The ODM and Define.xml

PhUSE

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CDISC℠

Setting the
Global Standard
for Clinical Data

Outline

ODM and Define.xml

- History
- The ODM
- ODM Touch Points
- Define.xml
- The Future
- Summary

Outline

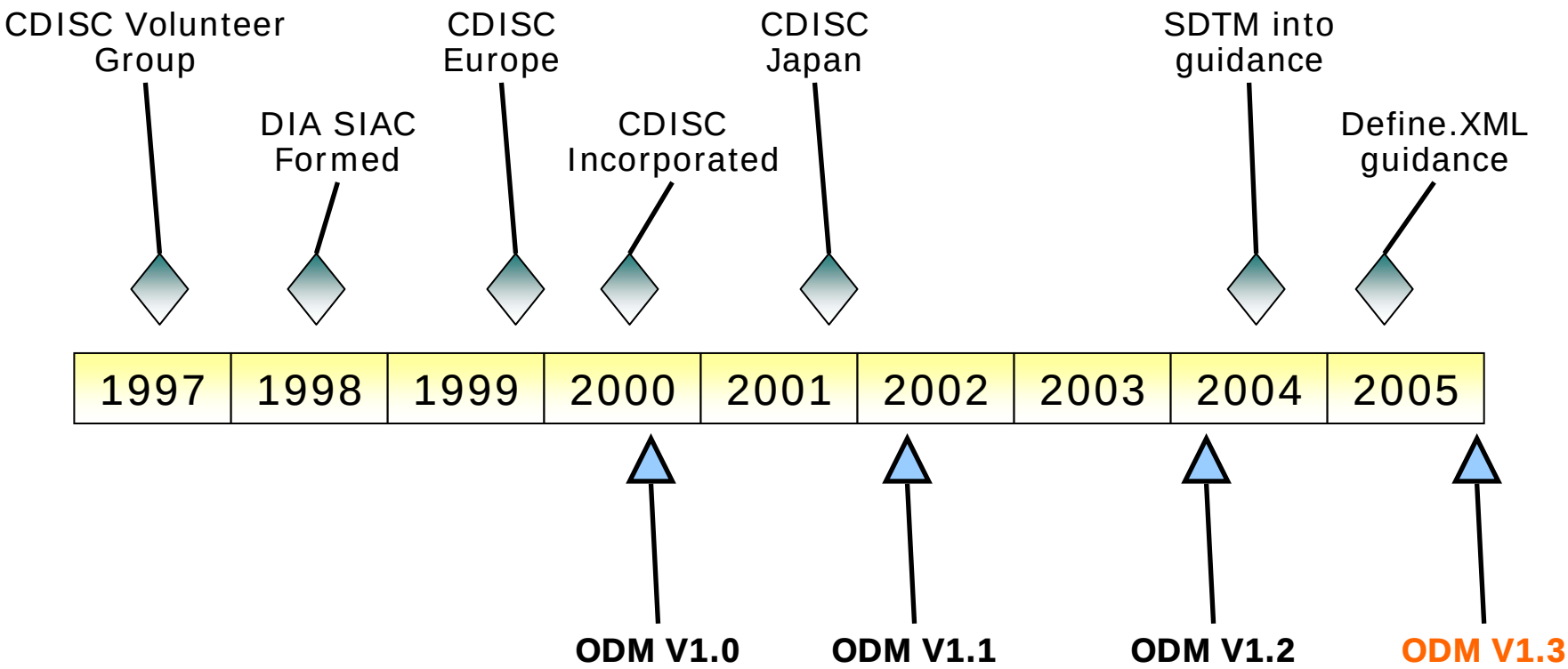
ODM and Define.xml

- **History**
- The ODM
- ODM Touch Points
- Define.xml
- The Future
- Summary

Operational Data Model (ODM)

- Support data interchange and archive
- Represent an entire clinical study
- Comply with 21 CFR Part 11 (and associated regulatory requirements)
- Be compatible with clinical data applications
- Platform and Vendor neutral

History


CDISC Volunteer Group
DIA SIAC Formed
CDISC Europe
CDISC Incorporated
CDISC Japan
SDTM into guidance
Define.XML guidance
1997
1998
1999
2000
2001
2002
2003
2004
2005
ODM V1.0
ODM V1.1
ODM V1.2
ODM V1.3

Outline

ODM and Define.xml

- History
- **The ODM**
- ODM Touch Points
- Define.xml
- The Future
- Summary

ODM: MetaData

Site Details

Site No.: _____

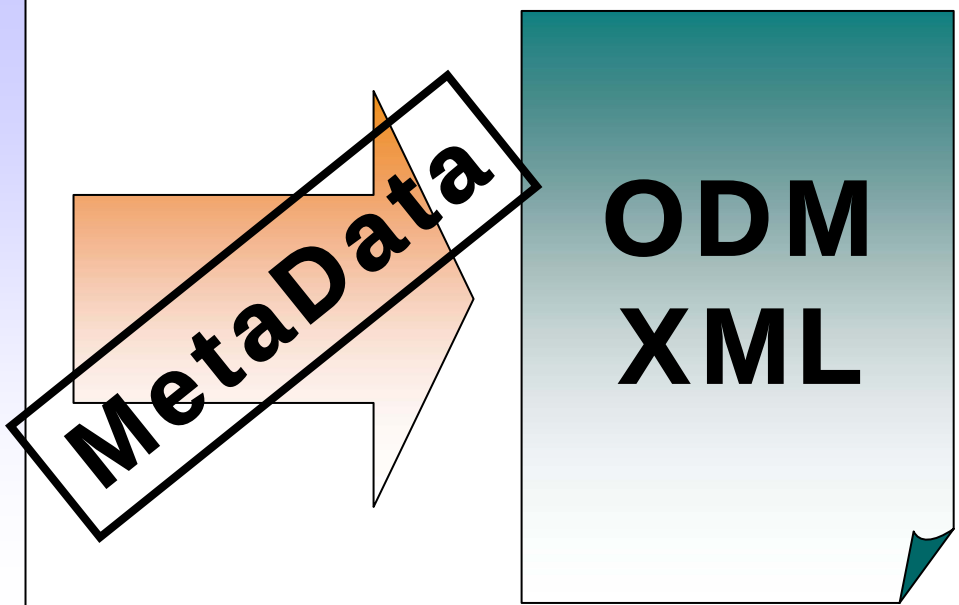
Subject's Characteristics

Number: _____

Sex: M [ ] F [ ]

Height: _____ cm

Weight: _____ kg



ODM: Data

Site Details

Site No.:___5___

Subject's Characteristics

Number:__12___

Sex: M [Y] F [ ]

