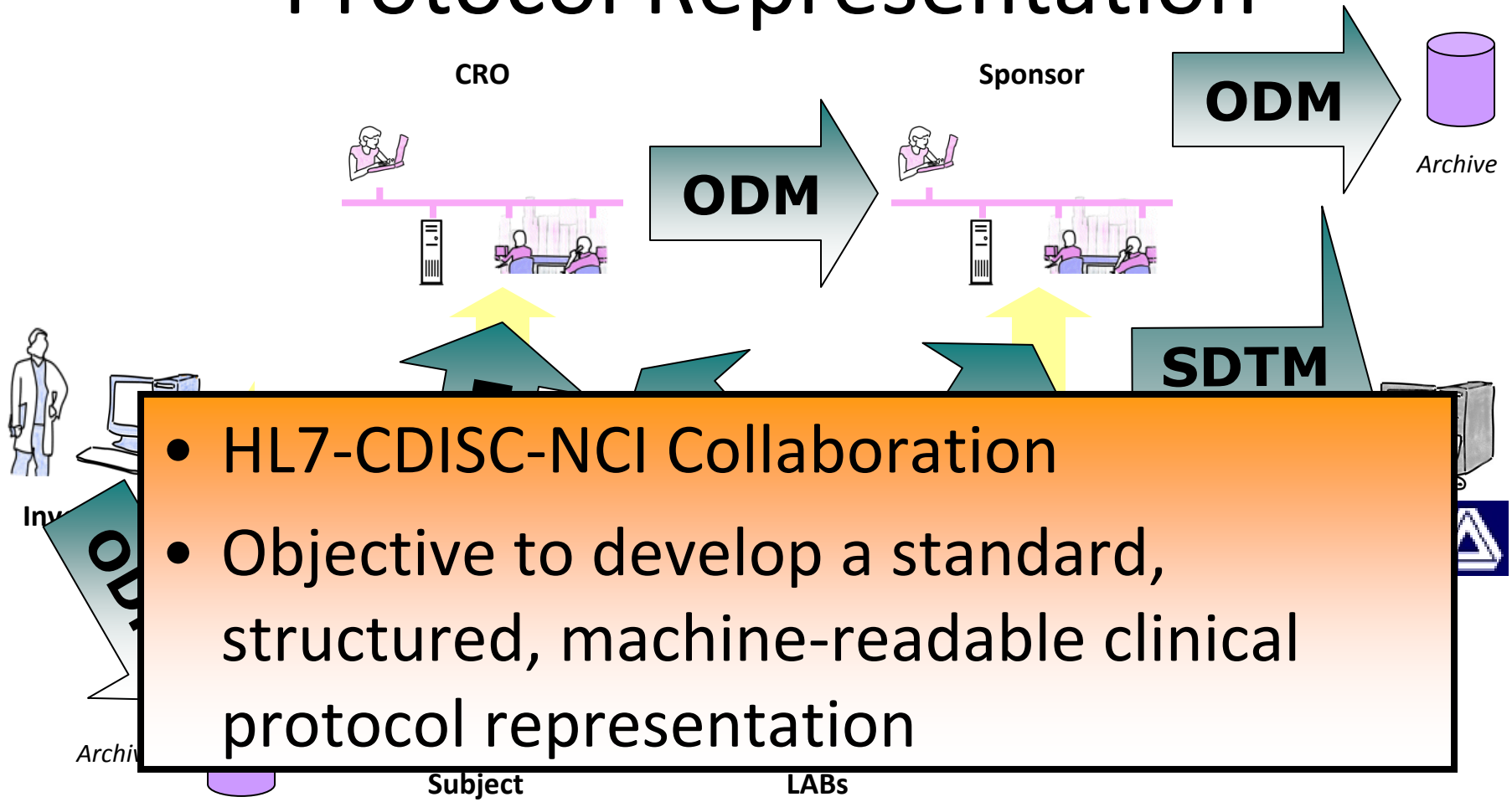
SDTM & ADaM Datasets

- SDTM:
  - observations from a clinical trial
  - are particularly useful in medical officer evaluation of safety (with appropriate tools)
- ADaM:
  - restructured and contain additional information (derived variables, flags, comments, etc.)
  - analysis-ready

CDASH

- FDA Critical Path Opportunity #45
- Continues ACRO's CRF Standardization Initiative
- Goal: To develop a set of 'content standards' (element name, definition, metadata) for a basic set of global data collection fields that will support clinical research studies. The initial scope will be the 'safety data domains' to support clinical trials.

Protocol Representation



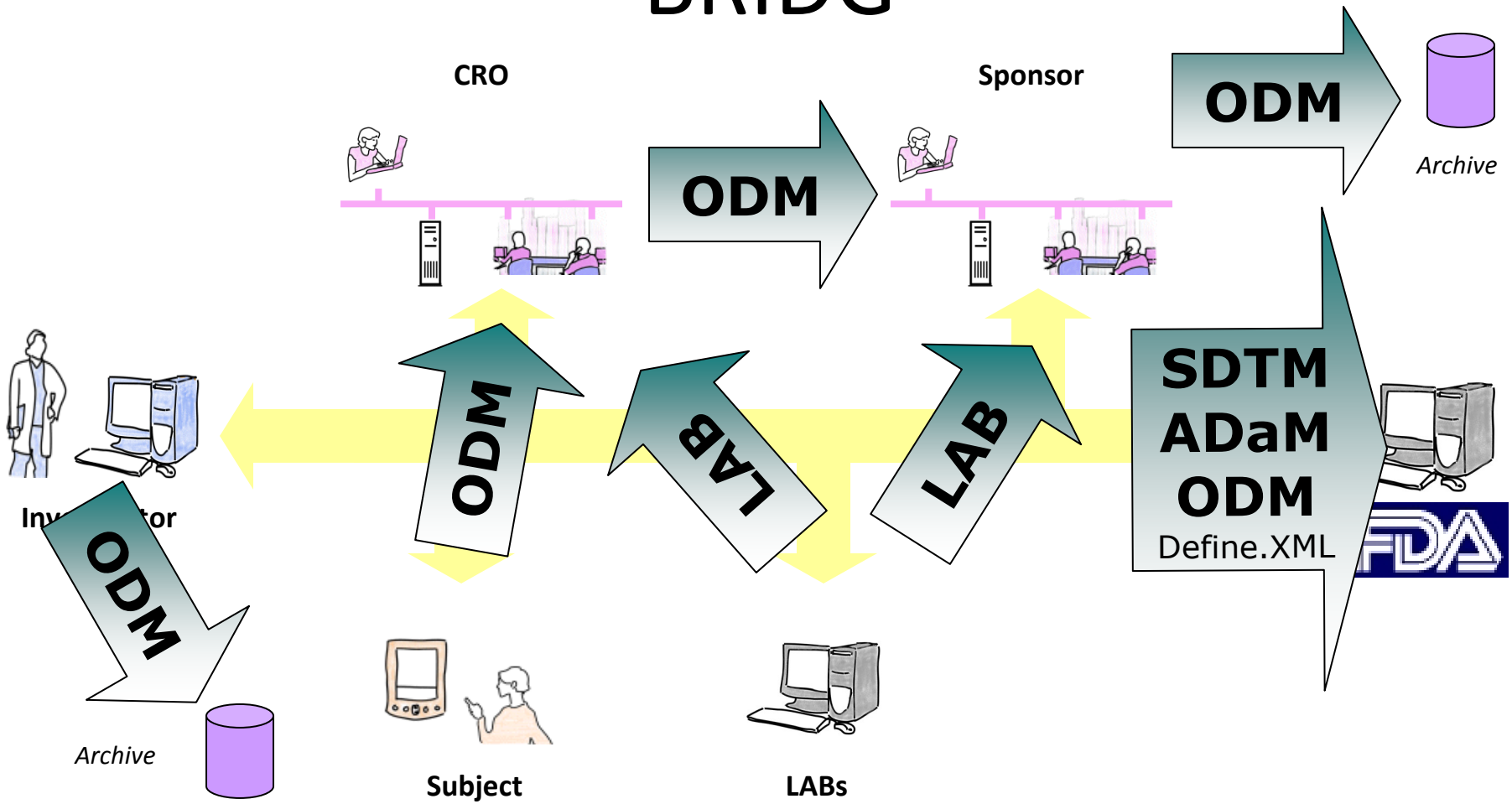
- HL7-CDISC-NCI Collaboration
- Objective to develop a standard, structured, machine-readable clinical protocol representation

