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

CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

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Kiel, Germany
29 March 2012

EHR4CR
A joint undertaking between Academia & Industry

imi
Innovative Medicines Initiative

CDISC®
Setting the
Global Standard
for Medical Research

SANOFI

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
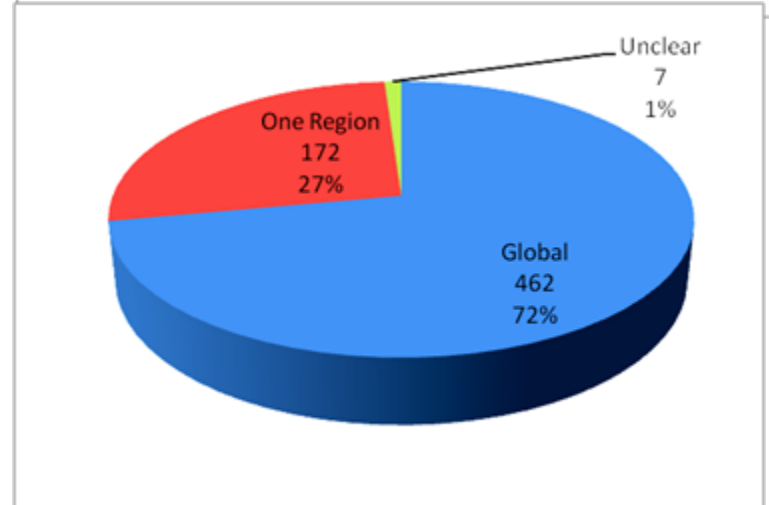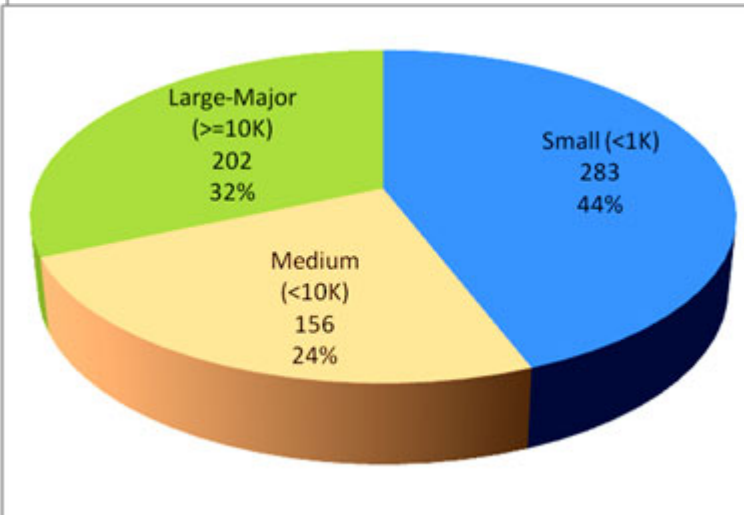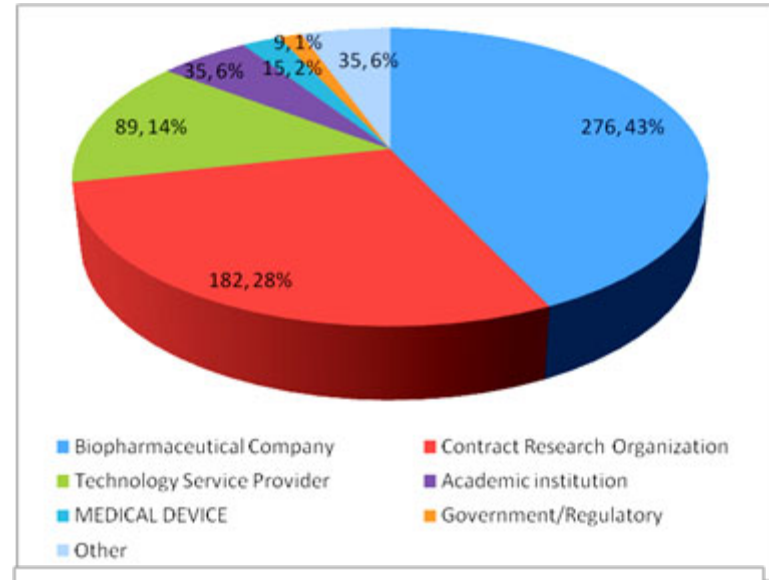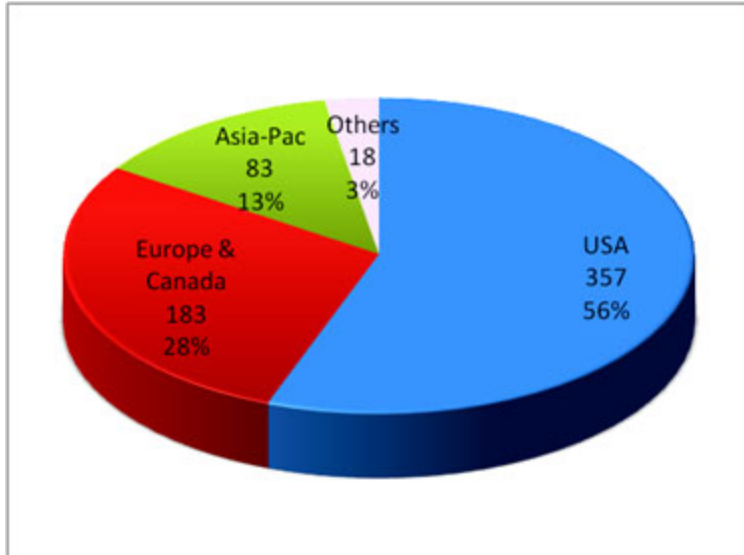 - Standards downloaded in over 65 countries

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

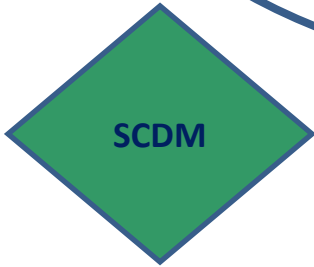# Implementation Survey (March 2010) Participants Demographics