Height: ___1560__ cm

Weight: ___87.2___ kg

ODM: Changes and Audit

Site Details

Site No.: ___5___

Subject's Characteristics

Number: __12___

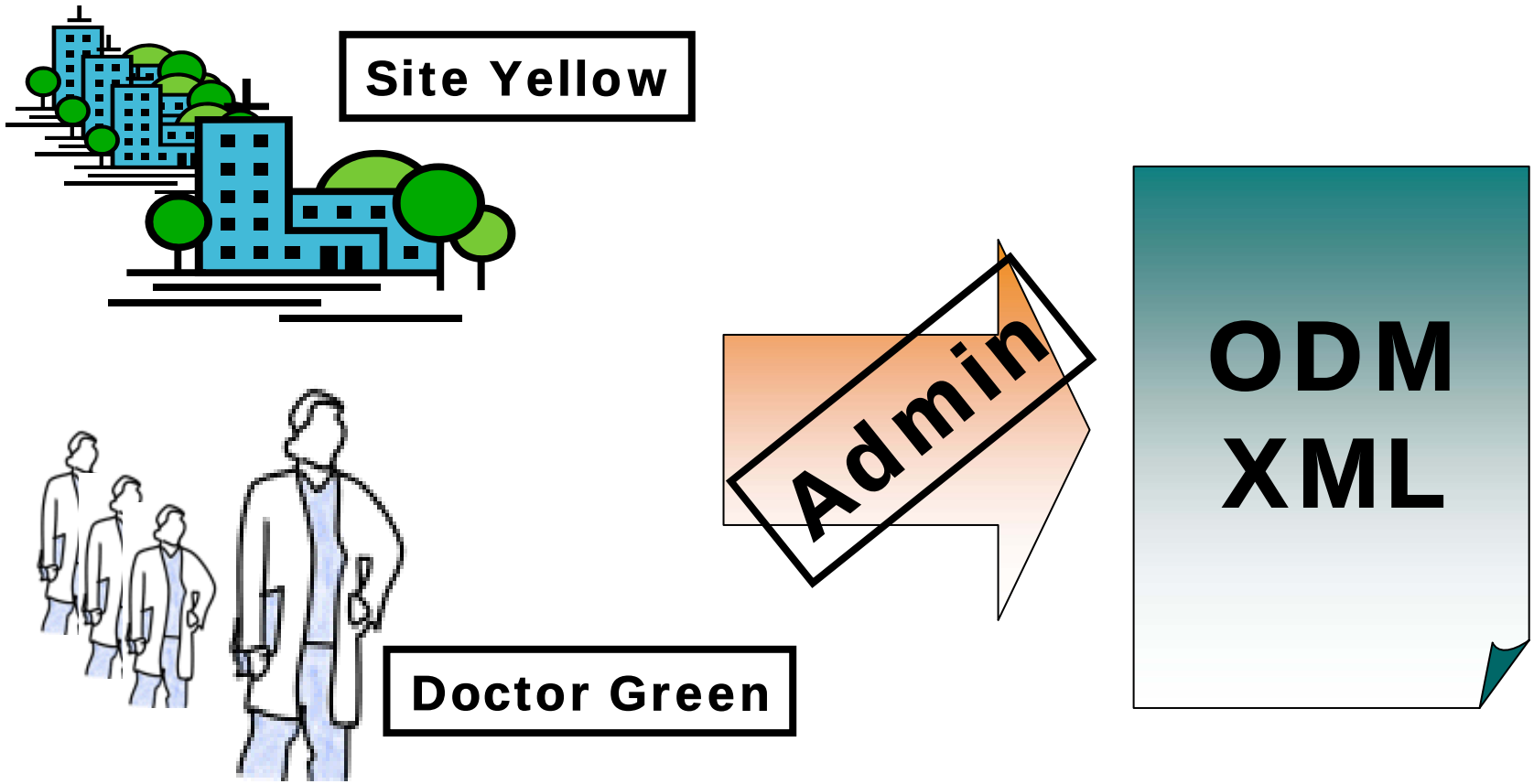
Sex: M [Y] F [ ]

Height: ___1560__ cm 156 ABC 1/1/2005

Weight: ___87.2___ kg

ODM XML

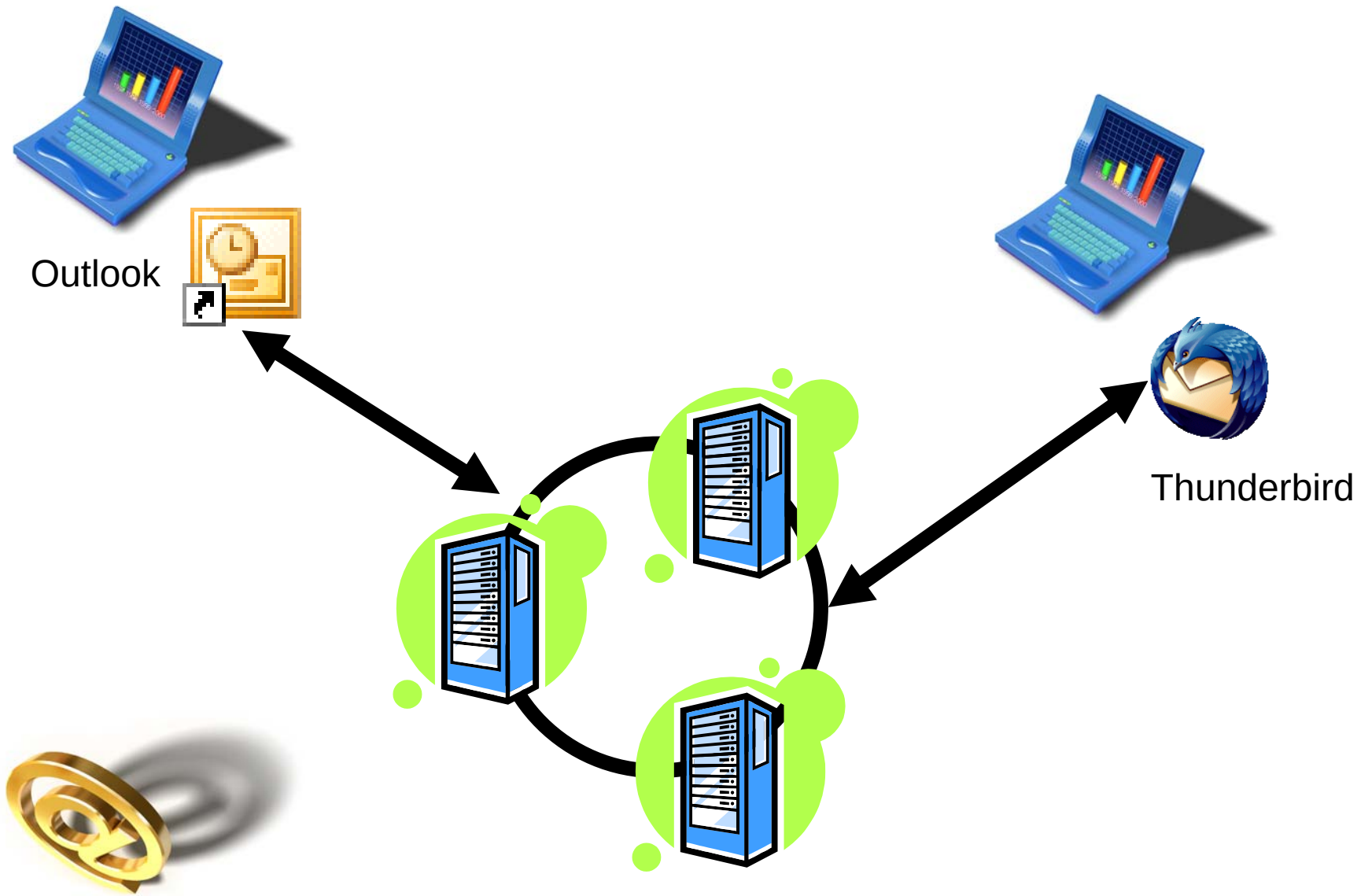
ODM: Administrative



ODM and Define.xml

- History
- The ODM
- **ODM Touch Points**
- Define.xml
- The CDISC Standard
- The Future
- Summary