Protocol & BRIDG

Main Protocol Use Cases

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

BRIDG

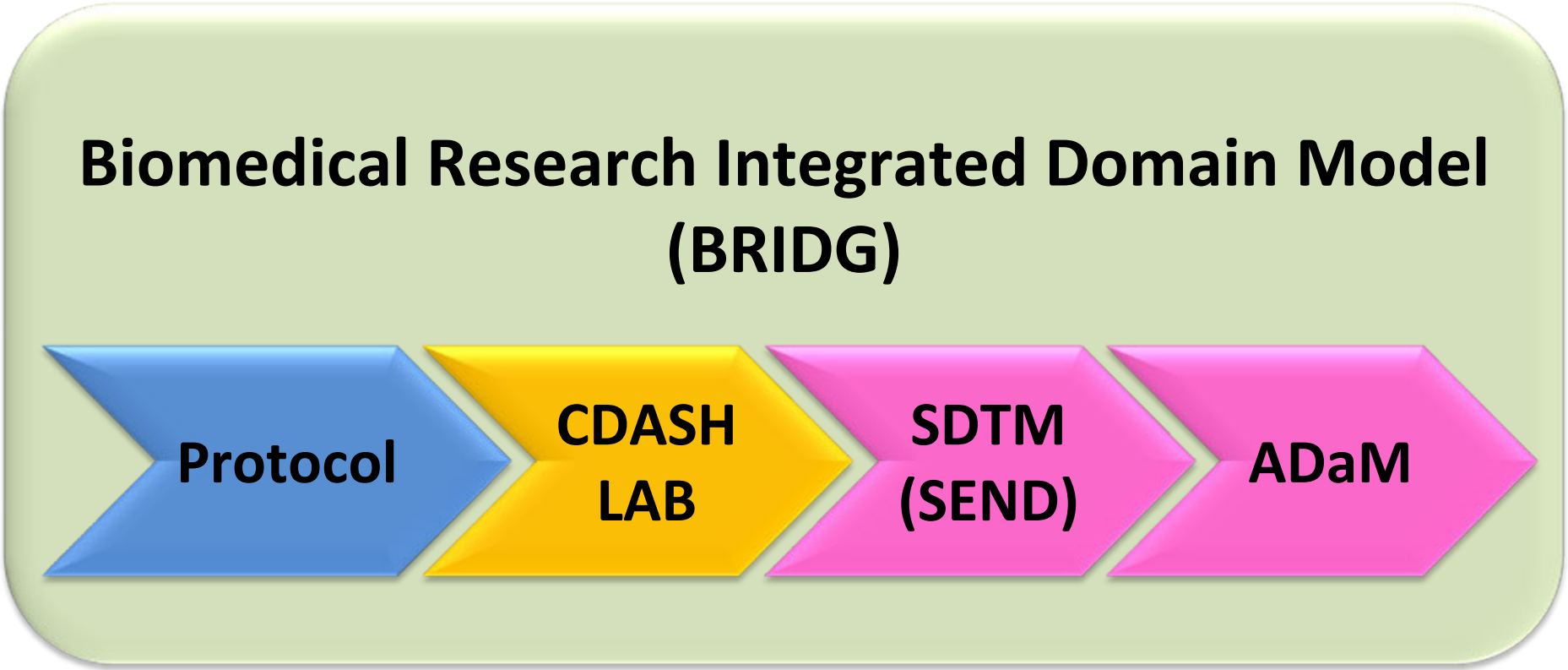


Protocol & BRIDG

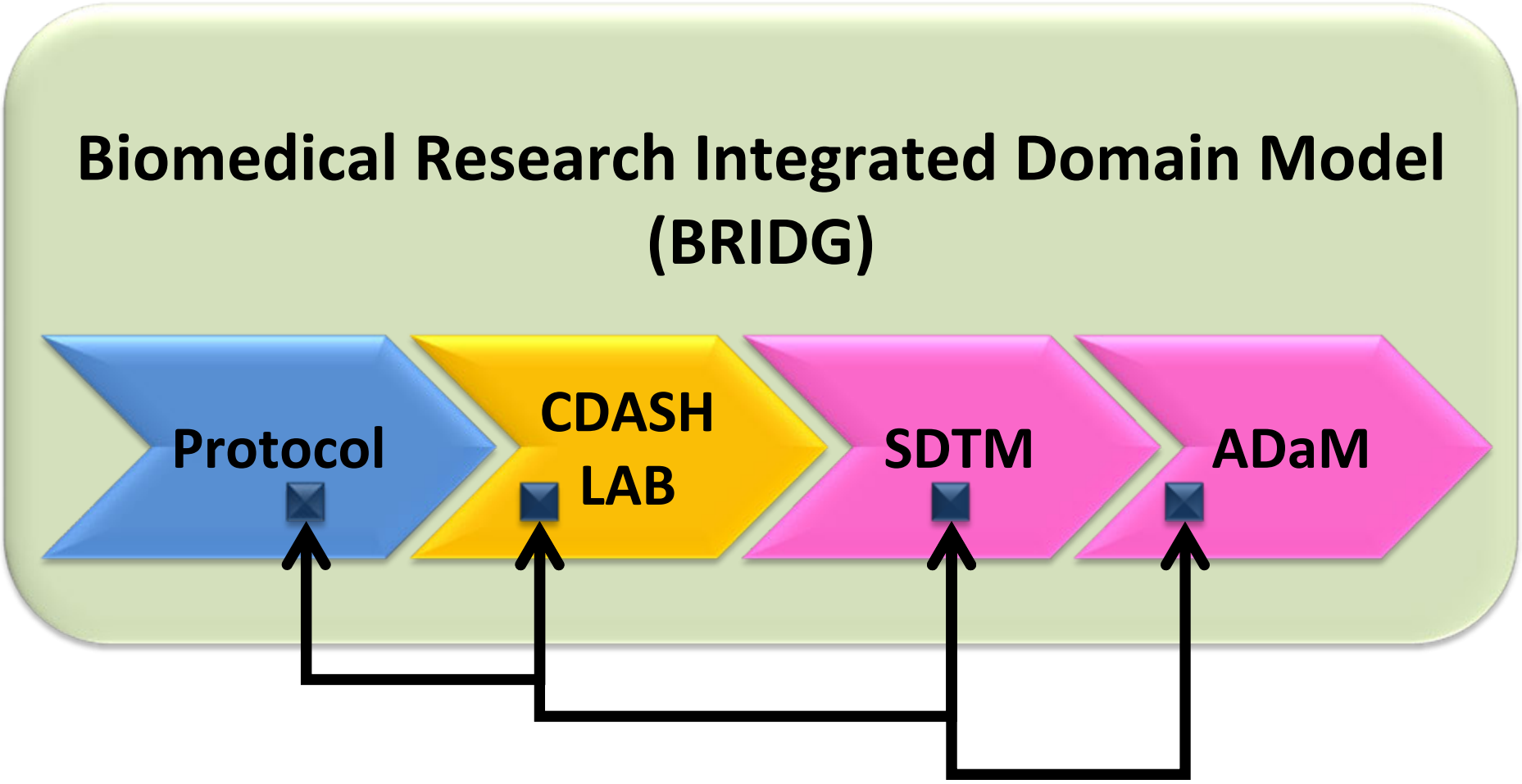
The BRIDG Model

- **Vision** : Create a domain analysis model for clinical research domain
  - **Key Goals**:
    - to harmonize clinical research standards among each other – i.e CDISC Standards
    - to harmonize standards between clinical/medical research and healthcare