Joint Initiative Council

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

Protocol	Form Setup & Config	Data Capture	Mapping	Analysis	Submission	Review

Protocol

CDASH

SDTM(SEND) & ADaM

ODM

LAB

XML

Controlled Terminology

Overview
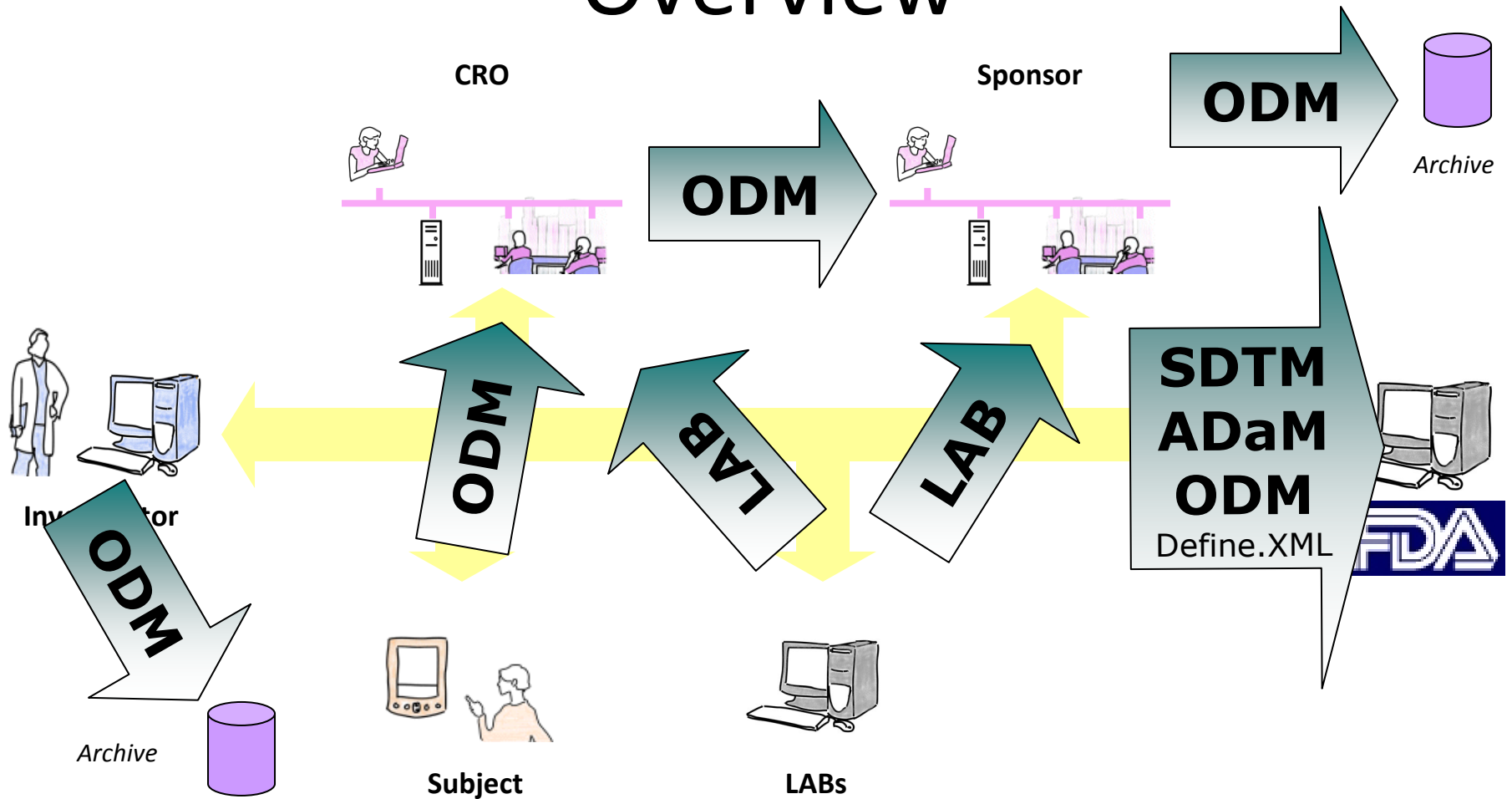
Protocol & BRIDG

Operational Data Model

CRO

Sponsor

ODM

Archive

ODM

Investigator

LAB

LAB

SDTM
ADaM
ODM
Define XML

ODM

Archive

Subject

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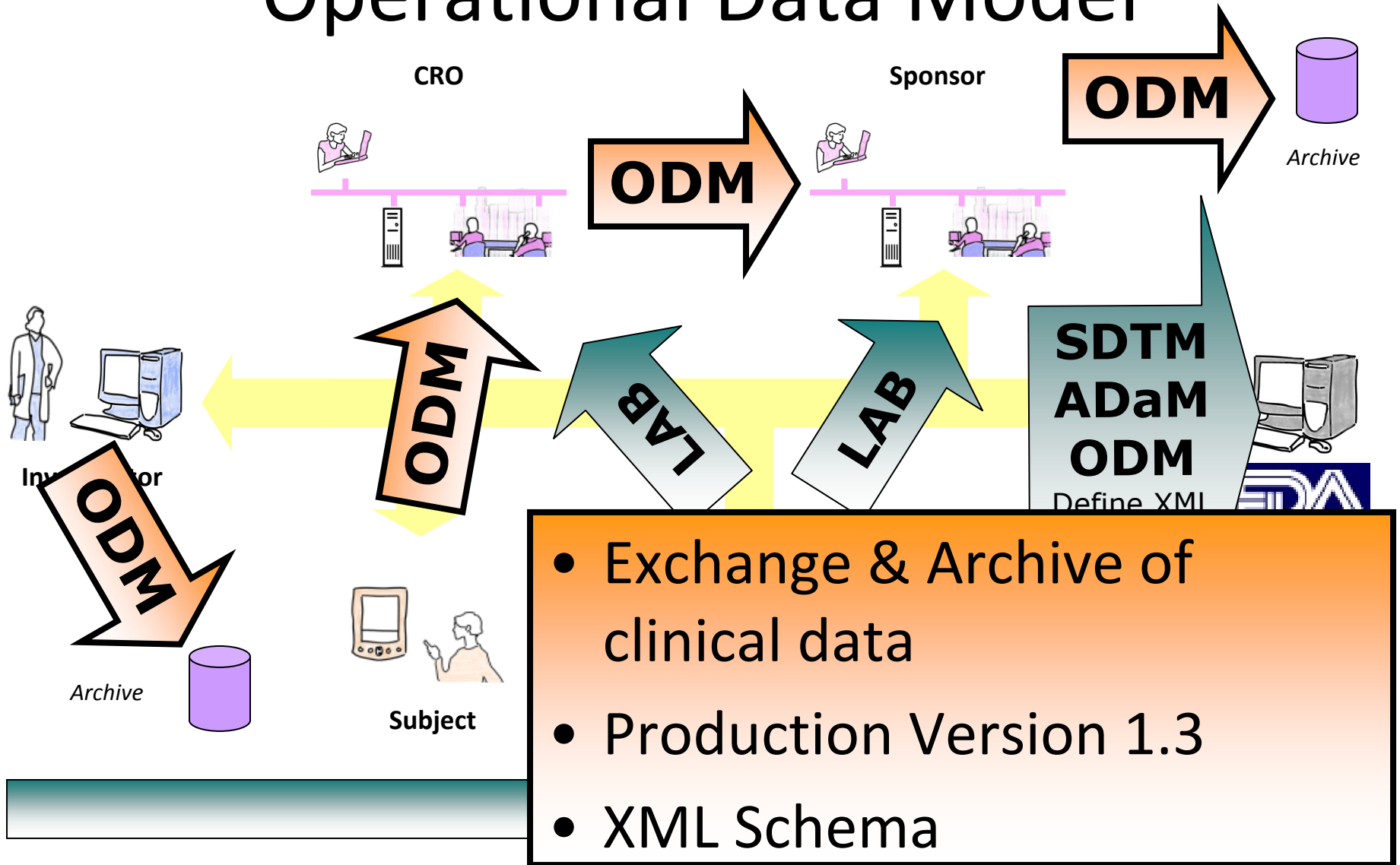
Original Use Cases

- 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

CDISC

CRO

Sponsor

ODM

ODM

Archive

LAB

LAB

**SDTM
ADaM
ODM**
Define.XML

FDA

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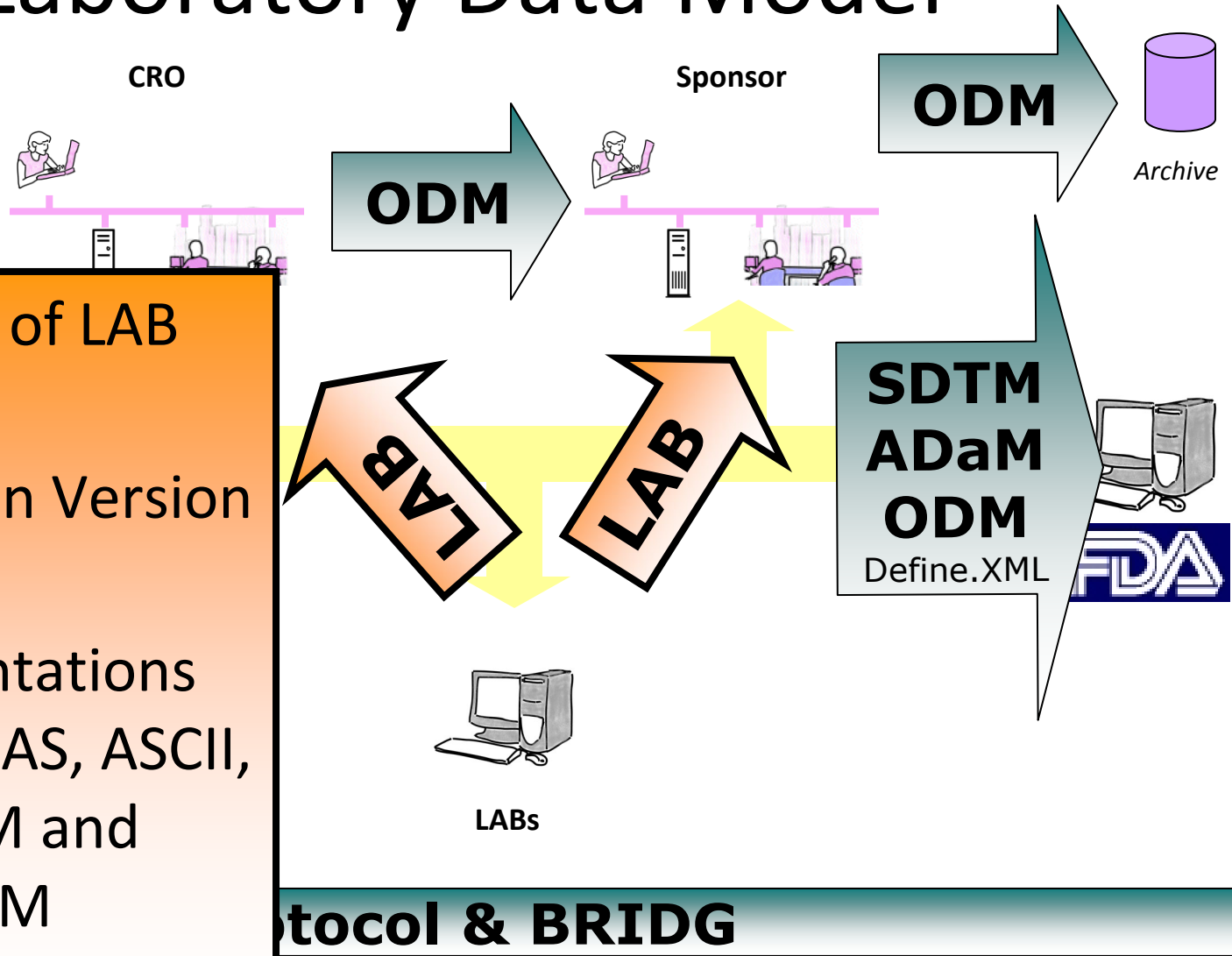
- Exchange of LAB data
- Production Version 1.0.1
- Implementations through SAS, ASCII, XML/ODM and HL7 V3 RIM message