Email



Email

Outlook

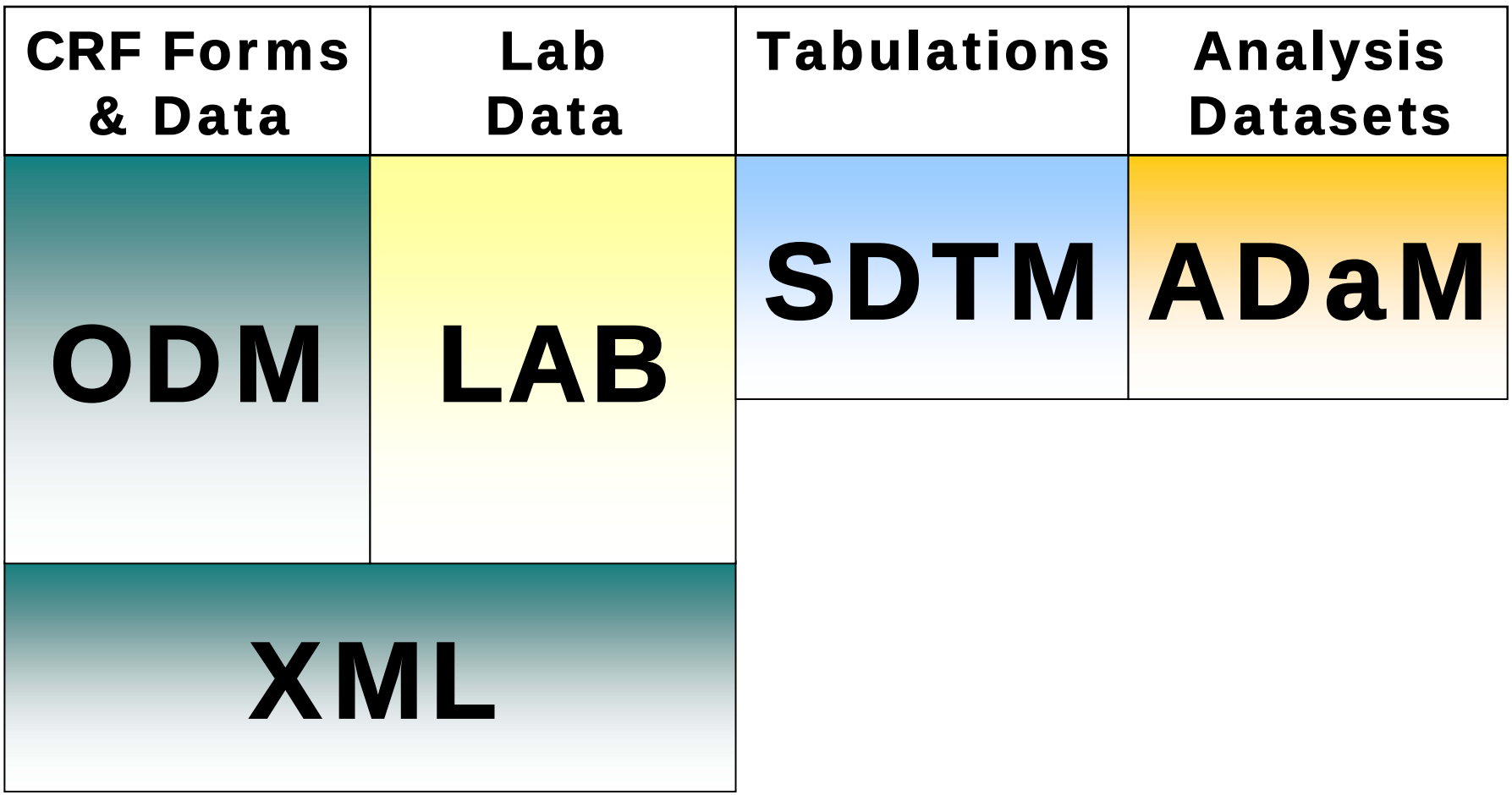
Thunderbird

- Email Content
  - From
  - To
  - Subject
  - Body
- Standards
  - SMTP & POP3

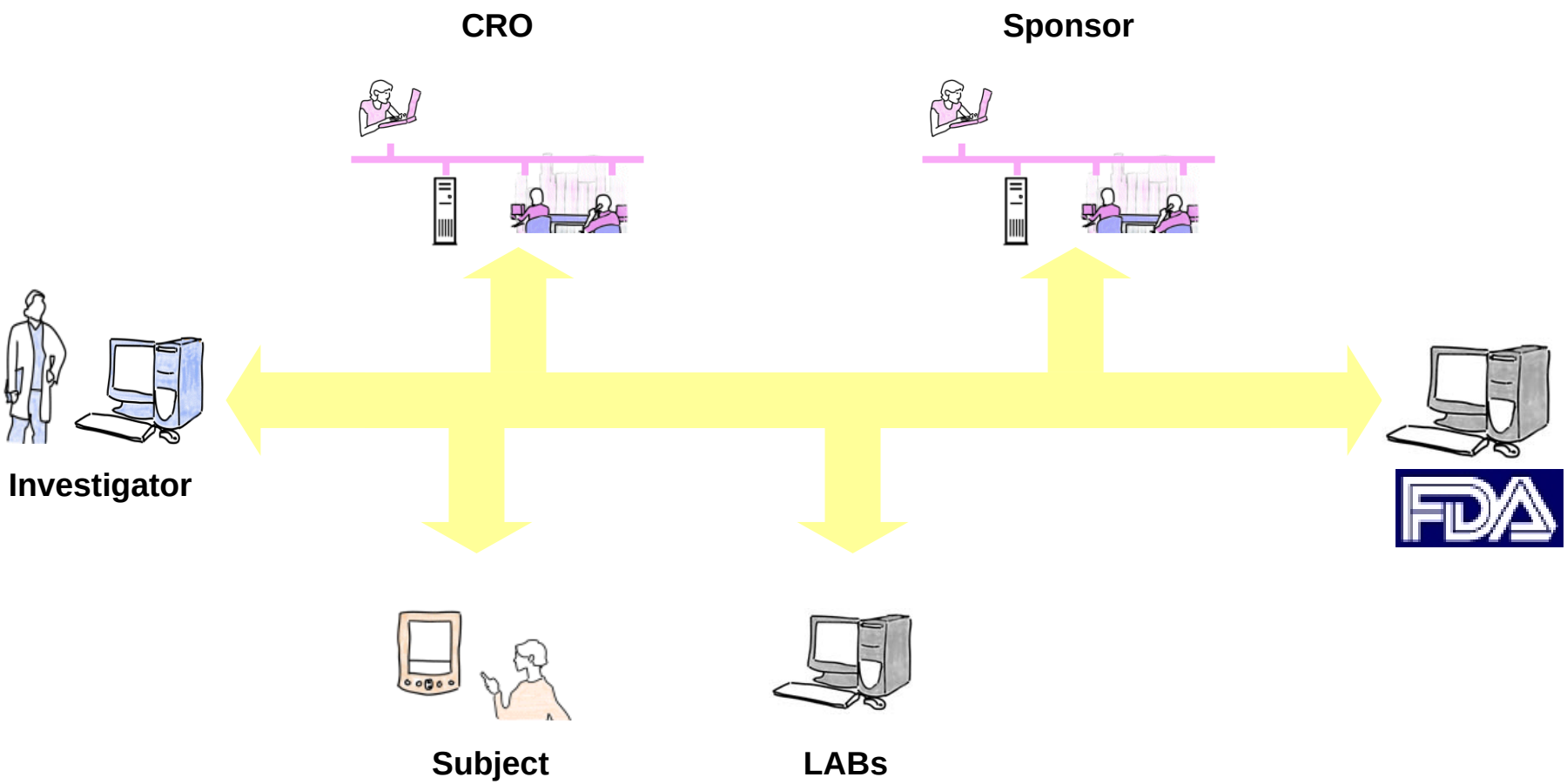
Standards

- Standards exist at varying levels within a hierarchy
- We do not necessarily need to understand the inner workings to benefit from them
- The CDISC Models sits at different levels
  - SDTM & ADaM are about “content”, ways of organising
  - LAB and ODM have a physical form, they are based on XML