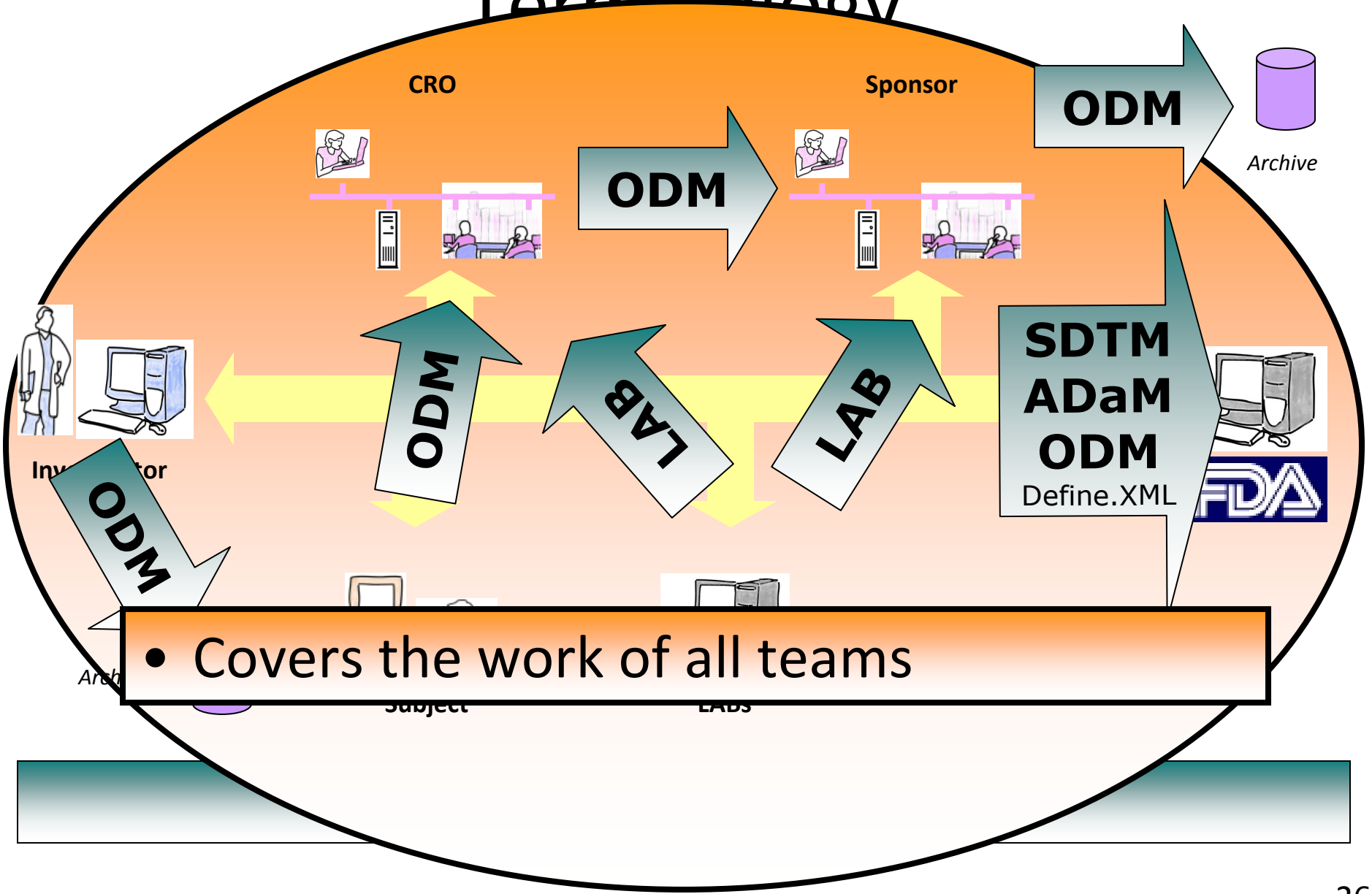
Aligned With and By BRIDG



Same Concept, Same Meaning

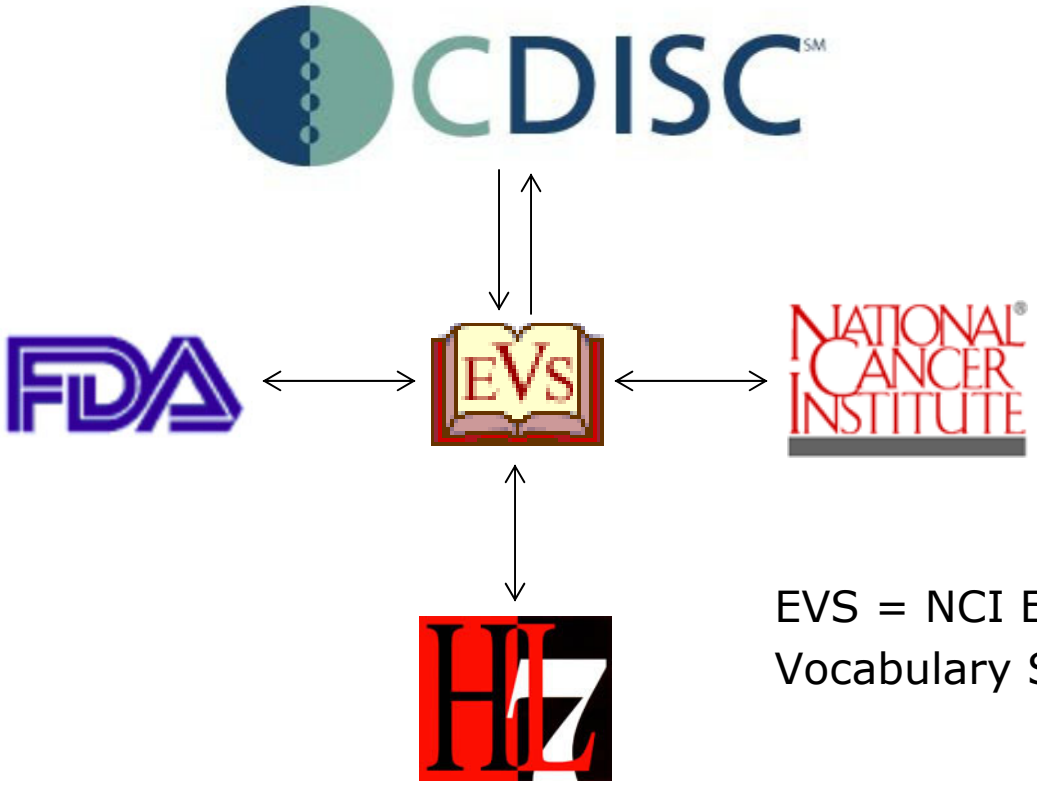


Terminology



- Covers the work of all teams

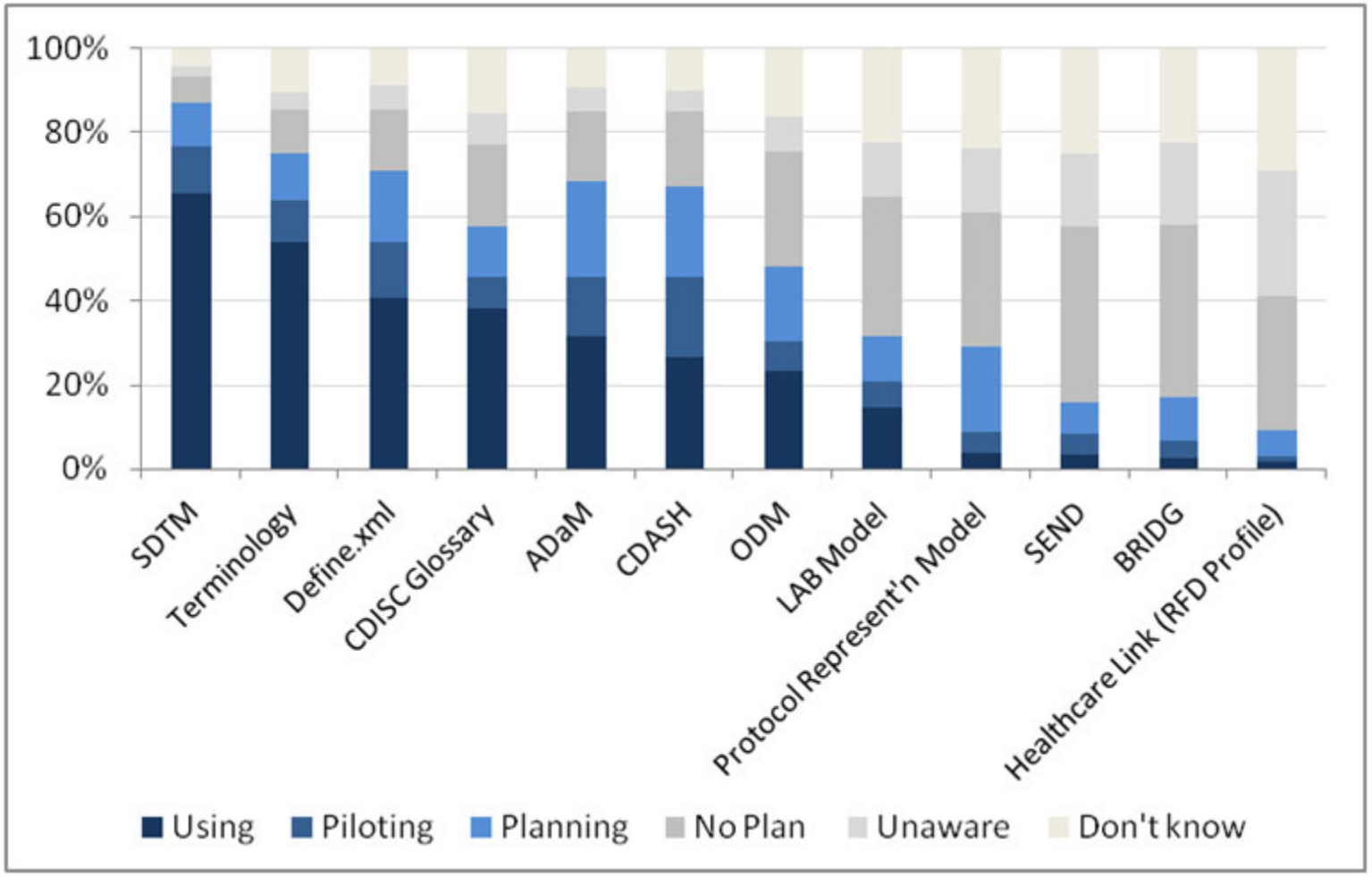
Terminology Collaboration



RCRIM

EVS = NCI Enterprise Vocabulary Services

Current Adoption of CDISC Standards



Quality Improvement

Enablers

CDISC is more than Data Standards!

Speed

Process Redesign

Workflow Integration

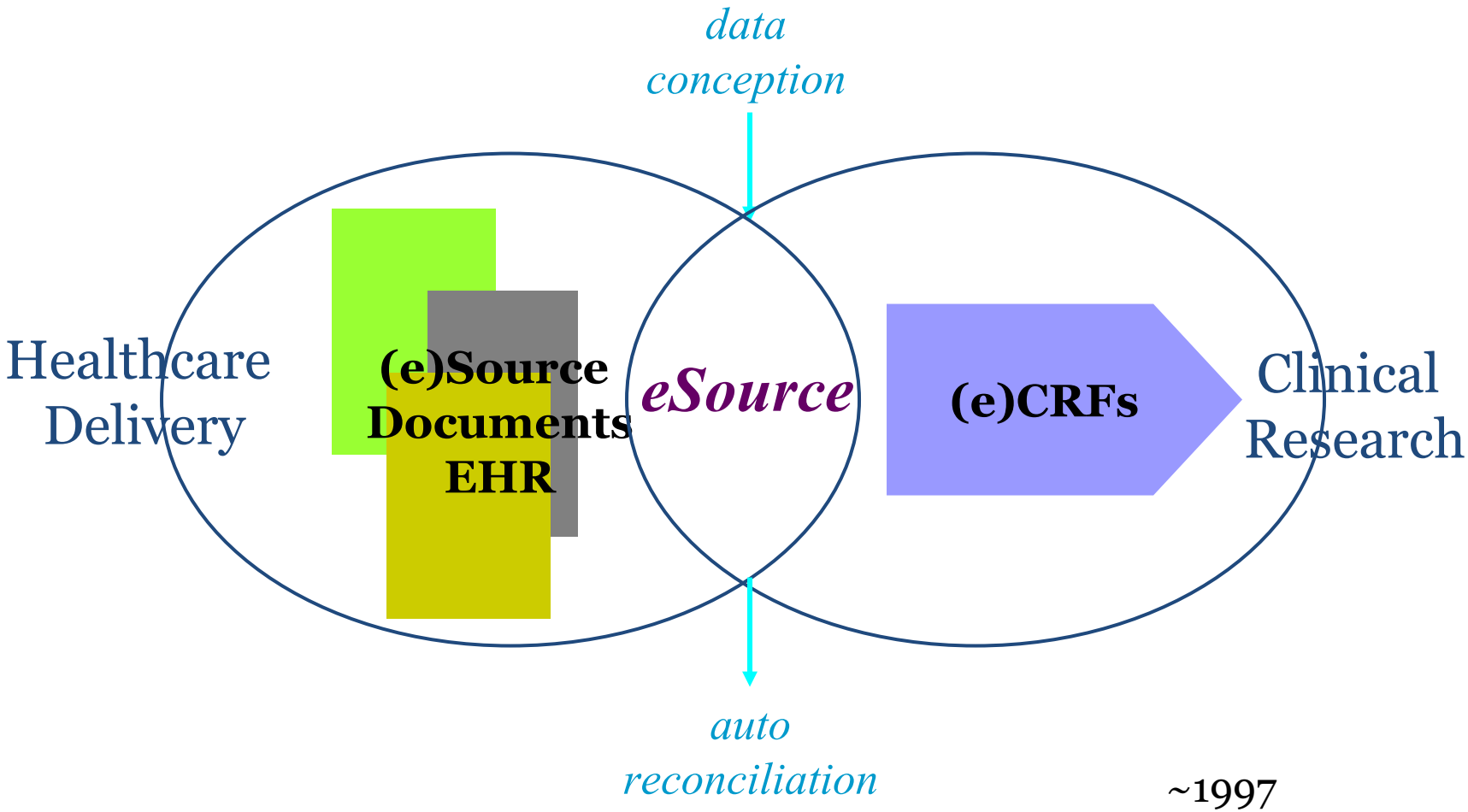
Resource Savings

Standards-inspired Innovation

Strength through collaboration

CDISC®

Optimizing the Process



~1997

eSource Data Interchange (eSDI) Initiative

- **Purpose:** FDA initiative to facilitate the use of electronic technology in the context of existing regulations for the collection of eSource data in clinical research