...tocol & BRIDG

Use Case

- Support the bulk transfer of laboratory data

Study Data Tabulation Model

CRO

Sponsor

ODM

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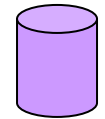
- Submission data (Case Report Tabulations; analysis data)
- SDTM Production Version 1.2, with Implementation Guide V. 3.1.2 (November 12, 2008);
- Referenced as a specification in FDA Guidance - 21 July 2004; updated – 30 October 2009
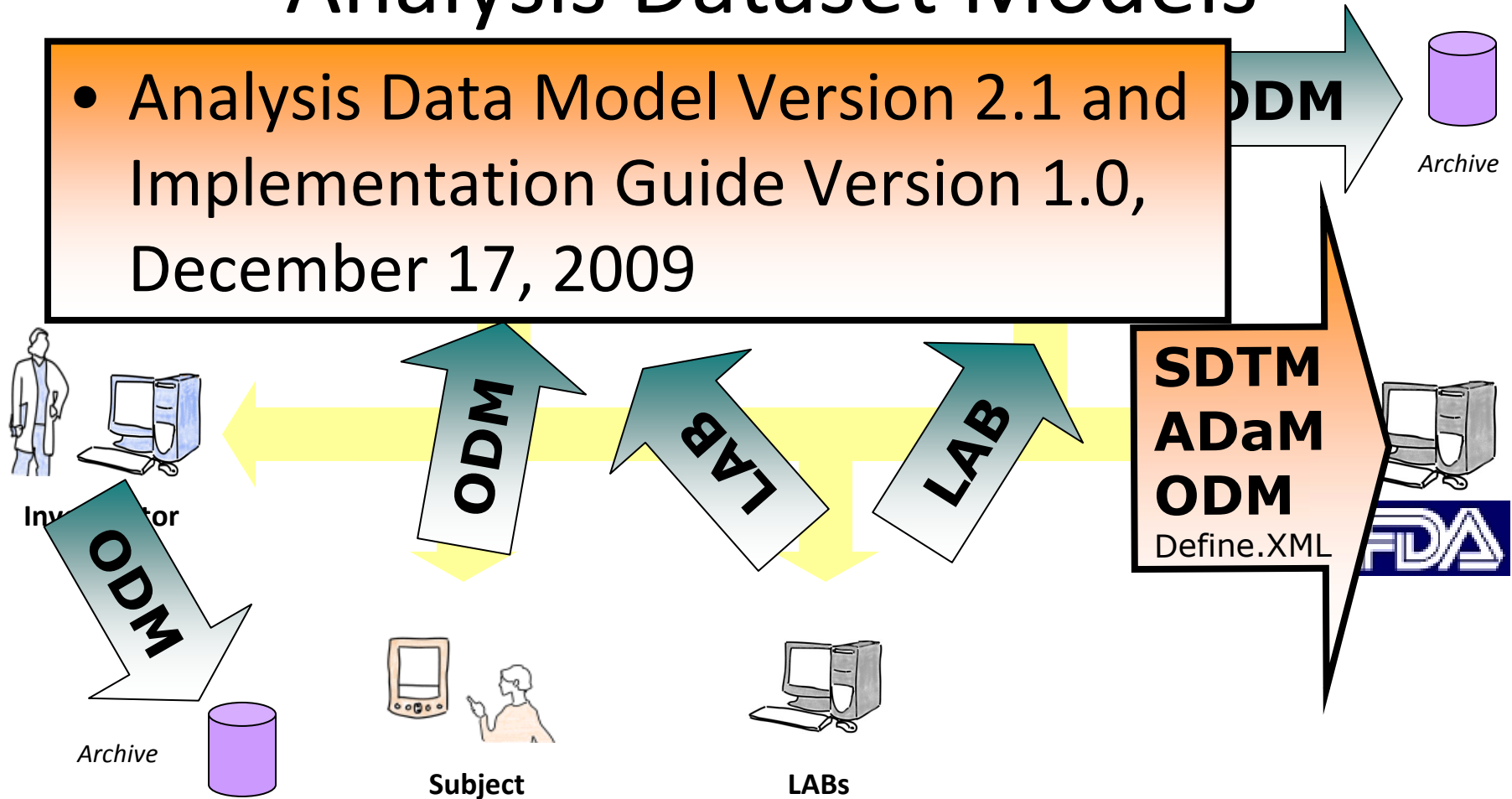
SDTM ADaM ODM Define.XML

FDA

Protocol & BRIDG

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Analysis Dataset Models

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

ODM

Archive

Investigator

ODM

LAB

LAB

SDTM
ADaM
ODM
Define.XML

FDA

ODM

Archive

Subject

LABs

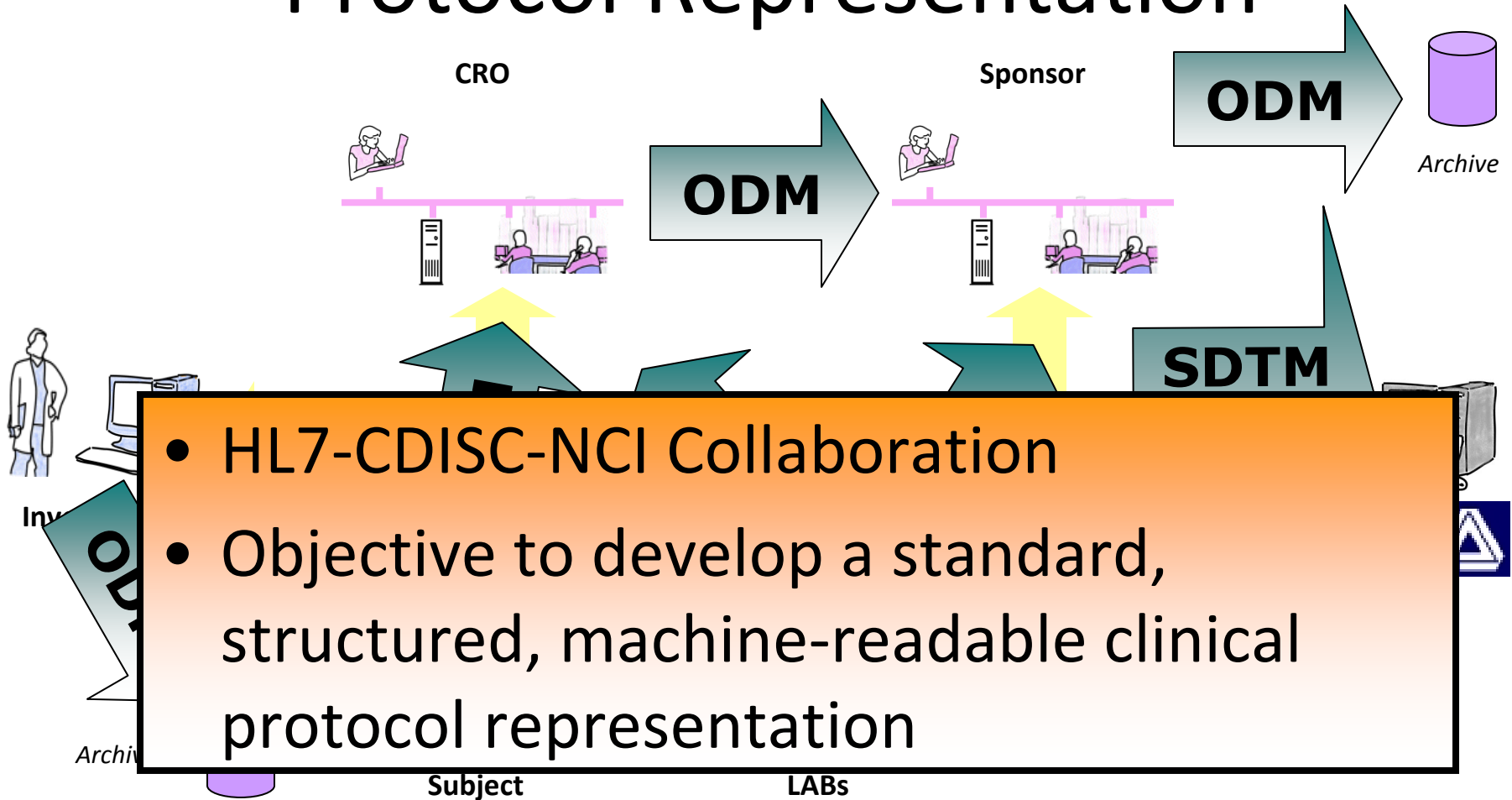**Protocol & BRIDG**

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

CRO — Sponsor — ODM — Archive — SDTM — Investigator — Subject — LABs

- 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
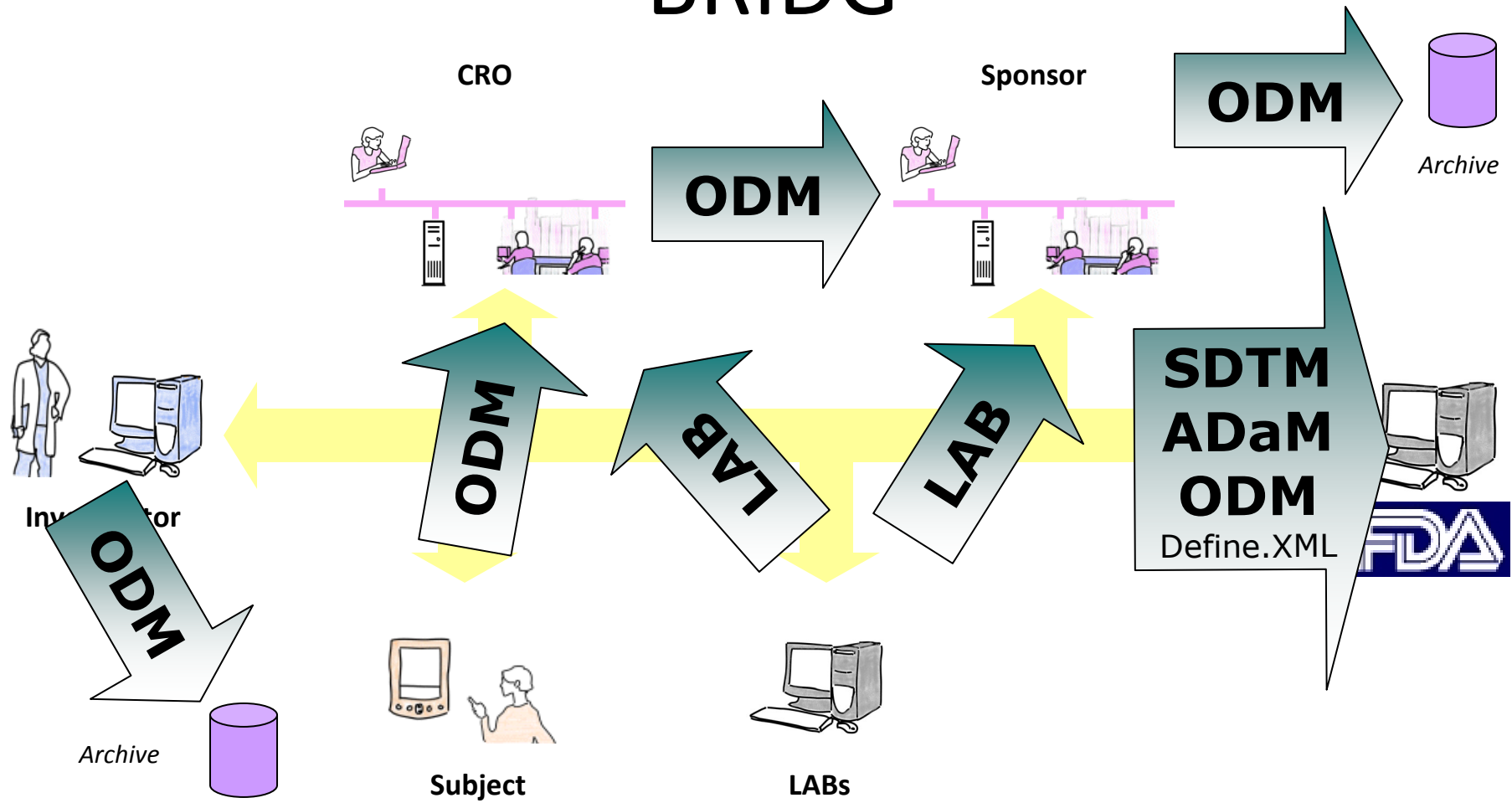
Protocol & BRIDG