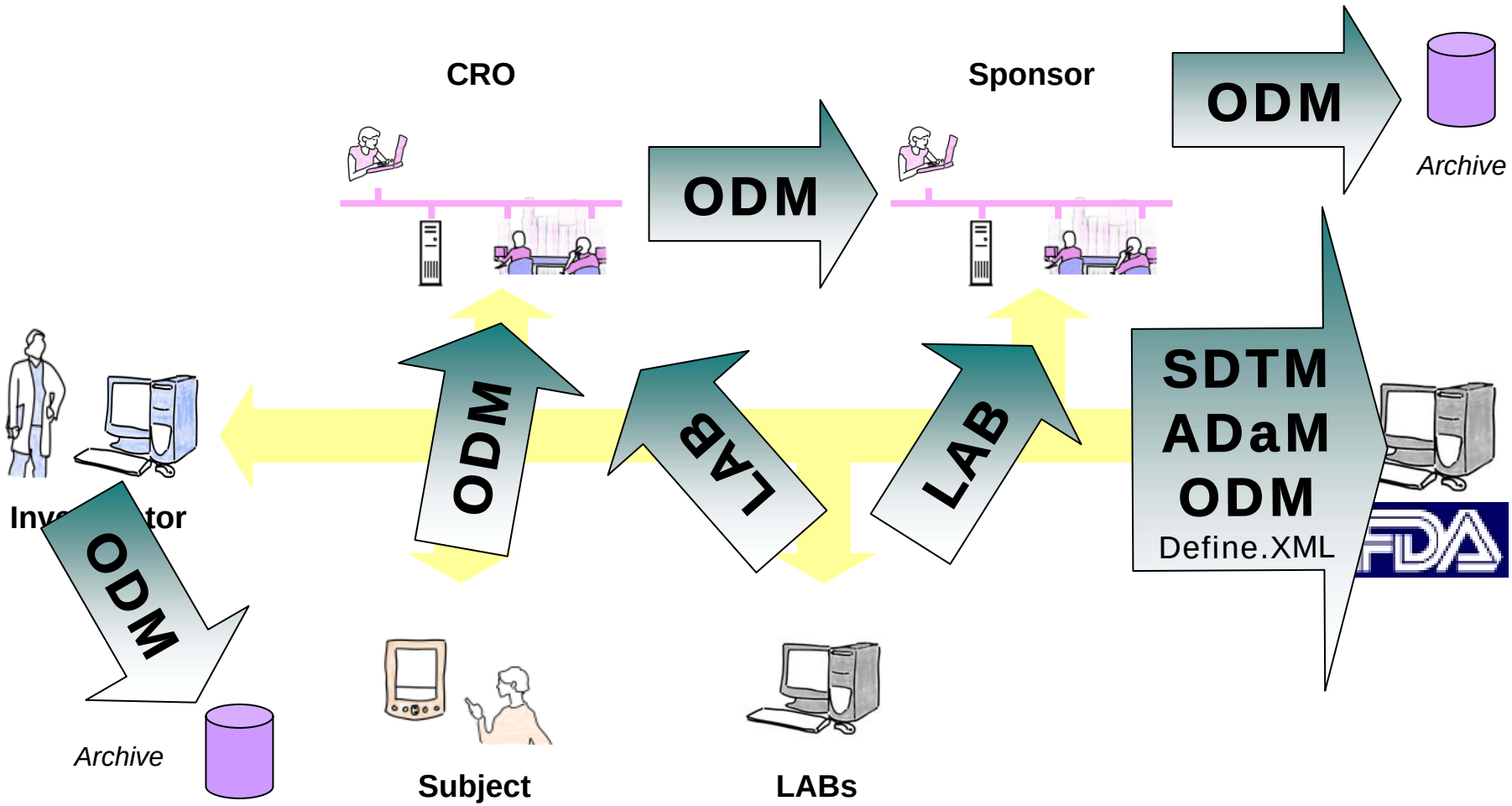
CDISC Models



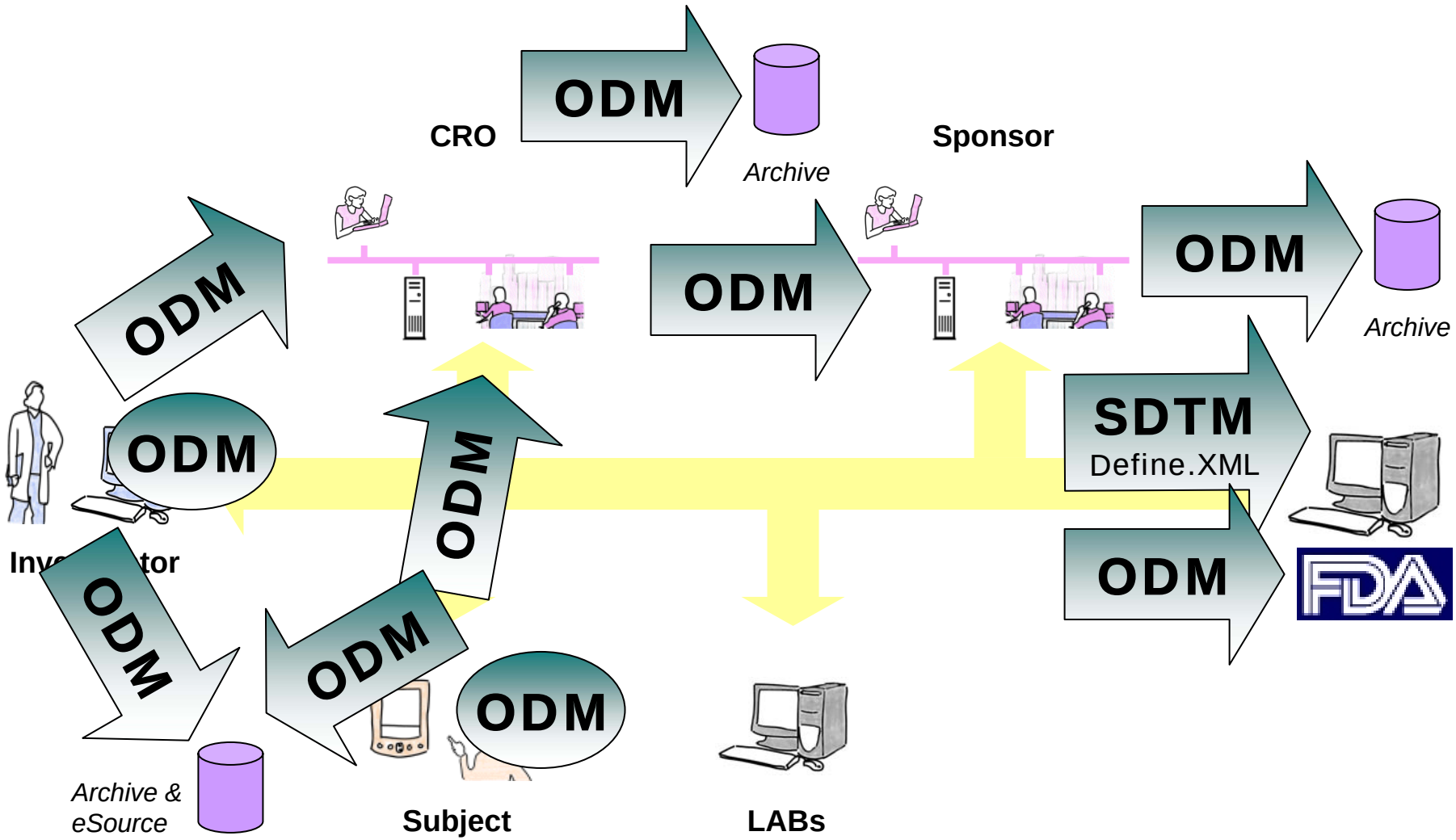
Touch Points



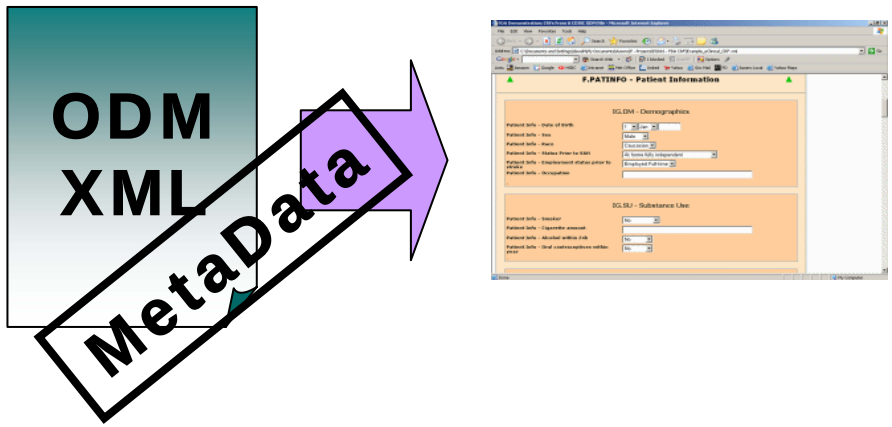
Standards


CRO
Sponsor
ODM
ODM
Archive
ODM
LAB
LAB
SDTM
ADaM
ODM
Define.XML
FDA
ODM
Archive
Subject
LABs

ODM Touch Points



Set Up



- Use of the ODM Metadata to configure tools
- eCRF systems
  - Several vendors using ODM-based mechanisms