  ***Note**: eSource pertains to collecting data electronically initially through eDiaries, ePatient Reported Outcomes, eData Collection, Electronic Health Records…*

- **Overarching Goals:**
  - to make it easier for physicians to conduct clinical research,
  - collecting data only once in an industry standard format for multiple downstream uses, and thereby
  - to improve data quality and patient safety
- **Product:** eSDI Document (with 12 requirements for eSource) (www.cdisc.org), which formed the basis for the Retrieve Form for Data Capture (RFD) Integration Profile

09 June 2010
EMA/INS/GCP/454280/2010
GCP Inspectors Working Group (GCP IWG)
Date for coming into effect 01 August 2010

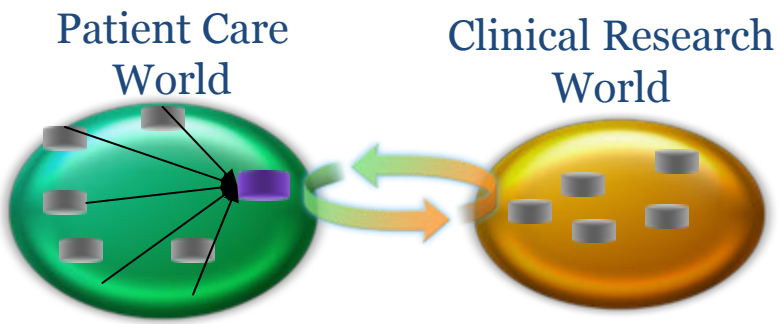
Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials

References

2. CDISC (Clinical Data Interchange Standards Consortium) Clinical Research **Glossary Version 8.0**, DECEMBER 2009 http://www.cdisc.org/stuff/contentmgr/files/0/be650811feb46f381f0af41ca40ade2e/misc/cdisc_2009_glossary.pdf.

3. **CDISC e-source standard requirements-CDISC** (Clinical Data Interchange Standards Consortium) Version 1.0 20 November 2006.

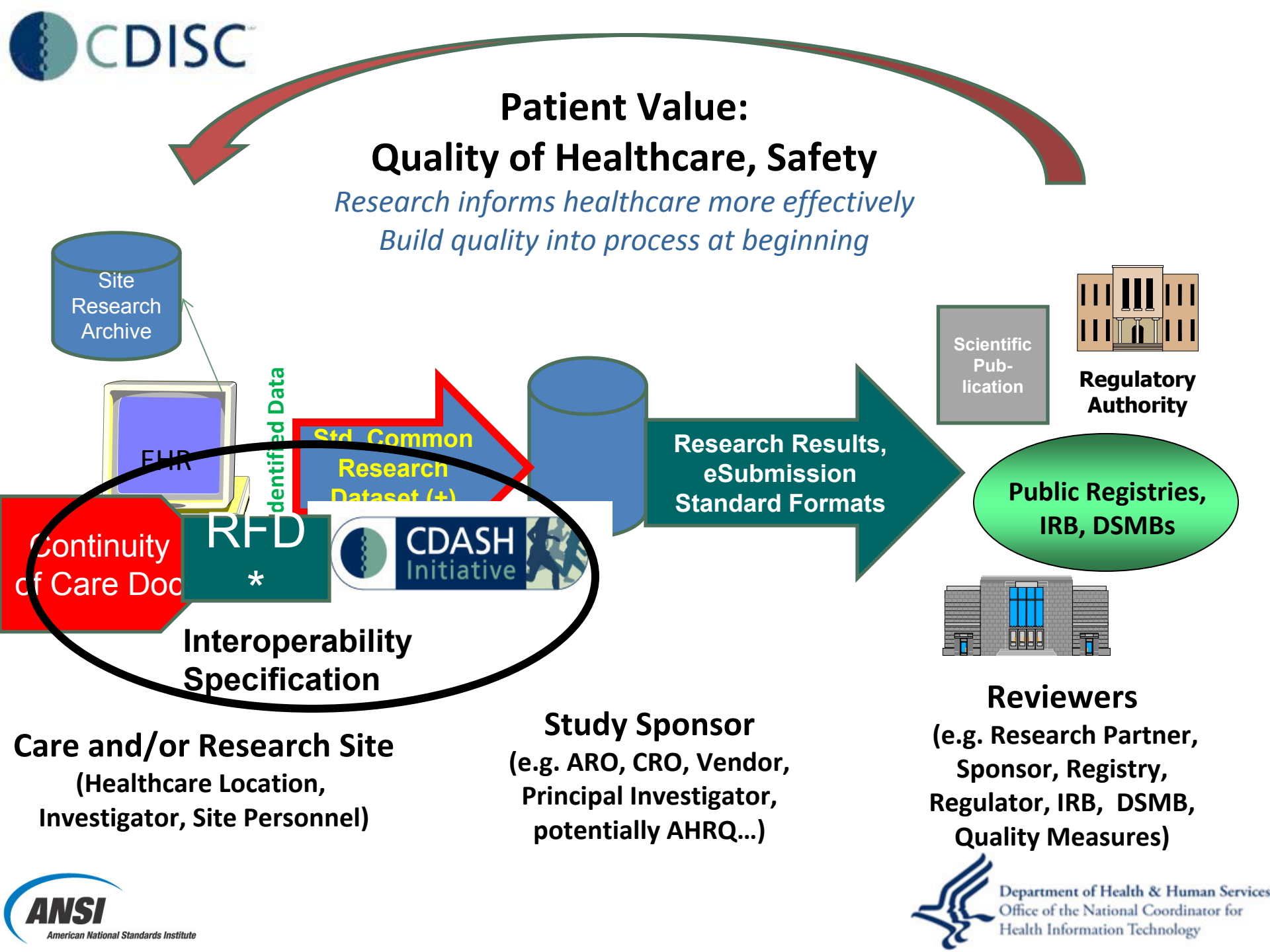
CDISC Initiative: Healthcare Link



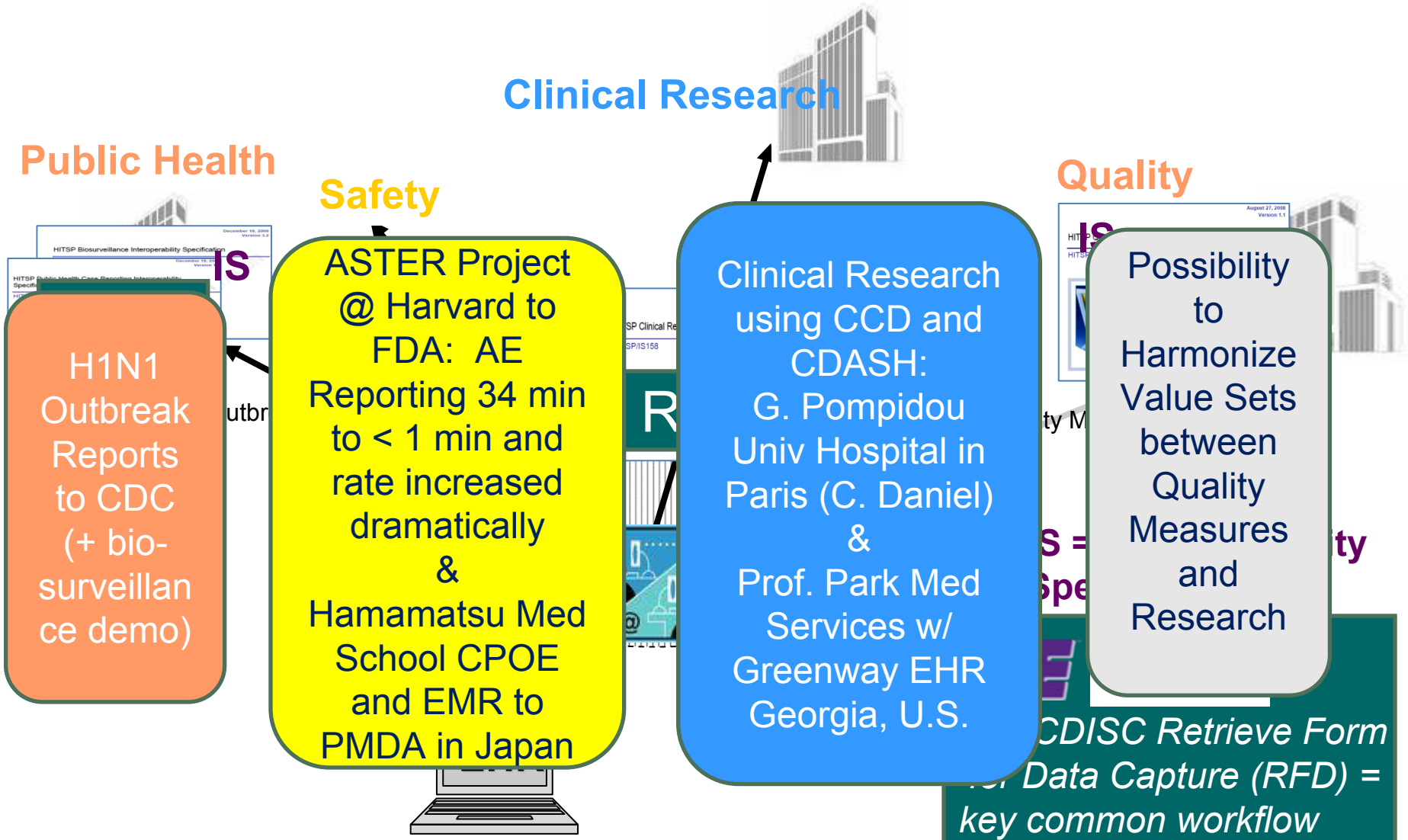
An industry initiative that successfully demonstrated clinical information interoperability between physician clinical systems (EHR) and pharmaceutical clinical trials systems based on open standards.
- Duke Clinical Research Institute, CDISC, Novartis, Merck, J&J, Microsoft.