The BRIDG Model

- **<u>Vision</u>** : Create a domain analysis model for clinical research domain
  - **<u>Key Goals</u>**:
    - 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

Biomedical Research Integrated Domain Model (BRIDG)

Protocol → CDASH LAB → SDTM (SEND) → ADaM

Same Concept, Same Meaning

Terminology

- Covers the work of all teams
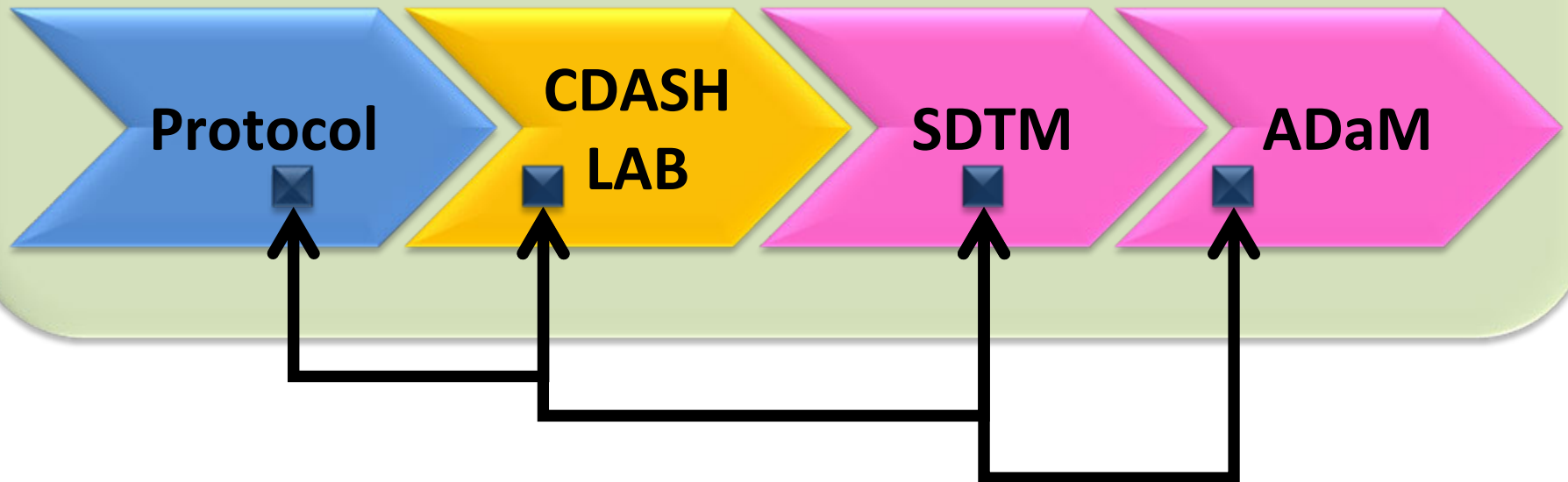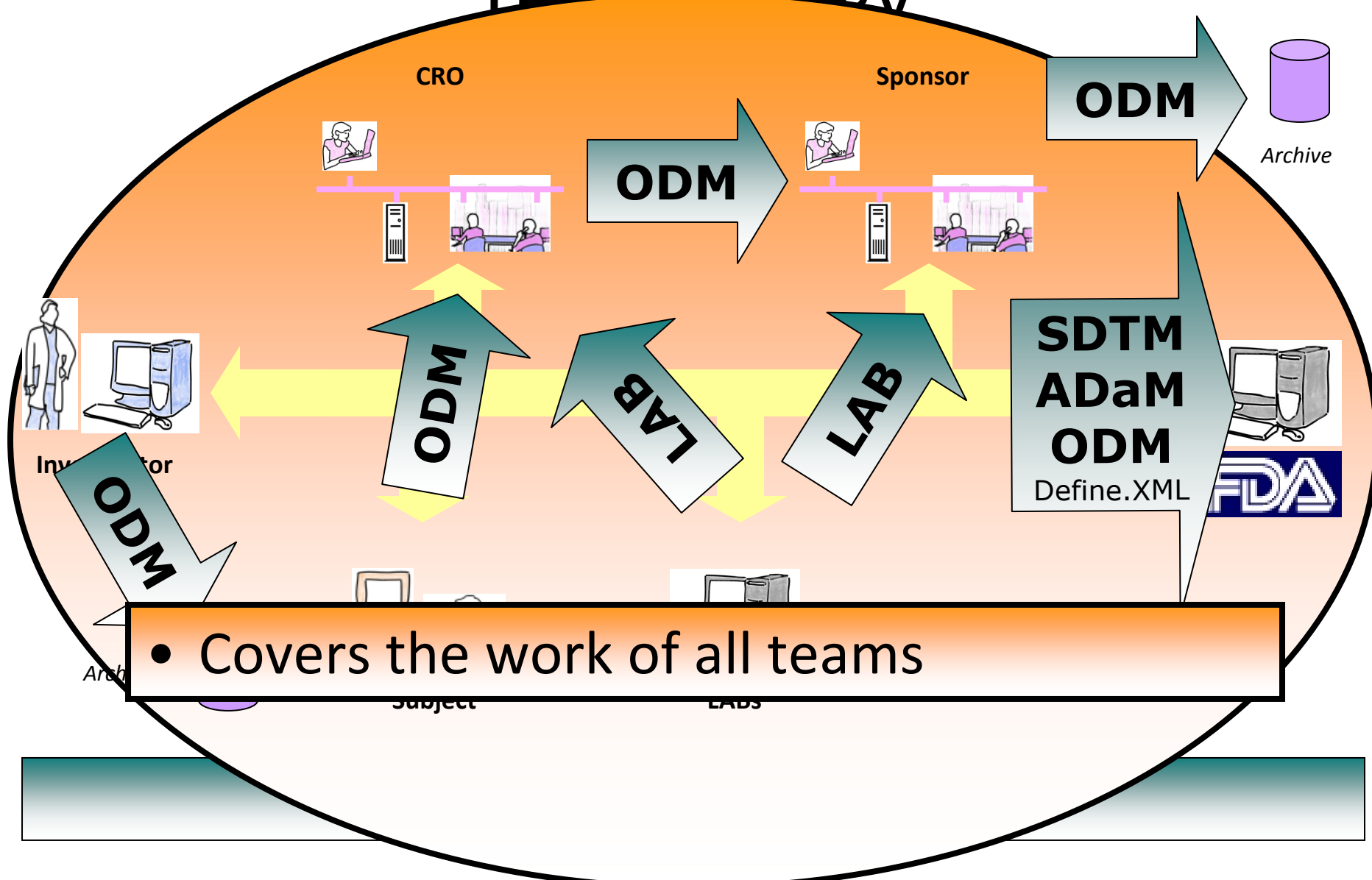
Terminology Collaboration