- eDiary systems
  - At least one system uses ODM for configuration purposes
- ODM Version 1.3 being developed to include additional support

Electronic Configuration (ACRO)

SPONSOR NAME

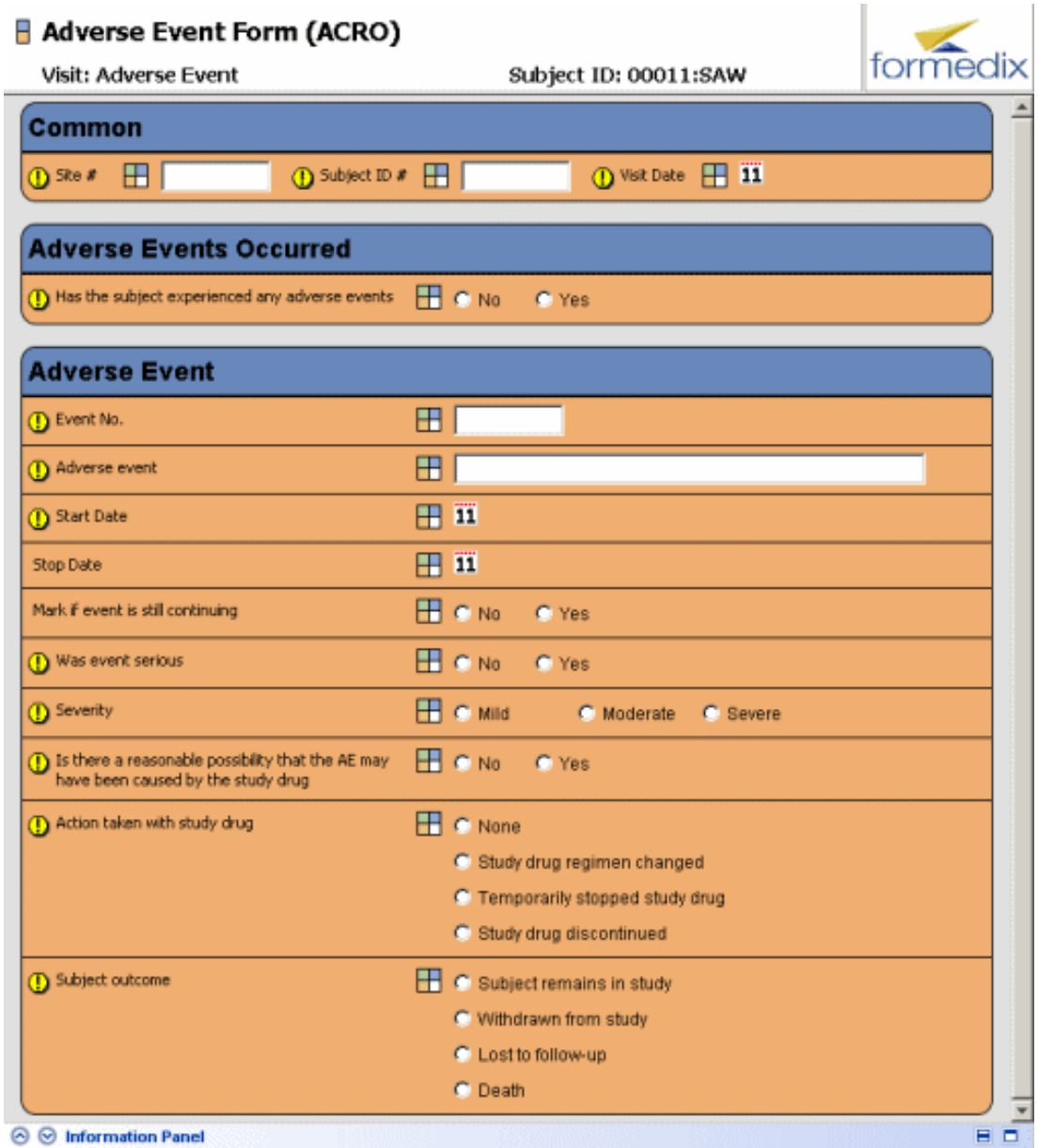
Protocol No.	Investigator No.	Subject No.	Subject Initials
ABC123	☐☐☐	☐☐☐	☐☐☐

ADVERSE EVENTS Has the subject experienced any adverse events? 1 ☐ Yes 0 ☐ No If Yes, describe below.