Next Step was the **Development and Demonstration of an Integration Profile called Retrieve Form for Data Capture (RFD)**

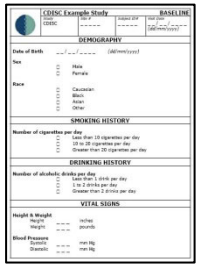
(*Project Leader: Landen Bain, lbain@cdisc.org, CDISC Liaison to Healthcare*)


Patient Value:
Quality of Healthcare, Safety
Research informs healthcare more effectively
Build quality into process at beginning
Site Research Archive
EHR
Identified Data
Std. Common Research Dataset (+)
Continuity of Care Doc
RFD *
CDASH Initiative
Interoperability Specification
Research Results, eSubmission Standard Formats
Scientific Pub-lication
Regulatory Authority
Public Registries, IRB, DSMBs
Care and/or Research Site
(Healthcare Location, Investigator, Site Personnel)
Study Sponsor
(e.g. ARO, CRO, Vendor, Principal Investigator, potentially AHRQ…)
Reviewers
(e.g. Research Partner, Sponsor, Registry, Regulator, IRB, DSMB, Quality Measures)

Integrating Workflow: EHRs and Clinical Research, Quality, Safety and Public Health



Standards-inspired Innovation: eSource Data Interchange and Archive



Transition – Paper, EDC, EHR

Site Research Archive

EHR

CCD

EDC

CDASH Initiative

RFD*

CDASH Initiative

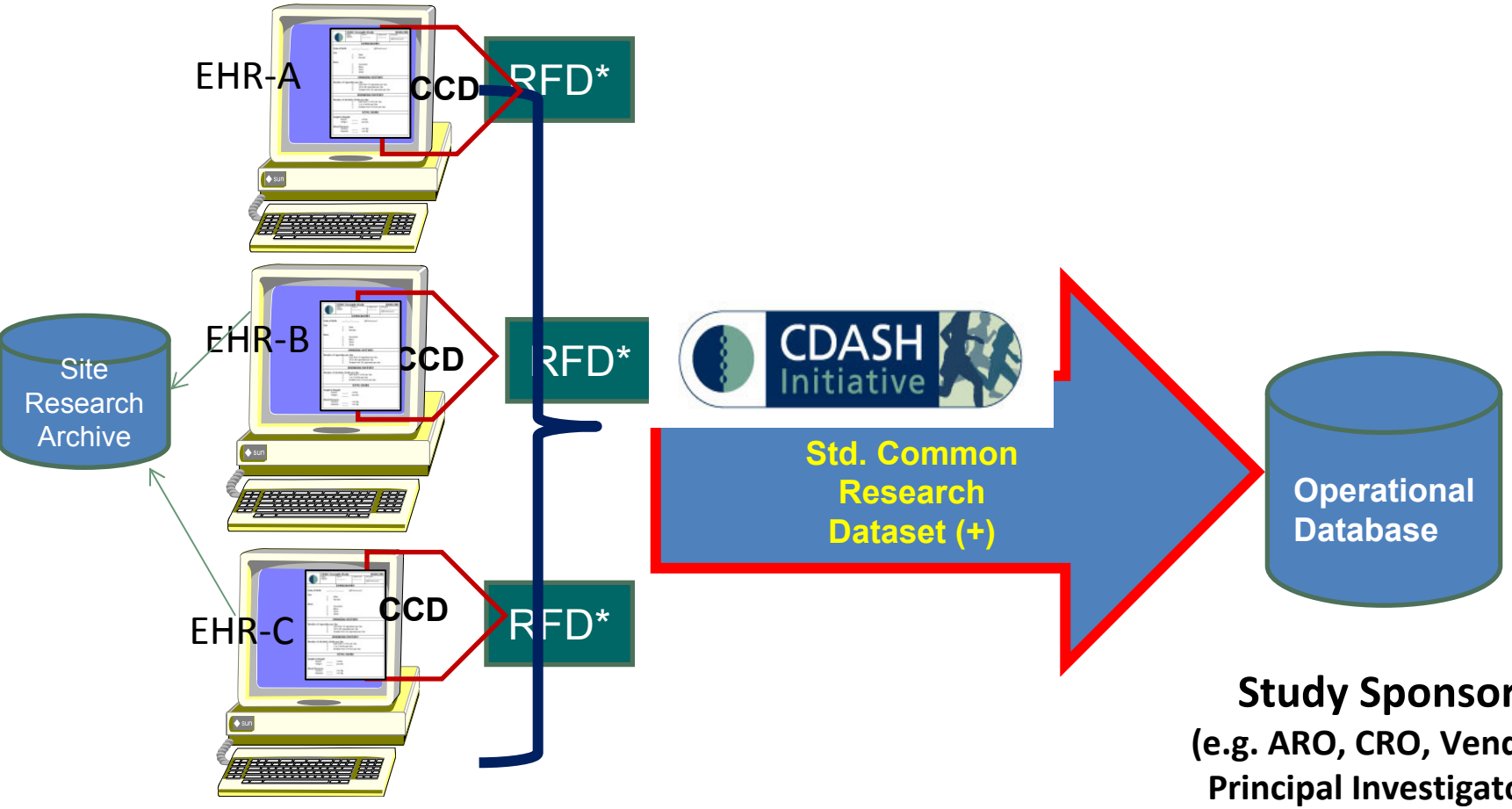
Std. Common Research Dataset (+)

Operational Database

Care and/or Research Site
(Healthcare Location, Investigator, Site Personnel)

Study Sponsor
(e.g. ARO, CRO, Vendor, Principal Investigator, potentially AHRQ…)

Standards-inspired Innovation: eSource Data Interchange and Archive

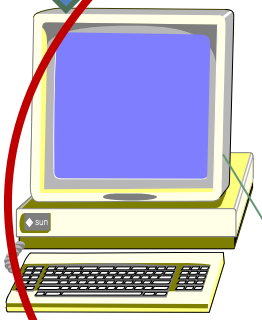


Care and/or Research Site
(Healthcare Location, Investigator, Site Personnel)

Study Sponsor
(e.g. ARO, CRO, Vendor, Principal Investigator, potentially AHRQ…)

Patient Value: Quality of Care, Safety

ePROTOCOL



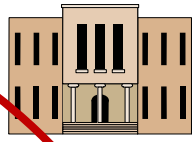
Research Site
(Healthcare Location Investigator, Site Personnel)

De-identified Data

Standards: To Streamline Workflow from Protocol through Reporting and to Ensure Useful Data, with Integrity and Meaning for Patients and anyone in Clinical Research

Site Research Archive

Scientific Publication



Regulatory Authority

Public Registries, IRB, DSMBs

eviewers
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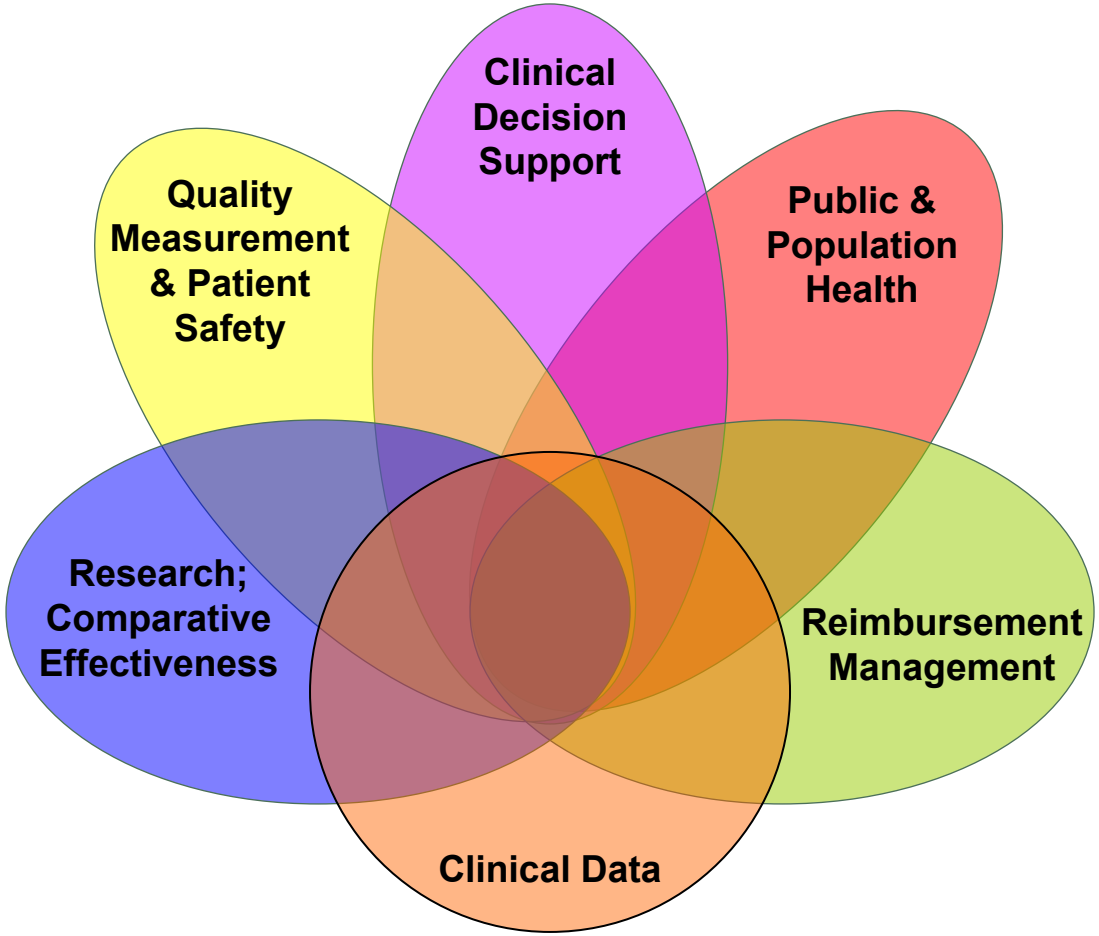
Efficiency: Collect Once, Repurpose Many Times



Aknowledgements

- CDISC Standards are developped by groups of volunteers and it would be impossible to name them all here, but we would like to thank them here for the great job they have done.
- This presentation uses a number of slides developped by important CDISC contributors: Steve Wilson, Dave Iberson-Hurst, Diane Wold, Philippe Verplancke, Susan Kenny, Julie Evans and Frank Newby. Many thanks to them!