EVS = NCI Enterprise Vocabulary Services
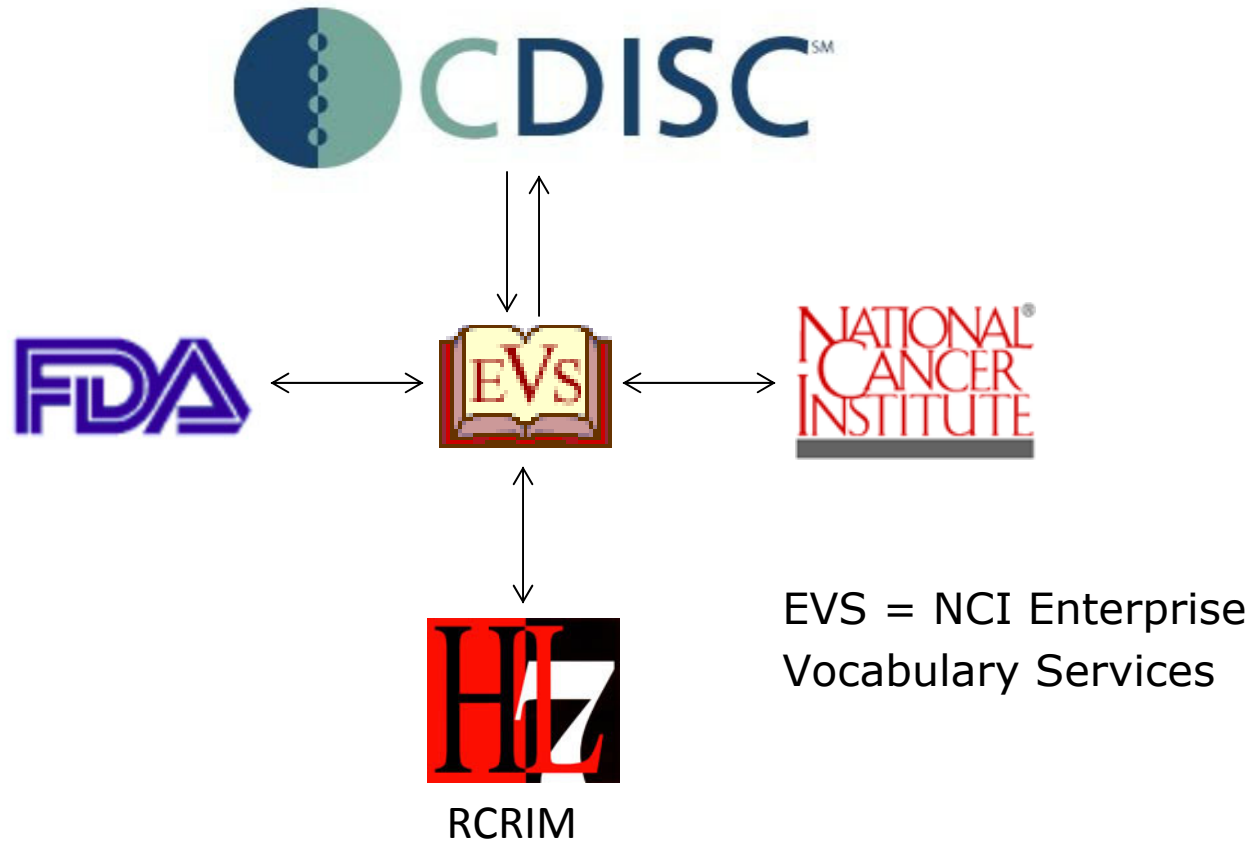
Current Adoption of CDISC Standards
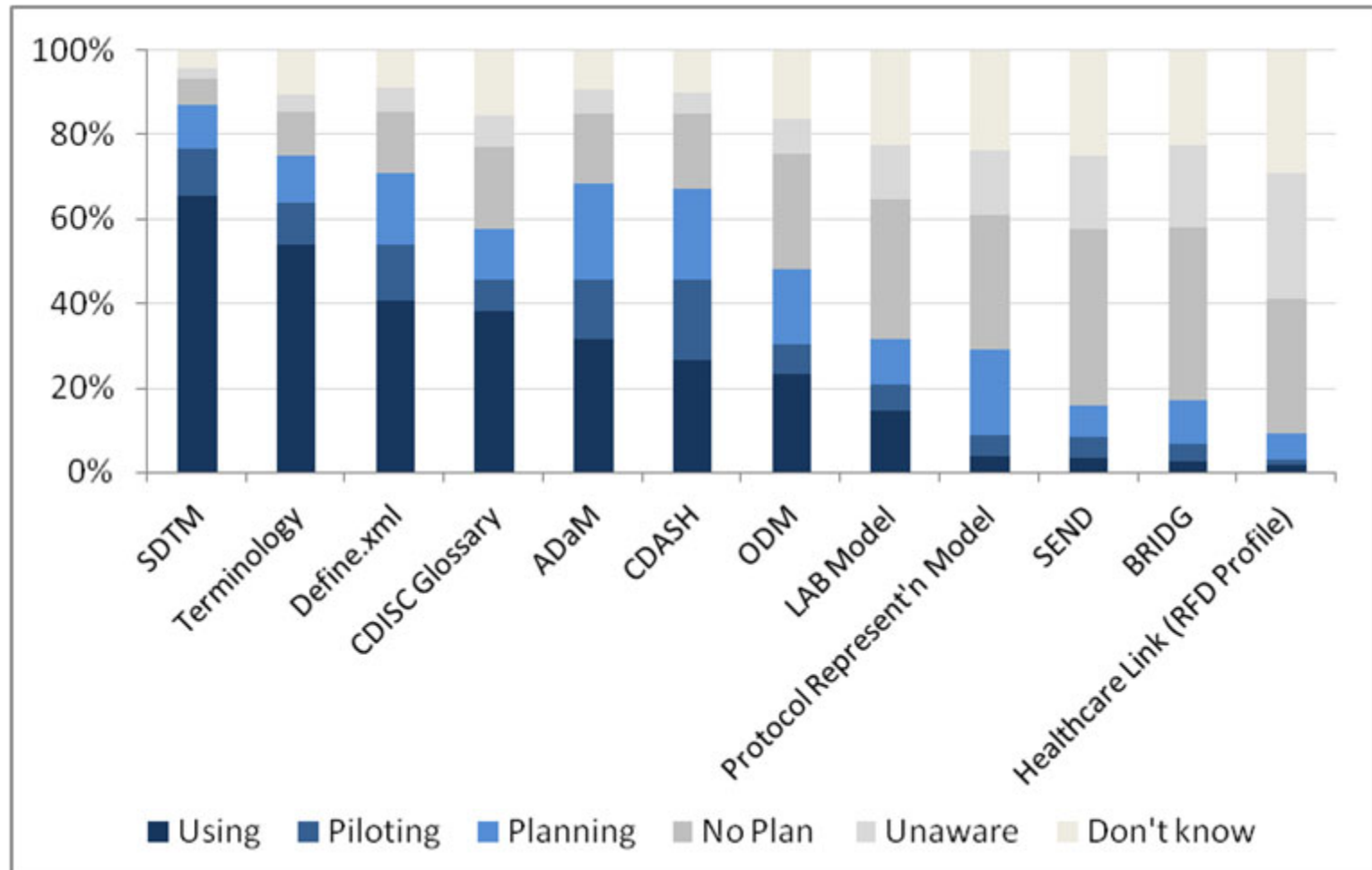
Optimizing the Process

data conception

Healthcare Delivery

(e)Source Documents EHR

eSource

(e)CRFs

Clinical Research

auto reconciliation

~1997
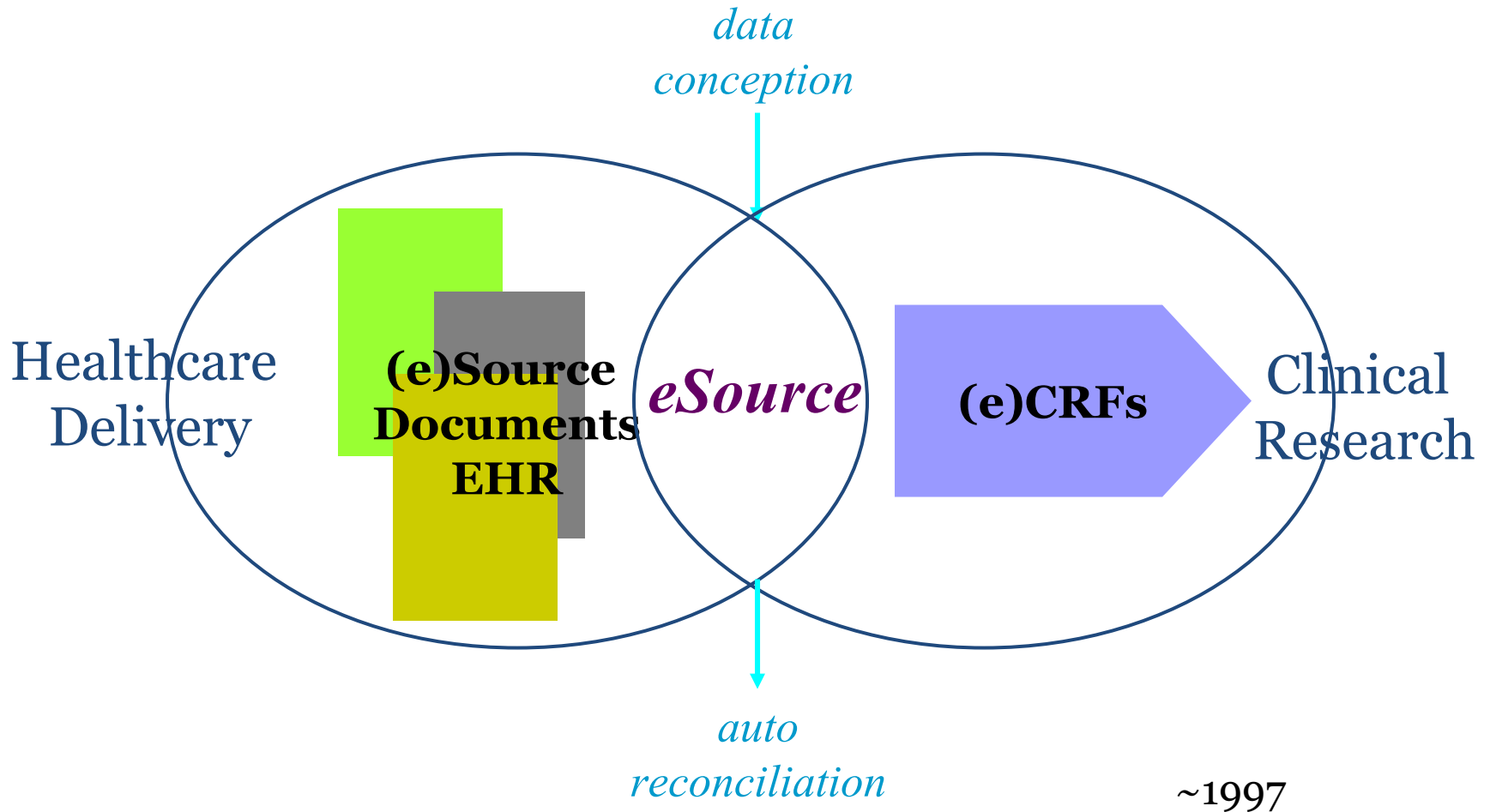
eSource Data Interchange (eSDI) Initiative