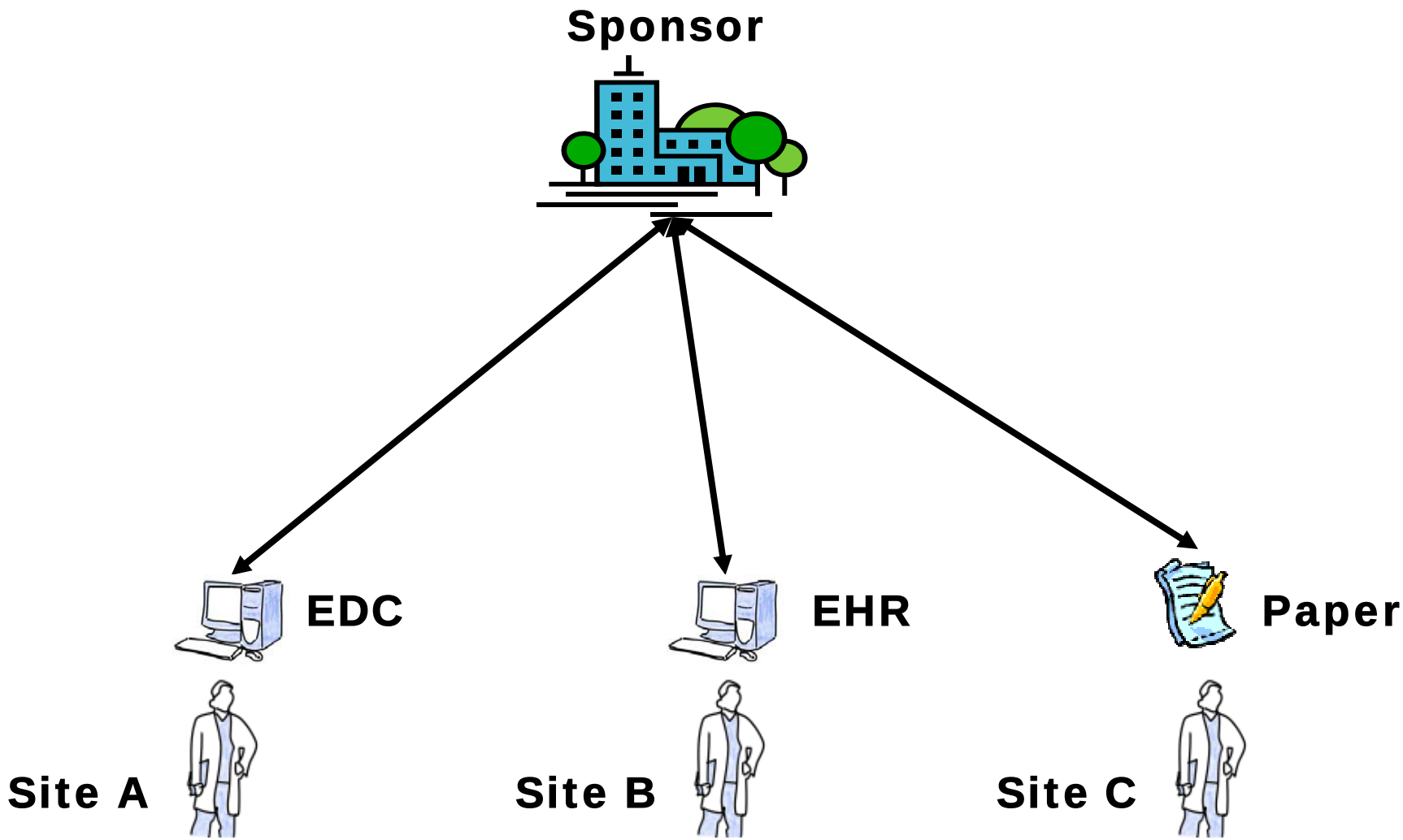
Event No.	Adverse Event	Start Date / Stop Date	Was Event Serious?	Severity	Is there a reasonable possibility that the AE may have been caused by the study drug(s)?*	Action Taken with Study Drug	Subject Outcome
	(Please list one event per line)	Either provide a stop date or mark box (√) if event is continuing ↓	Mark only 1 response 0 = No 1 = Yes	Mark only 1 response 1 = Mild 2 = Moderate 3 = Severe	Mark only 1 response 0 = No 1 = Yes	Mark only 1 response 0 = None 1 = Study drug regimen changed 2 = Temporarily stopped study drug 3 = Study drug discontinued	Mark only 1 response 0 = Subject remains in study 1 = Withdrawn from study 2 = Lost to follow-up 3 = Death
		☐☐-☐☐☐-☐☐☐☐ day month year ☐☐-☐☐☐-☐☐☐☐ day month year 1 ☐	0 ☐ 1 ☐	1 ☐ 2 ☐ 3 ☐	0 ☐ 1 ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐
		☐☐-☐☐☐-☐☐☐☐ day month year ☐☐-☐☐☐-☐☐☐☐ day month year 1 ☐	0 ☐ 1 ☐	1 ☐ 2 ☐ 3 ☐	0 ☐ 1 ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐
		☐☐-☐☐☐-☐☐☐☐ day month year ☐☐-☐☐☐-☐☐☐☐ day month year 1 ☐	0 ☐ 1 ☐	1 ☐ 2 ☐ 3 ☐	0 ☐ 1 ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐

*A "reasonable possibility" means you cannot rule out a relationship between the event and the study drug.

Electronic Configuration (ACRO)