A joint undertaking between Academia & Industry

Innovative Medicines Initiative

Overview of the EHR4CR project

Electronic Health Record for Clinical Research

About IMI

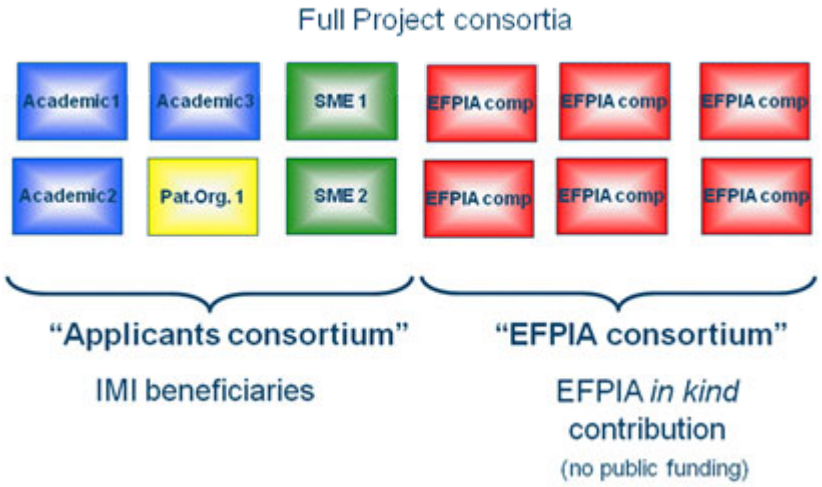
Innovative Medicines Initiative

- A Public-Private Partnership between EU and EFPIA focused in research on needs common to the Pharmaceutical Industry and Patients at European level (2007-2017)
- Aims to removing major bottlenecks in drug development, where pre-competitive research is the key, and to re-invigorate the European bio-pharmaceutical sector
- IMI projects offers industry an opportunity to build new business models based on collaboration and transparency
- Coordinated research efforts with shared funding (EFPIA contributes with in-kind resources). Research focuses on fields of high industrial and policy relevance
- The IMI 2009 Call for proposal has 9 topics proceeding to stage 2 (final stage to become a project) addressing the two strategic pillars:
  - Predictivity of Efficacy Evaluation and
  - Knowledge Management (call topics 7,8 and 9).

Overall Structure of IMI Research Projects

IMI Call topics for proposals are conducted through a 2-stage process

- The first stage of the call process is addressing 'Applicant Consortia' (e.g. collaborations between academia, SMEs, patient organisations, non EFPIA industry, etc), to submit to the IMI JU an Expression of Interest in response to a call
- The second stage, following the first stage peer review, the 'Applicant Consortium' of the best Expression of Interest, and the 'EFPIA consortium' that already are associated to the topic, will be invited to form a full 'Project Consortium'
- The full project proposals will be evaluated based on consistency with the original Expression of Interest, on scientific excellence, the quality of the implementation plan and the potential impact
- Only full project proposals that have been favorably reviewed in the evaluation process can be selected for funding and will be invited to conclude a Grant Agreement governing the relationship between the selected project consortium and the IMI JU.



The IMI project principles are to ensure shared leadership roles (research) but to be coordinated by EFPIA

Innovative Medicines Initiative

Project objective & outputs

The EHR4CR project will develop a platform and business model for re-using EHR data for supporting medical research.

<u>Output</u>:

- **Requirements Specification and Business Model**
- **Technical Platform (a set of tools and services)**
- **Different Pilots for validating the solutions:**
  - ✓ for different scenarios (e.g. patient recruitment);
  - ✓ across different therapeutic areas (e.g. oncology);
  - ✓ across several countries (under different legal frameworks).

Vision: Scalable Organisational Model for EHR re-use

Regional interoperability

National interoperability

Cross EU States interoperability

Connect different sources and services of EHR for support clinical research

Federation of service providers – TTPs using the EHR4CR Business model

Benefits

- Accreditation and certification will enable research and clinical trials to be delivered more cost effectively. Both vendors of certified products and hospitals (source data) that will be accredited will have a competitive advantage.
- A new business model for re-using EHR data in research will aim at offering benefits for "**all**" stakeholders and strengthen the collaboration amongst "**all**" the partners in Research... !

Benefits (cont.)

Patients and health care perspective:

- Closer co-ordination between care providers and patients, resulting in safer and more evidence-based diagnosis and treatment
- Significantly facilitate re-use of EHR data to allow more efficient management of public health issues

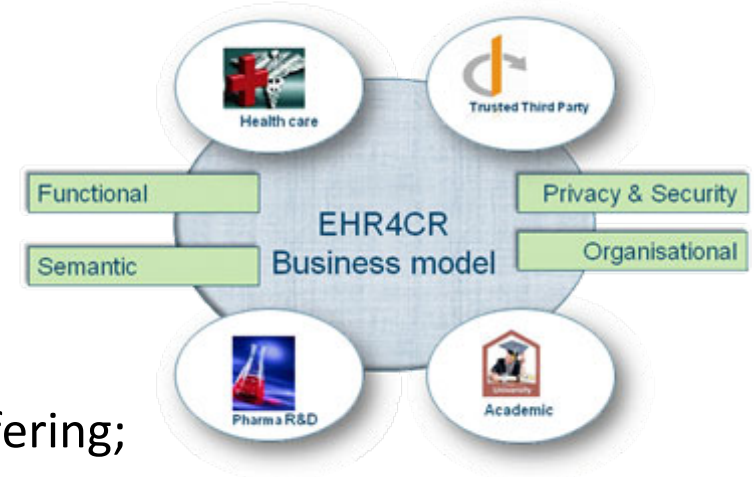
Academic perspective

- Provide tools and services to better plan and conduct academic trials (investigator-initiated trials)
- Facilitate comparative effectiveness research, e.g. paediatric trials, trials on rare diseases, trials with biotherapy)

Pharmaceutical perspective:

- Improve speed and quality of clinical patient recruitment process and study design by accurate understanding of real patient populations
- Support to conduct observational and outcomes research studies in real-world settings

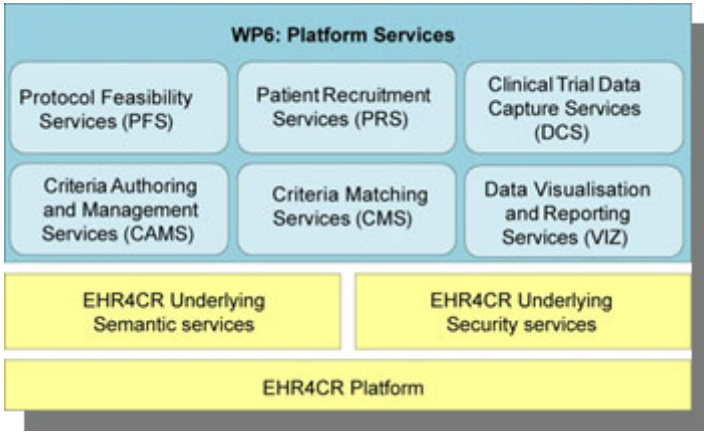
Business model



It will:

- Specify in detail the product and service offering;
- Include analyses and an impact analysis on multiple stakeholders;
- Deliver a self-sustaining economic model including sensitivity analysis;
- Define appropriate governance arrangements for the platform services and for pan-European EHR4CR networks;
- Define operating procedures and trusted third party service requirements;
- Identify the value proposition and incentives for each of the key players and stakeholders impacted by EHR4CR;
- Define accreditation and certification plans for EHR systems capable of interfacing with the platform;
- Provide a framework to define public and private sector roles in reusing EHRs for clinical research;
- Define a roadmap for pan-European adoption and for funding future developments.

Technical Platform



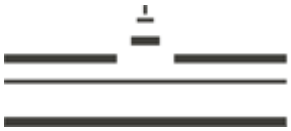
It will:

- Support the feasibility, exploration, design and execution of clinical studies and long-term surveillance of patient populations;
- Enable trial eligibility and recruitment criteria to be expressed in ways that permit searching for relevant patients across distributed EHR systems, and initiate confidentially participation requests via the patients' authorised clinicians;
- Provide harmonised access to multiple heterogeneous and distributed clinical (EHR) systems and integration with existing clinical trials infrastructure products (e.g. EDC systems);
- Facilitate improvements of data quality to enable routine clinical data to contribute to clinical trials, and importantly vice versa, thereby reducing redundant data capture.