- **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

Patient Care World

Clinical Research World

HL7   Single Source   CDISC
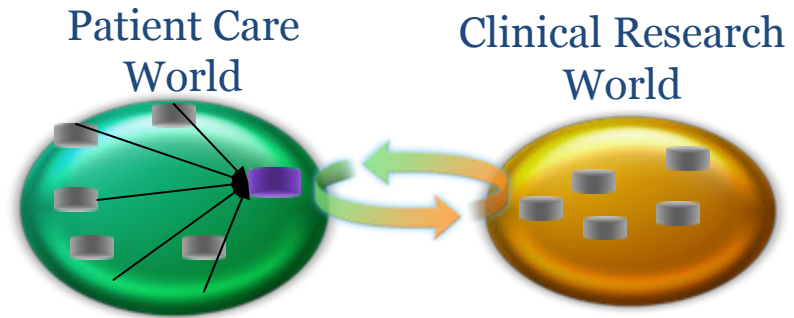
An industry initiative that successfully demonstrated clinical information interoperability between physician clinical systems (EHR) and pharmaceutical clinical trials systems based on open standards.
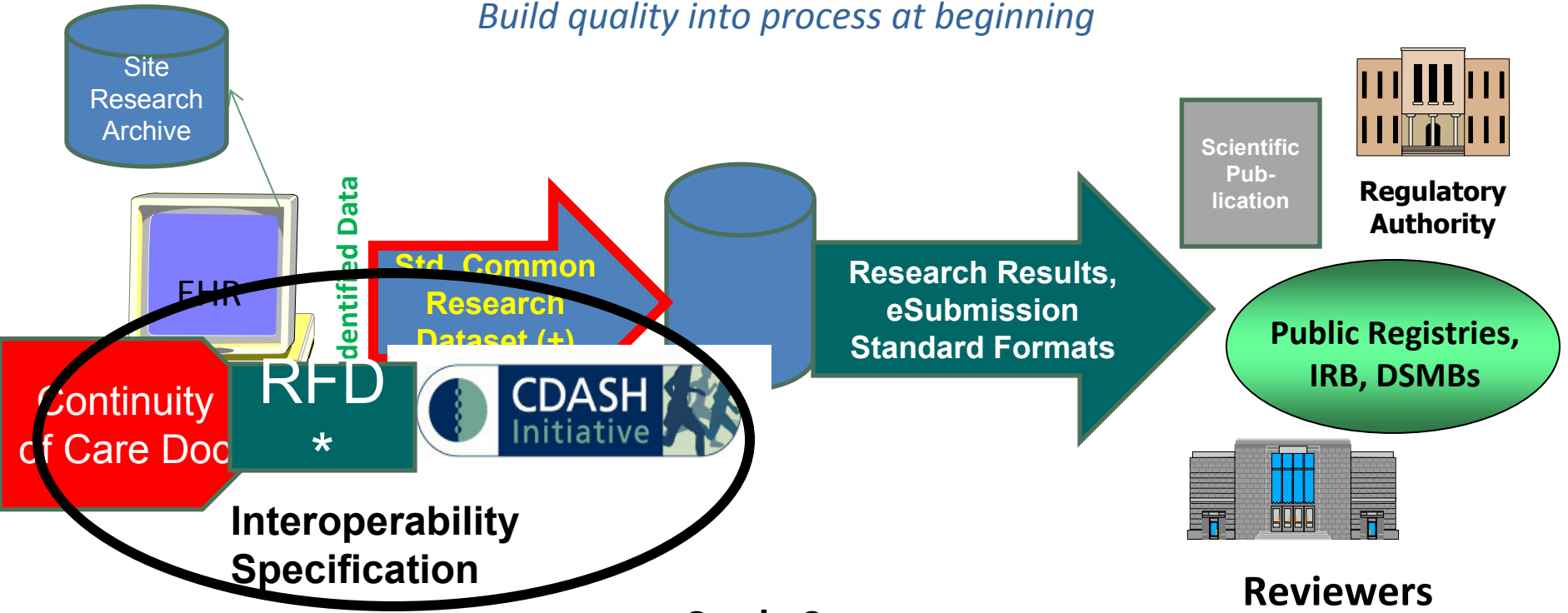*- Duke Clinical Research Institute, CDISC, Novartis, Merck, J&J, Microsoft.*

IHE

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)

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

Clinical Research

Public Health

Safety

Quality

H1N1 Outbreak Reports to CDC (+ bio-surveillance demo)

ASTER Project @ Harvard to FDA: AE Reporting 34 min to < 1 min and rate increased dramatically & Hamamatsu Med School CPOE and EMR to PMDA in Japan

Clinical Research using CCD and CDASH: G. Pompidou Univ Hospital in Paris (C. Daniel) & Prof. Park Med Services w/ Greenway EHR Georgia, U.S.

Possibility to Harmonize Value Sets between Quality Measures and Research

CDISC Retrieve Form for Data Capture (RFD) = key common workflow integration profile (easy for EHRs to implement)

Standards-inspired Innovation:
eSource Data Interchange and Archive

Transition – Paper, EDC, EHR

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

Std. Common Research Dataset (+)

Operational Database

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

CDISC
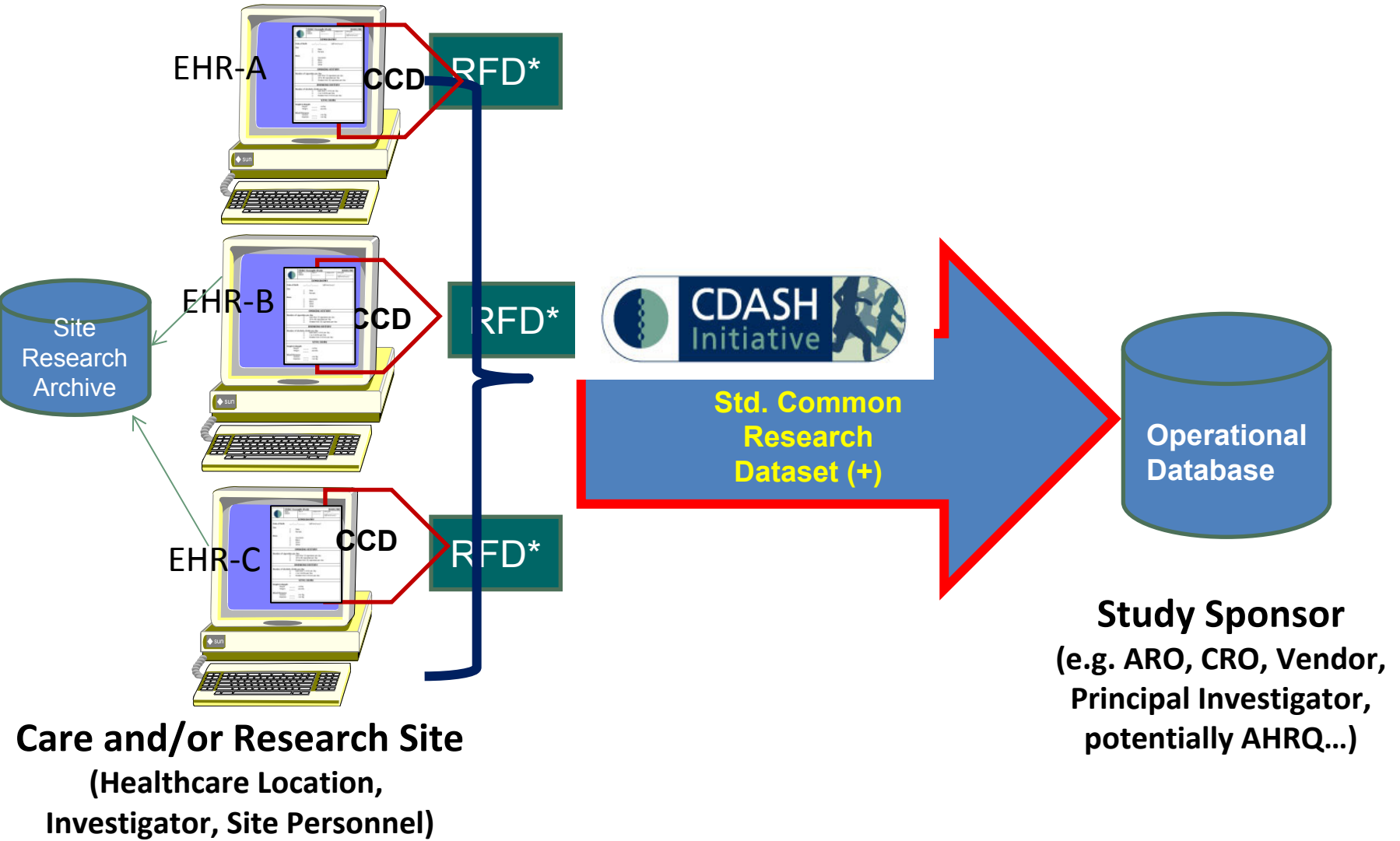
Patient Value: Quality of Care, Safety

eProtocol
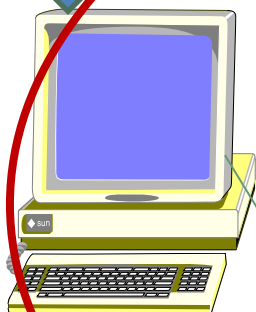
De-identified Data

Scientific Publication

Regulatory Authority

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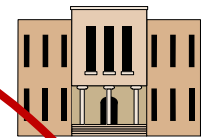
Public Registries, IRB, DSMBs

Research Site
(Healthcare Location, Investigator, Site Personnel)

Site Research Archive
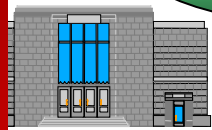
Reviewers
(Research Partner, Sponsor, Registry, Regulator, IRB, DSMB)
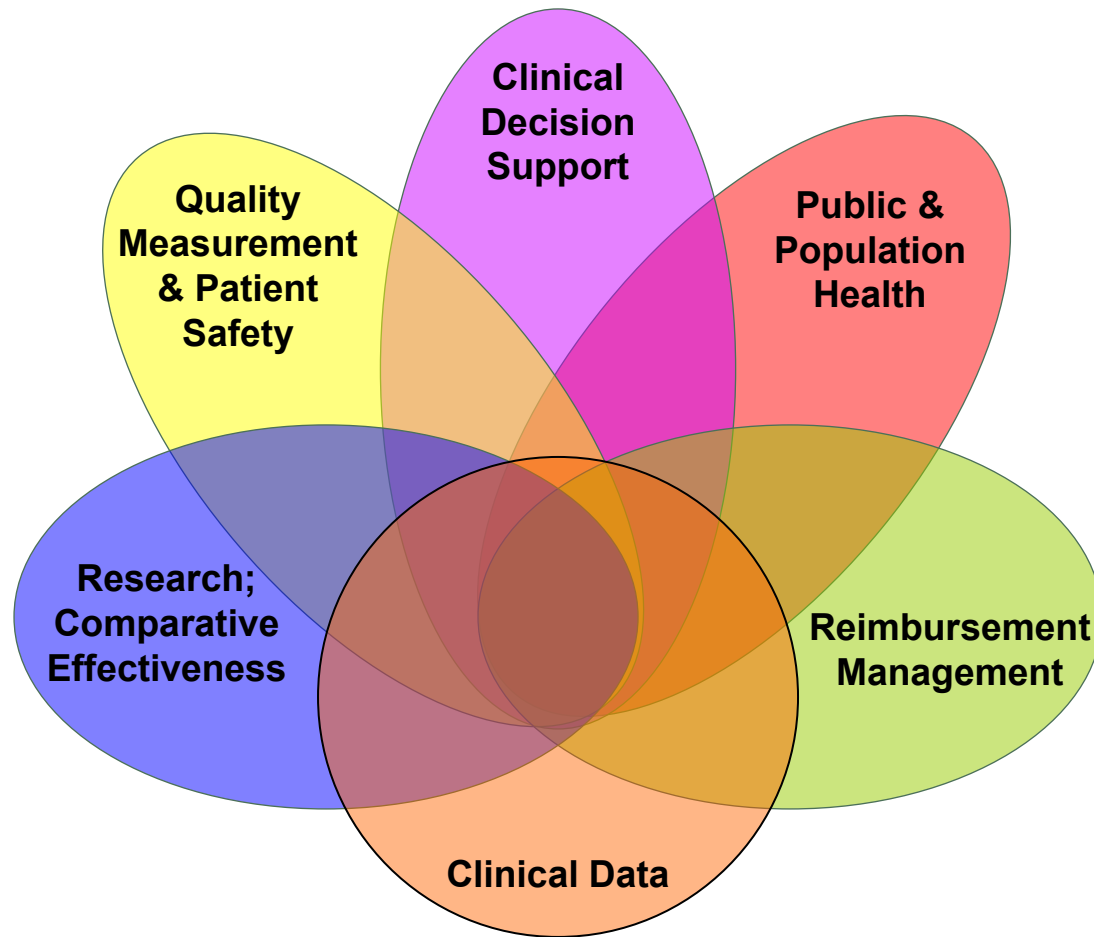
Aknowledgements

- 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!