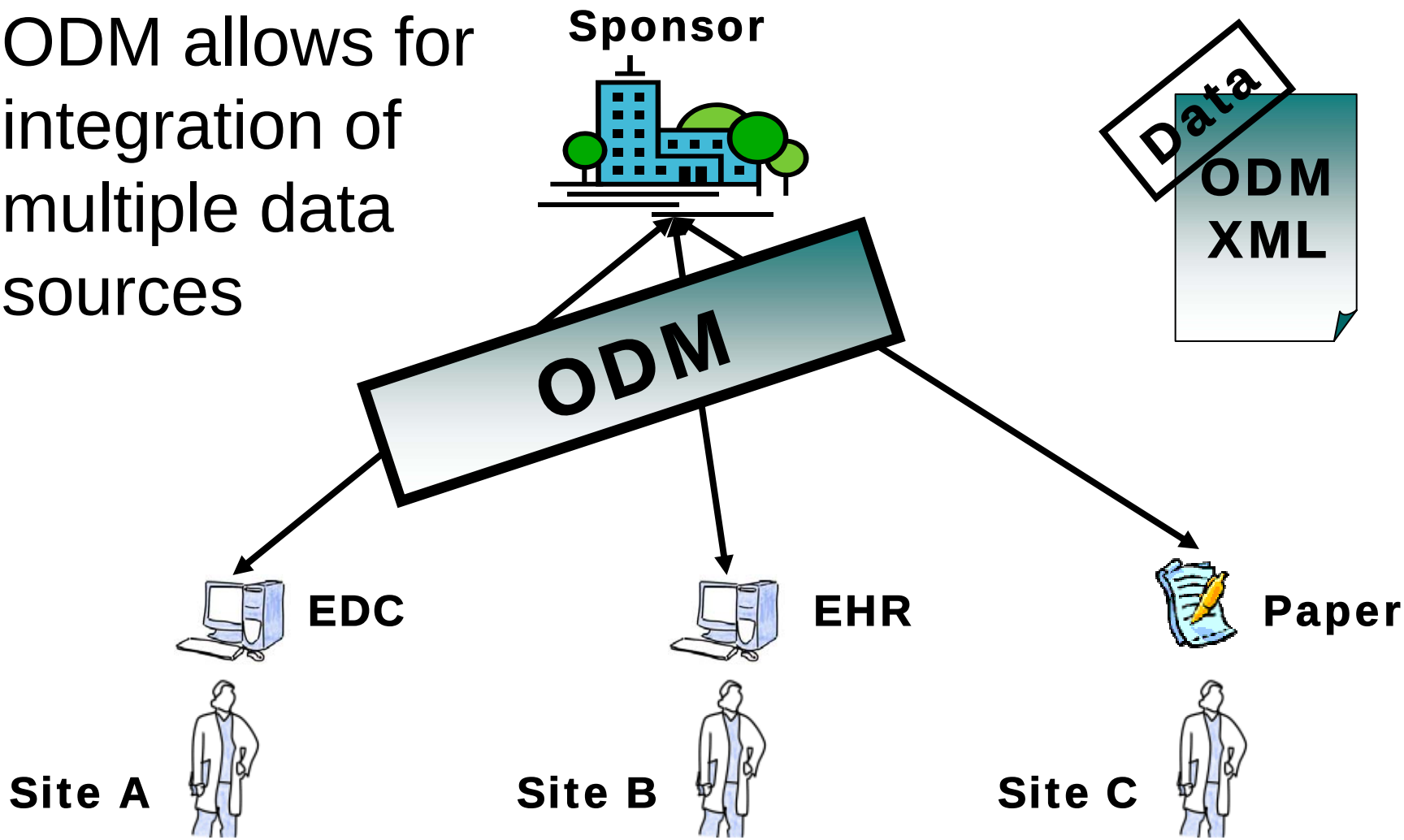


Acquisition



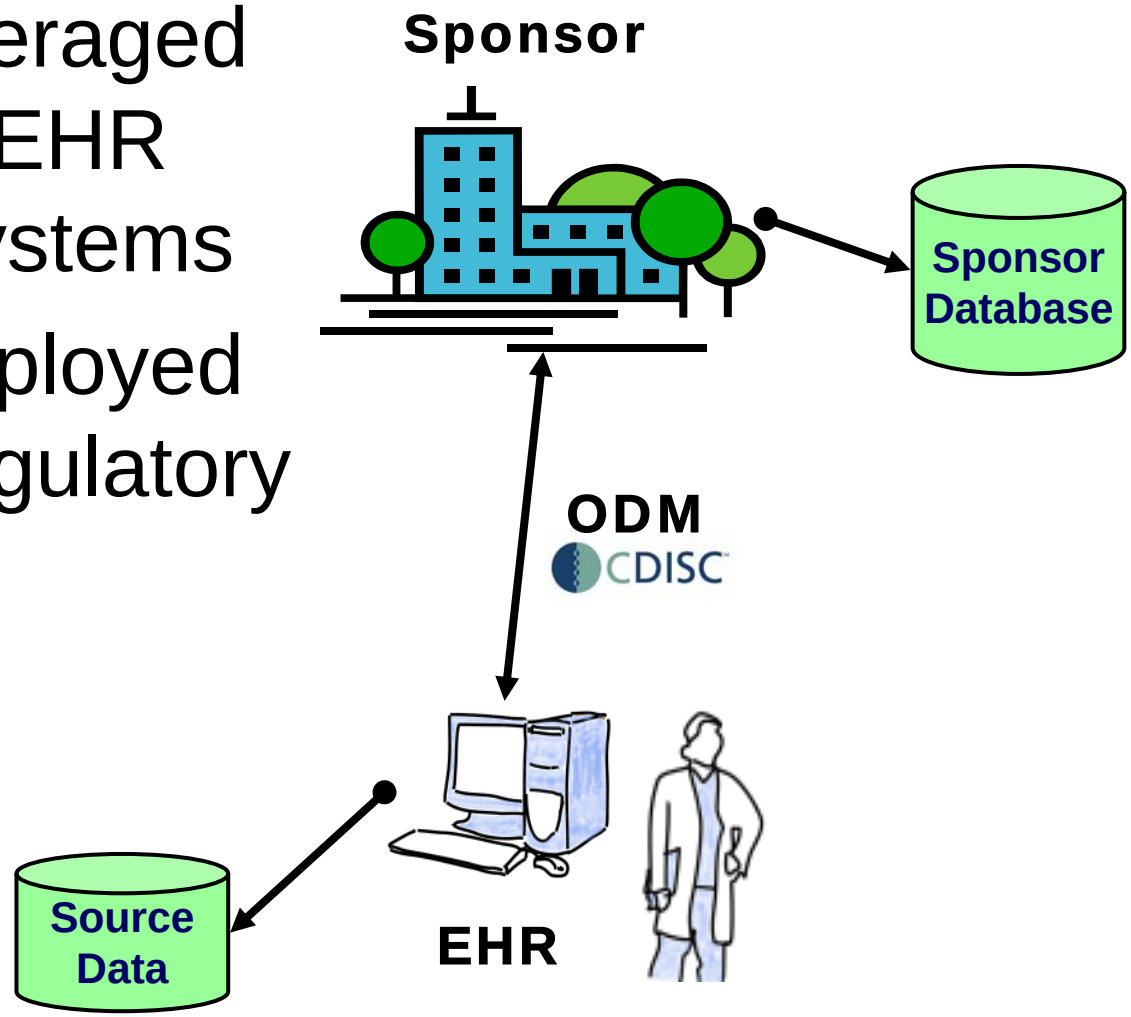
Acquisition

- ODM allows for integration of multiple data sources



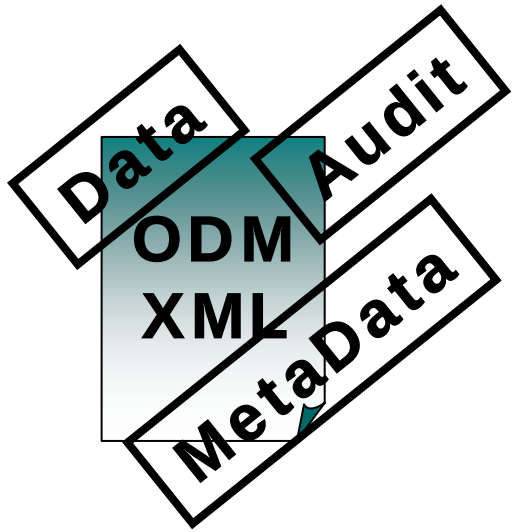
Example Development

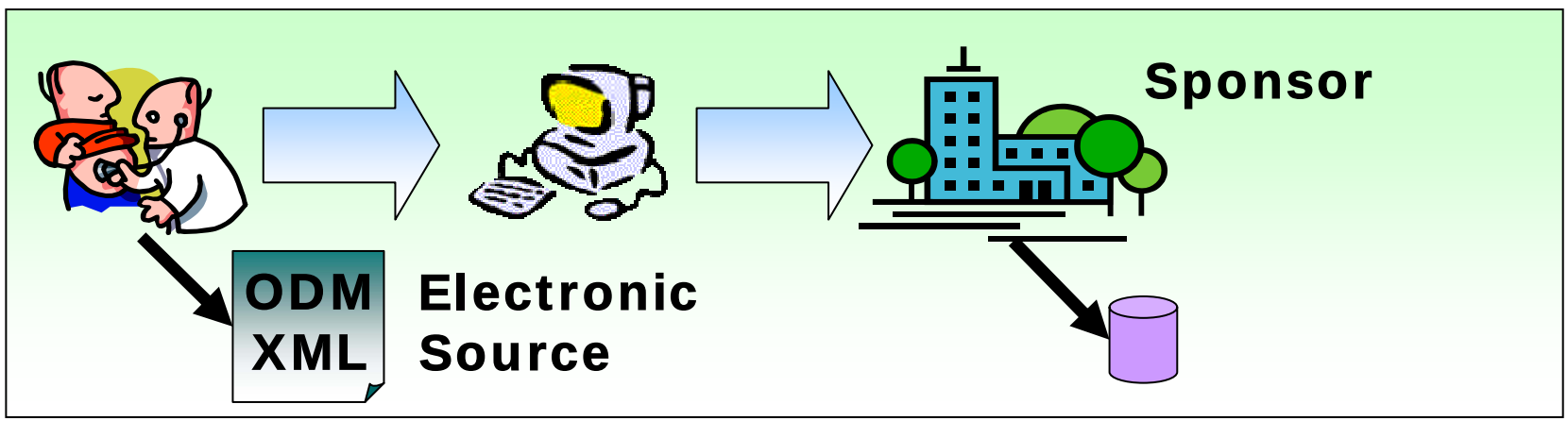
- ODM being leveraged to integrate an EHR with sponsor systems
- ODM being employed to help meet regulatory requirements