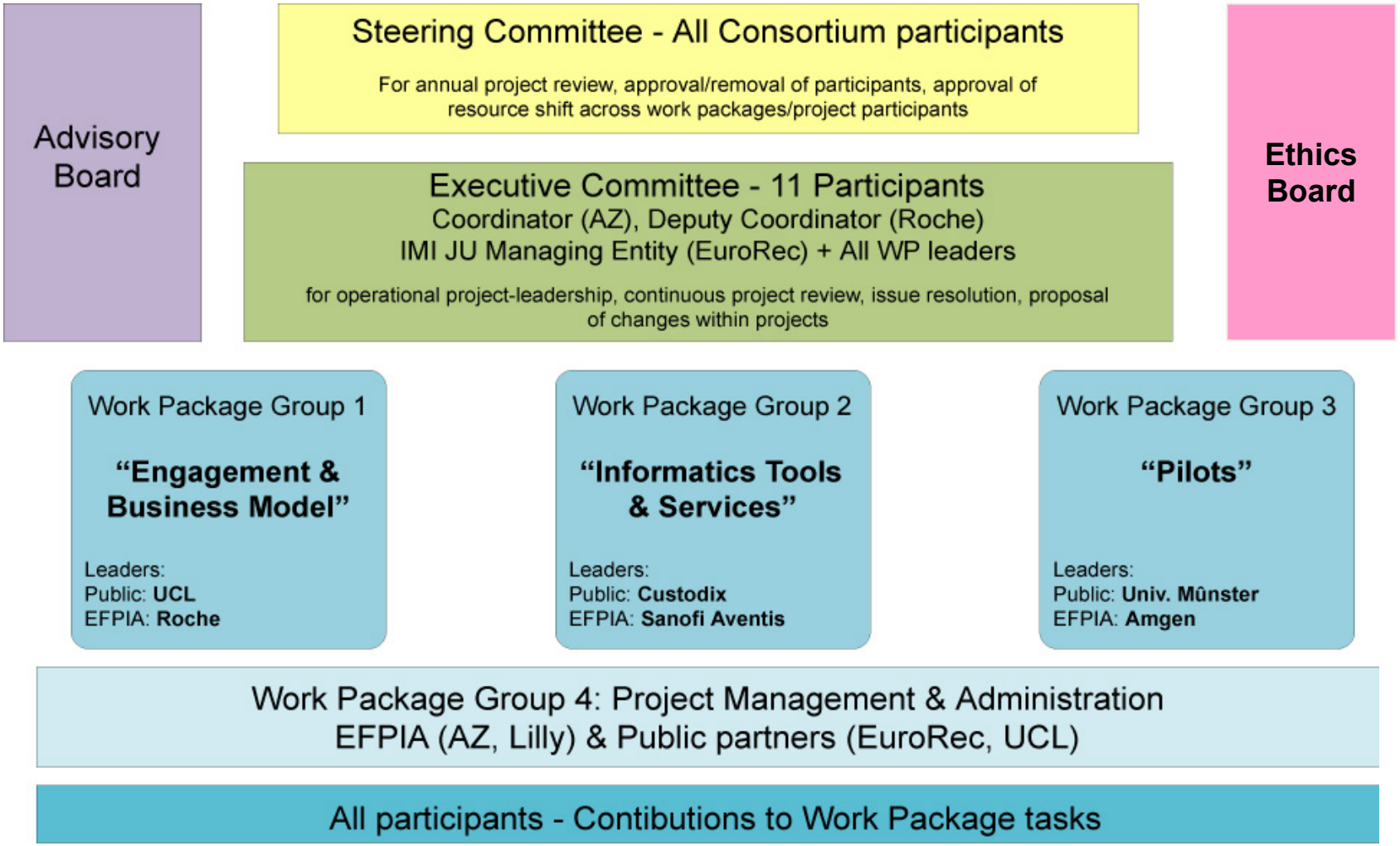
EHR4CR
A joint undertaking between Academia & Industry

The partners





Governance structure



Overview of Work Package Groups

Work Package Group 1

Engagement & Business Model

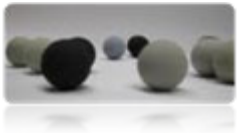
Objectives

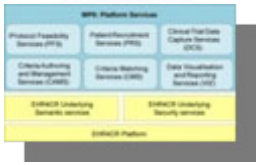
- **WP 1 (Specification & Evaluation)**
  - Review the ethical, legal and regulatory landscape in Europe
  - Define the use case scenarios applicable to the EHR4CR platform and business model.
- **WP 2 (Business model & Strategic road map)**
  - Develop a roadmap specifically for the EHR4CR platform, focusing on benefits, investments and adaptations needed
  - Develop a comprehensive business model to establish a durable European service to include specialized products requiring key partnerships for services to be provided
- **Example of tasks**
  - Governance Success Factors (e.g. identify the regulations and cross-border legislative issues that EHR4CR must address and comply with
  - Evaluation of the Pilots
  - Develop a Business model including product and service offering, governance arrangements, operating procedures, third party service requirements and proposals, accreditation and certification plans

Work Package Group 2
Technology Platform & Tools

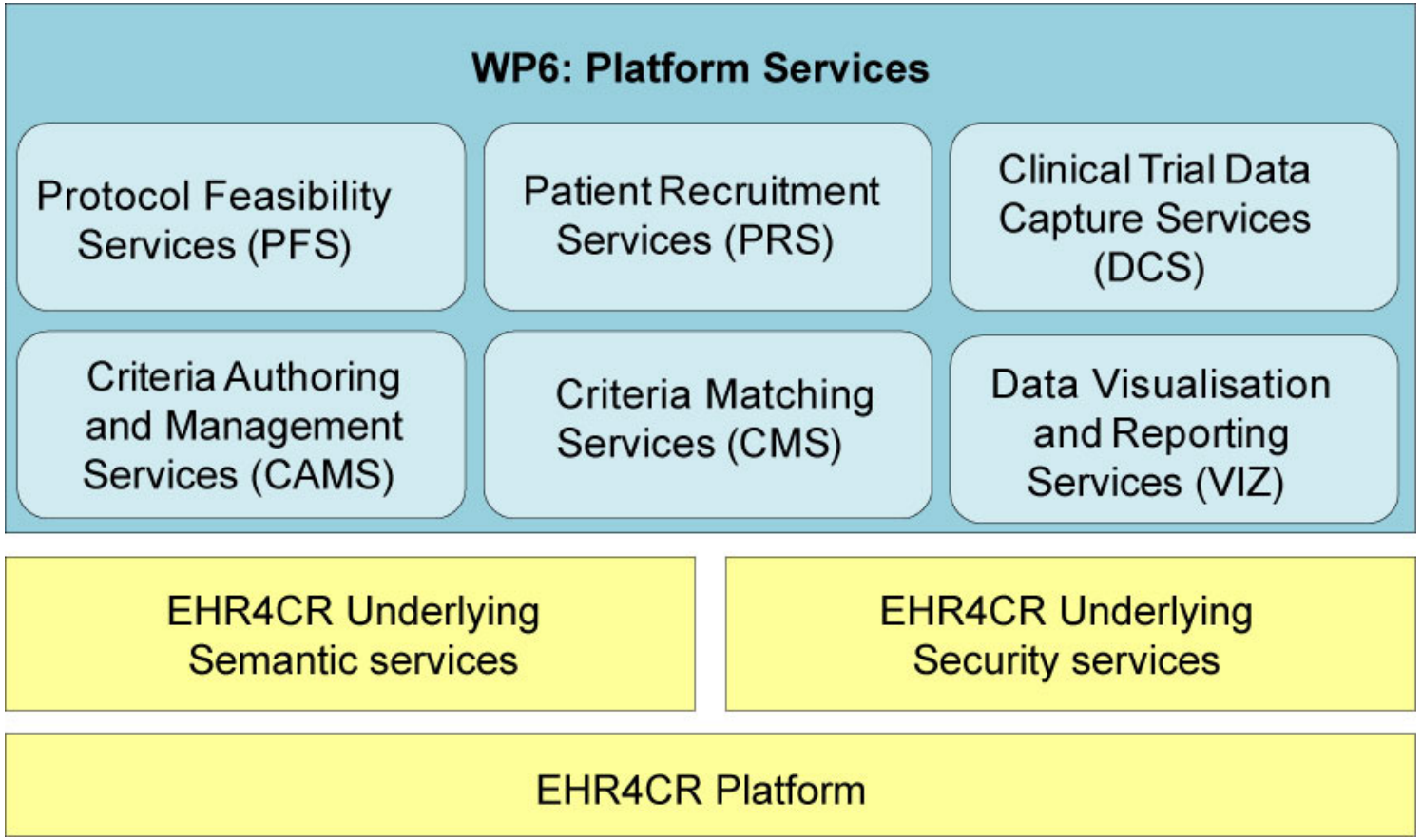
Objectives

- **WP3 (Architecture and Integration)**
  - Define the architecture of the EHR4CR platform, provide a reference implementation and oversee the overall EHR4CR platform integration and operation.
- **WP 4 (Semantic Interoperability)**
  - Provide tools and services to ensure semantic interoperability between varying and disparate data sources (EHRs and CDMS), allowing for consistent interpretation of data
- **WP5 (Data protection, Privacy & Security)**
  - Provide the core security services for the EHR4CR platform and ensure that data and process flows are optimised for data protection and compliance
- **WP 6 (Platform Services)**
  - Design and implement end-to-end solutions (tools and services) that address the requirements of the different EHR4CR scenarios (e.g. clinical trial protocol feasibility)