Overview of the EHR4CR project

Electronic Health Record for Clinical Research

About IMI

- 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).
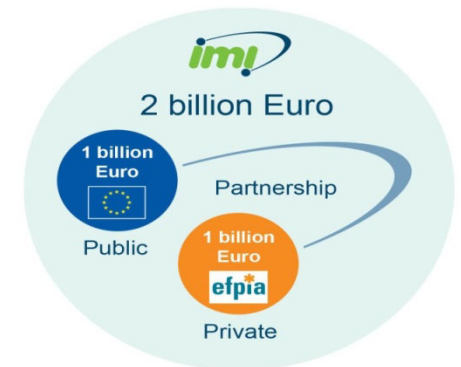
Overall Structure of IMI Research Projects

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.

Full Project consortia

Academic1 Academic3 SME 1 EFPIA comp EFPIA comp EFPIA comp
Academic2 Pat.Org. 1 SME 2 EFPIA comp EFPIA comp EFPIA comp

"Applicants consortium" "EFPIA consortium"

IMI beneficiaries EFPIA *in kind* contribution (no public funding)
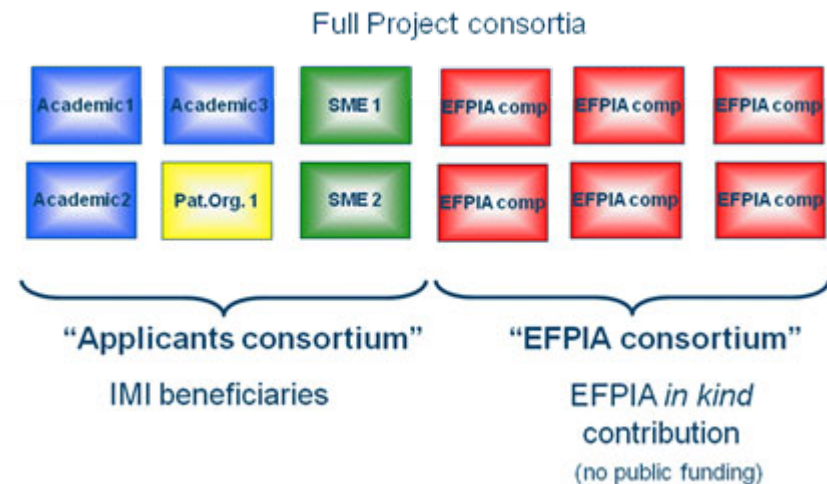
The IMI project principles are to ensure shared leadership roles (research) but to be coordinated by EFPIA

Innovative Medicines Initiative

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Project objective & outputs

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

Output:

- **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
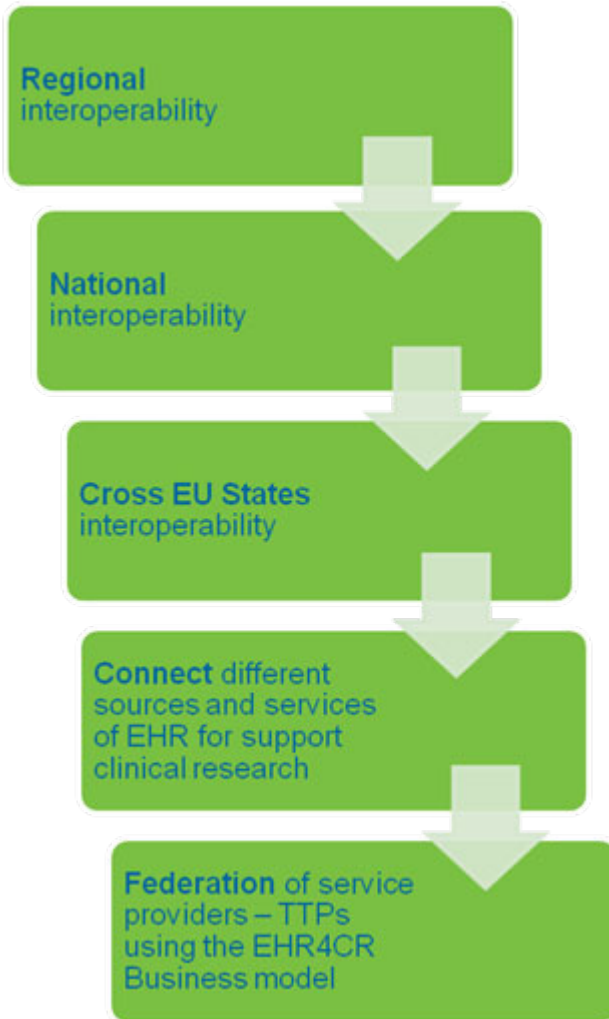
Benefits

- 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
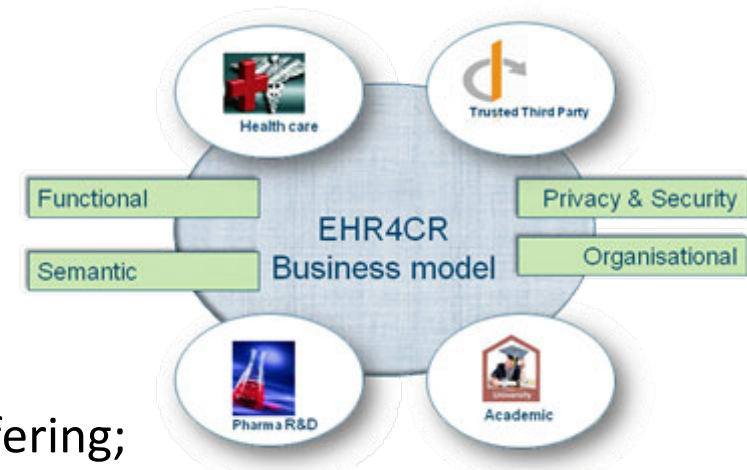
It will:

- 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.
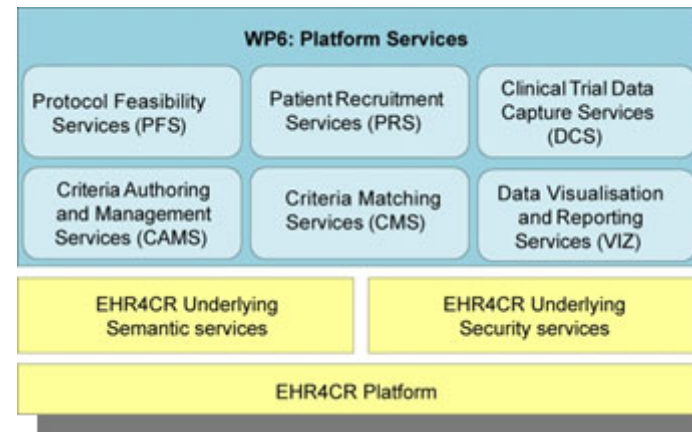
The partners

Governance structure

Steering Committee - All Consortium participants

For annual project review, approval/removal of participants, approval of resource shift across work packages/project participants

Advisory Board

Ethics Board

Executive Committee - 11 Participants
Coordinator (AZ), Deputy Coordinator (Roche)
IMI JU Managing Entity (EuroRec) + All WP leaders

for operational project-leadership, continuous project review, issue resolution, proposal of changes within projects

Work Package Group 1

"Engagement & Business Model"

Leaders:
Public: **UCL**
EFPIA: **Roche**

Work Package Group 2

"Informatics Tools & Services"

Leaders:
Public: **Custodix**
EFPIA: **Sanofi Aventis**

Work Package Group 3

"Pilots"

Leaders:
Public: **Univ. Münster**
EFPIA: **Amgen**

Work Package Group 4: Project Management & Administration
EFPIA (AZ, Lilly) & Public partners (EuroRec, UCL)

All participants - Contibutions to Work Package tasks

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
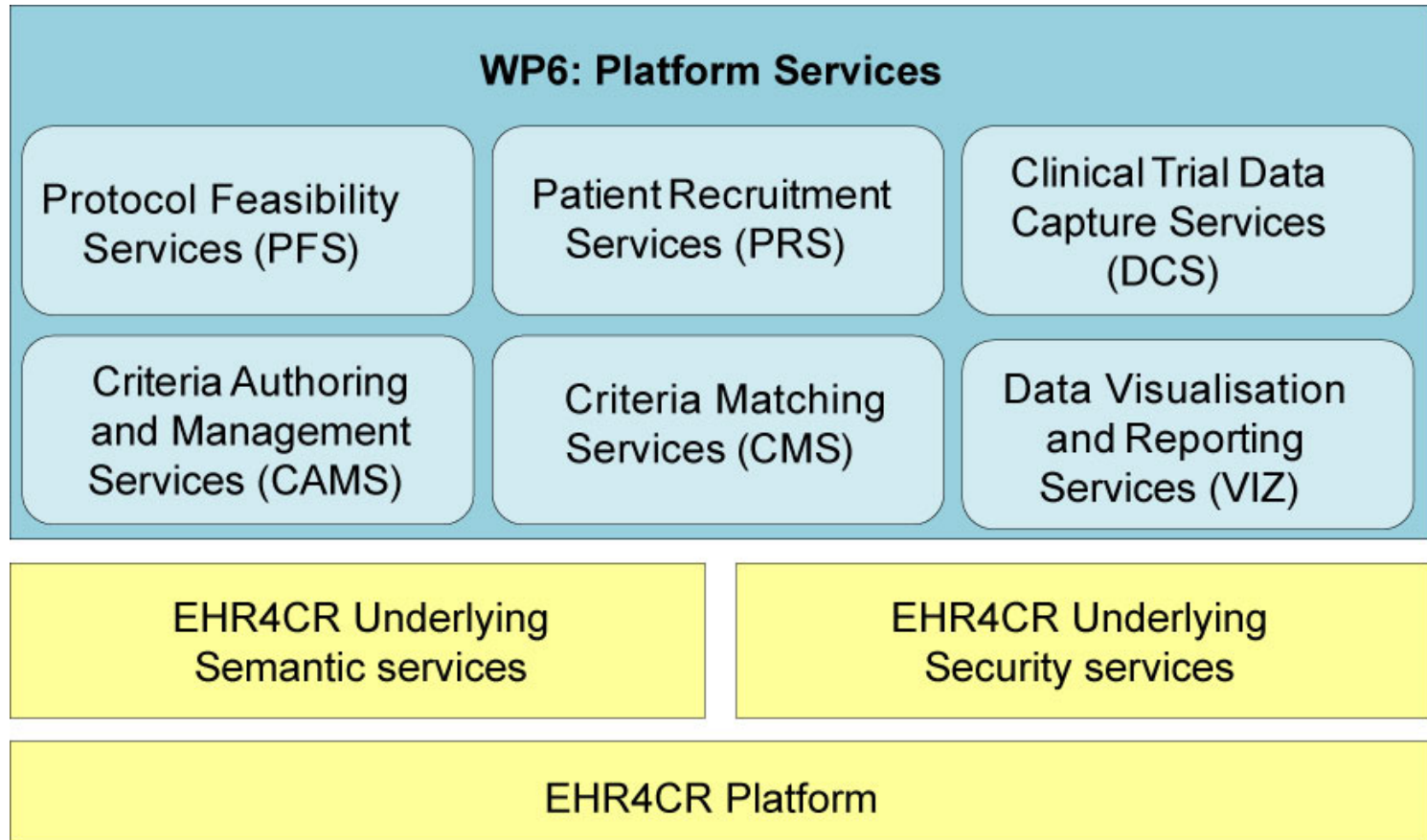
Work Package Group 2
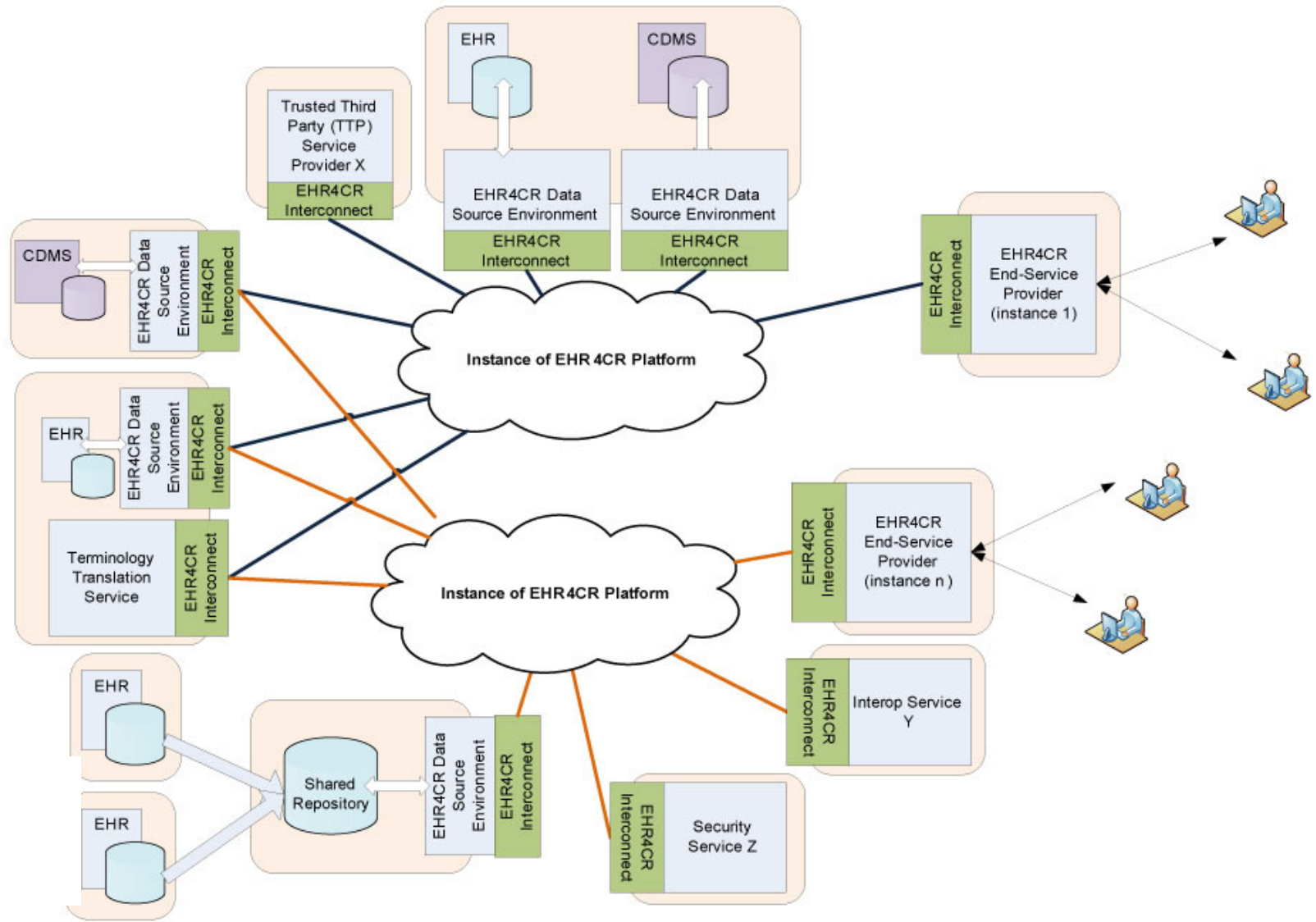# Technology Platform & Tools

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

WP6: Platform Services

Protocol Feasibility Services (PFS)	Patient Recruitment Services (PRS)	Clinical Trial Data Capture Services (DCS)
Criteria Authoring and Management Services (CAMS)	Criteria Matching Services (CMS)	Data Visualisation and Reporting Services (VIZ)

EHR4CR Underlying Semantic services
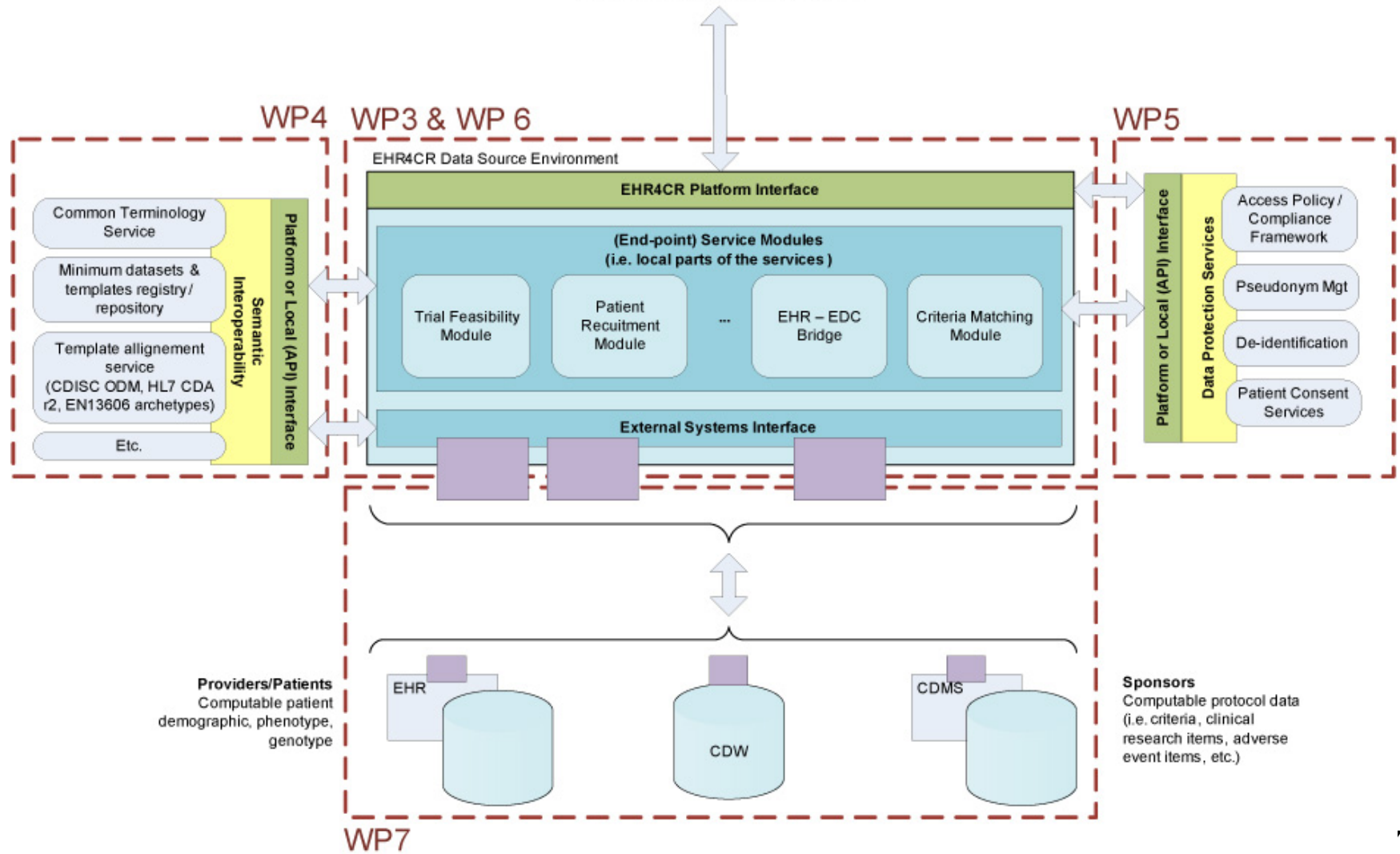
EHR4CR Underlying Security services

EHR4CR Platform

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

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