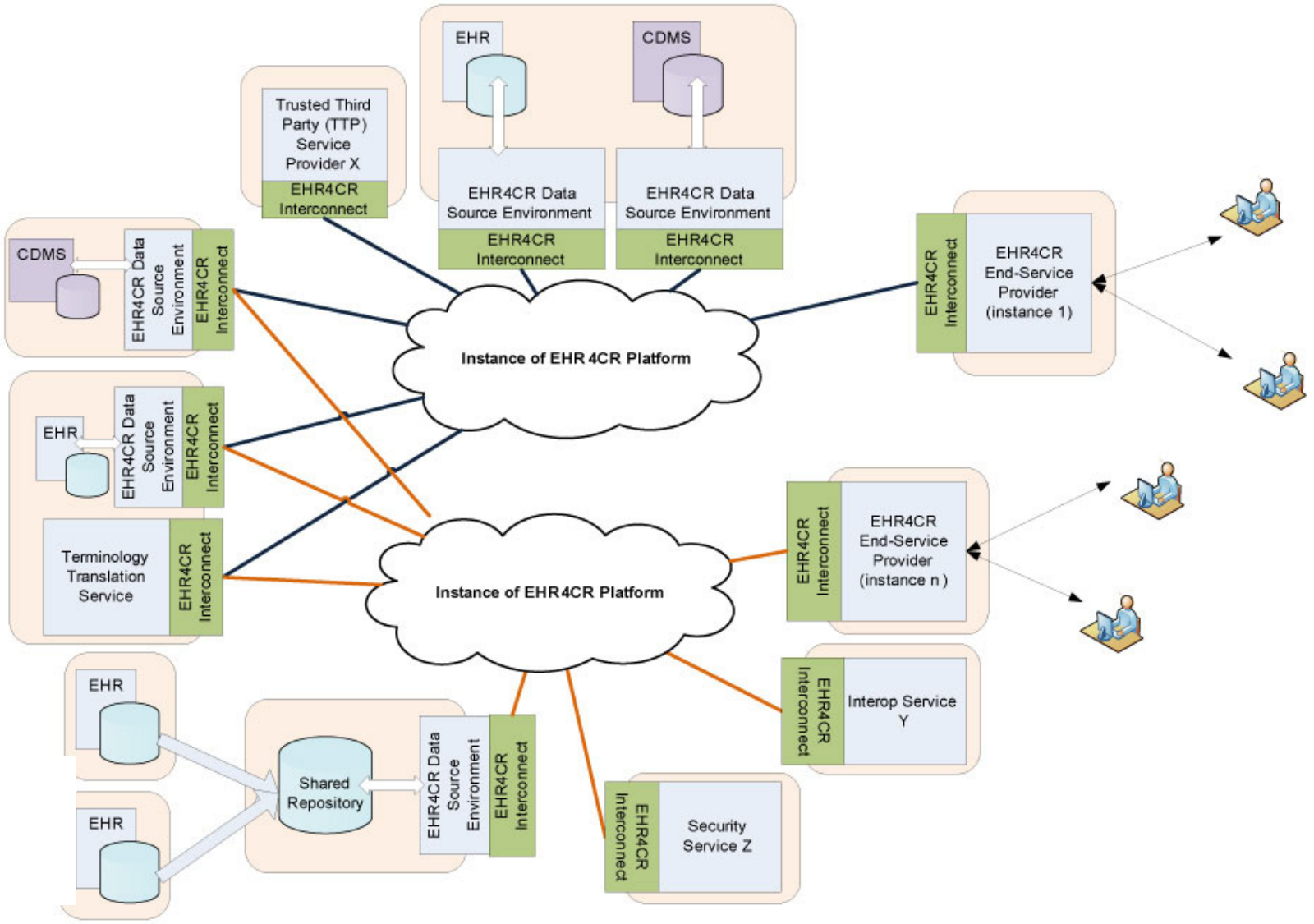




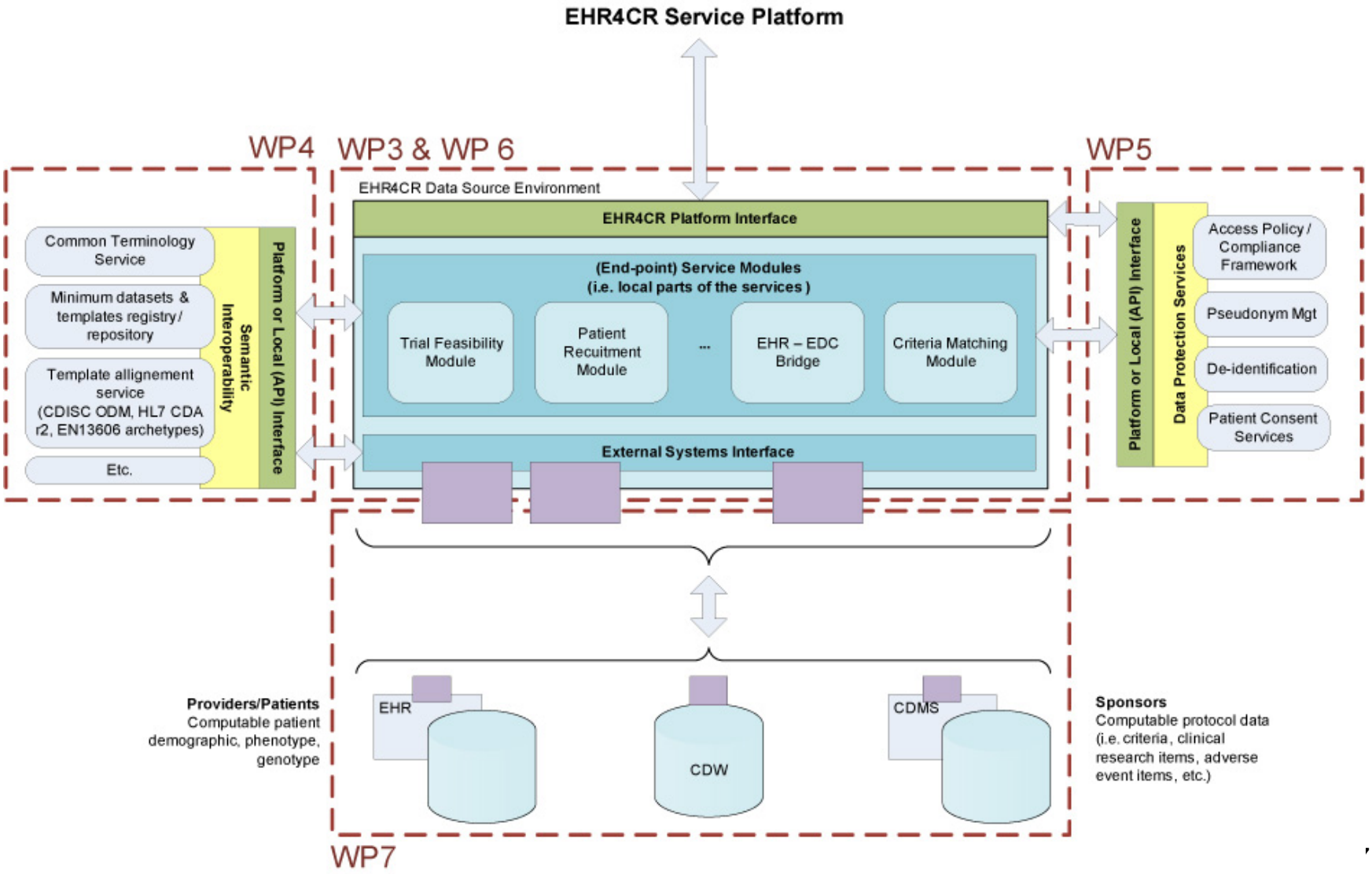
Overview of Platform services



concept overview



data source flow



Work Package Group 3
Pilots

Objectives

- **WP7 (Pilots)**
  - Demonstrate the functionality of the tools and services provided by Work Packages 3-6 and to evaluate the EHR4CR platform in terms of clinical study design and execution with a specific focus towards a set of mutually acceptable medical domains agreed between the pilot sites and the EFPIA partners
  - Pilots evaluations will occur at several large academic hospitals, interfacing with EHR systems, with a specific focus towards a set of mutually agreed medical domains between the pilot sites and EFPIA partners (e.g. Diabetes, Oncology).

- **Example of tasks**
  - Develop Interfaces between local EHR/CDW and CDMS systems and the uniform access layer
  - Execute pilots on
    - Protocol Feasibility, Patient Recruitment, Clinical Trial Execution, Drug Safety Monitoring)
  - of the inventory of local data sources and the matching of EFPIA clinical studies with suitable clinical data providers

Work Package Group 4
Management

Objectives

- **WP 8 (Training & Communication)**
  - Support the communication and training between all EHR4CR Work Package Groups and Work Packages and promote EHR4CR services to prepare for EHR4CR platform exploitation
  - Widely disseminate the EHR4CR outcomes and communicate with other EC FP or IMI projects in Europe and globally

- **WP 9 (Management)**
  - Coordinate the work of the EHR4CR project, administer day-to-day operations, manage the collaborative efforts of the Work Packages
  - Ensure that the scientific work being conducted is delivered on time and on budgets through optimal project management, including quality monitoring, planning, reporting and financial control

- **Example of tasks**
  - Project Website development and maintenance, Project collaboration space
  - Dissemination and liaison activities in EU
  - Coordination and managing of IMI JU funding, Project management office
  - Total quality management
  - Computer systems validation

Consortium Status 2011

Consortium status

- Background
  - Forming one EHR4CR consortia of 34 private and public partners to develop a full project proposal for 2009 IMI call topic 9, including finalizing stage 2 (March-September)
  - The project is coordinated by AZ and EuroRec acts as managing entity for public partners. Roche acts as deputy coordinator and Eli Lilly to cover Project Management
- Project Agreement and Grant Agreement finalised March 15th
  - Professional Service Agreement finalised between Efpia and Data Mining International, March 15th
- Establishing chairman's for the Advisory Board and Ethical boards, February 15th

Progress 2011-2012

Project start March 1st 2011

- Kick-off meeting
  3 & 4 March, AstraZeneca, Göteborg, Sweden

Work Package Group 1:

Engagement & Business Model

- Task 1.2 Kick-Off Workshop,
  5 & 6 April 2011, Novartis, Basel, Switzerland

Work Package Group 2:

Technology Platform & Tools

- Kick-Off Meeting,
  4-6 May 2011, Sanofi, Paris, France

Progress 2011-2012

Work Package Group 3: **Pilots**

- Kick-Off Meeting June 23-24, 2011 at Novartis in Basel

Work Package Group 4: **Management**

- Workshop for developing a integrated project plan for the first 18th months, May 16th (Finalised on June 7th)

Project Alignement

- Meeting of the Steering Committee, Ethics and all Work Packages on October 18-21, 2011 (Sanofi Frankfurt, Germany)

Status March 2012

- All Work Packages Deliverables on time, on budget
- Phase 1 Requirements Finalized,
  Platform Build starting

MORE INFO?

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http://www.cdisc.org

http://www.imi.org

http://www.ehr4cr.eu