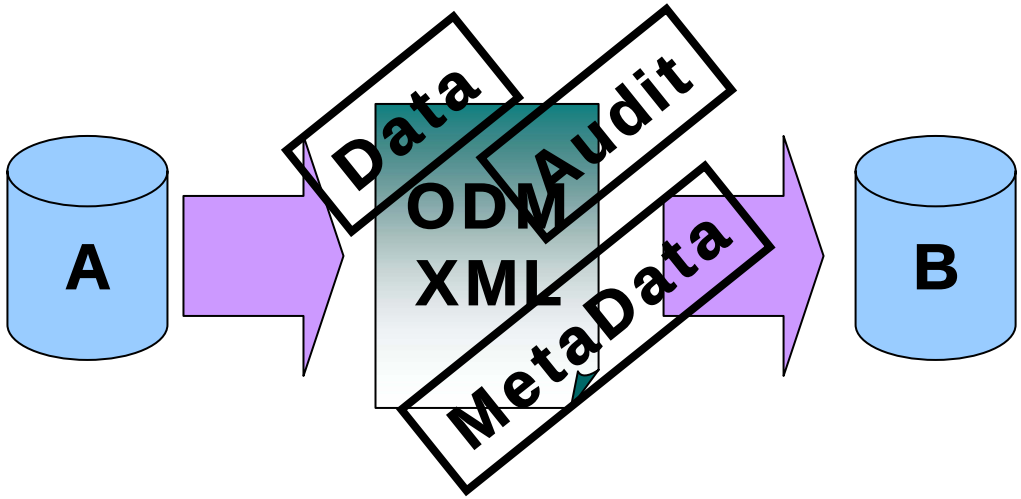
eSource

- Investigator is obliged to
  - Maintain source data (accurate)
  - Retain source data
  - Prevent its destruction
  - Allow access to inspectors



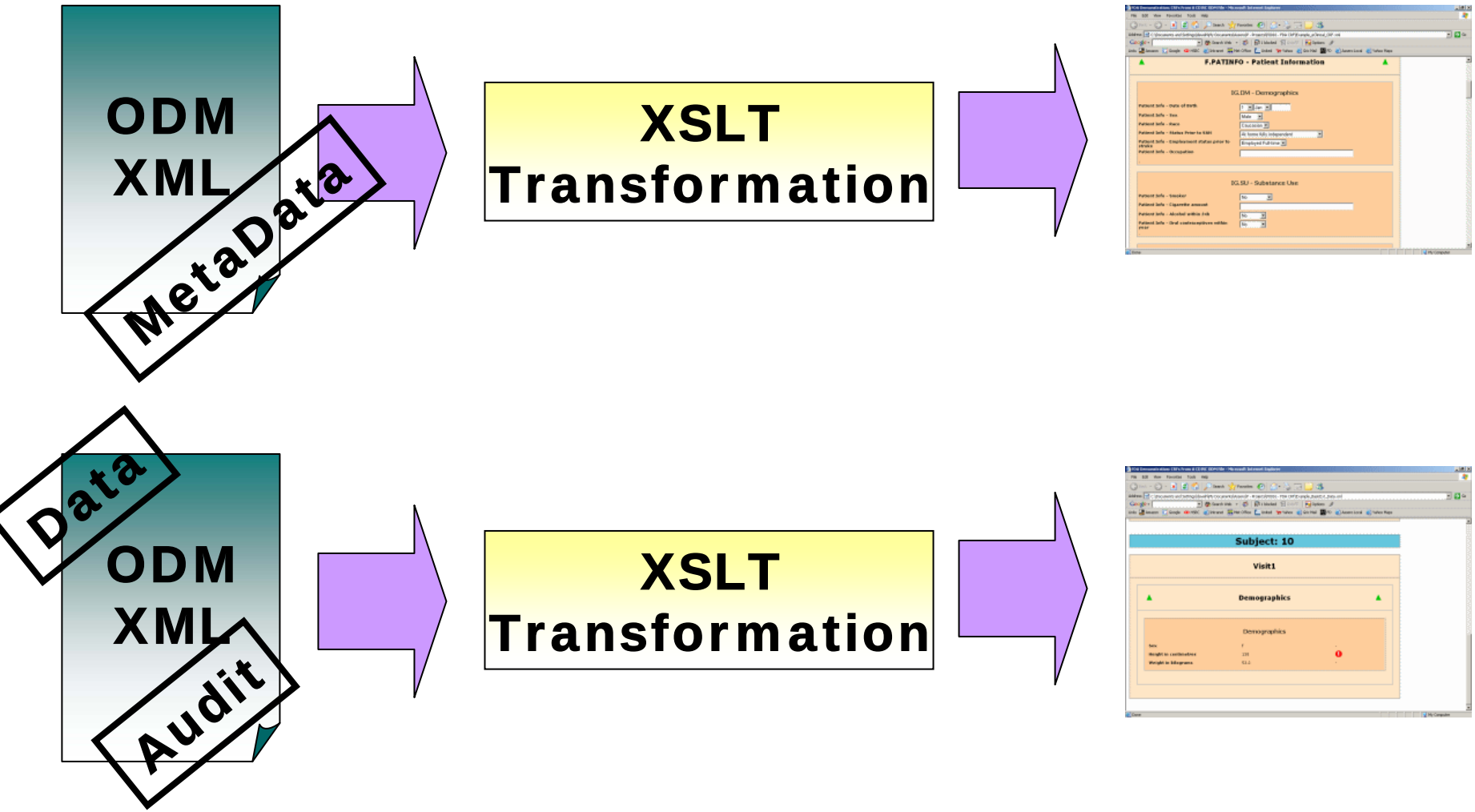


Interchange



- One of the original use cases for the model
- Ability to interchange Metadata and / or Clinical Data

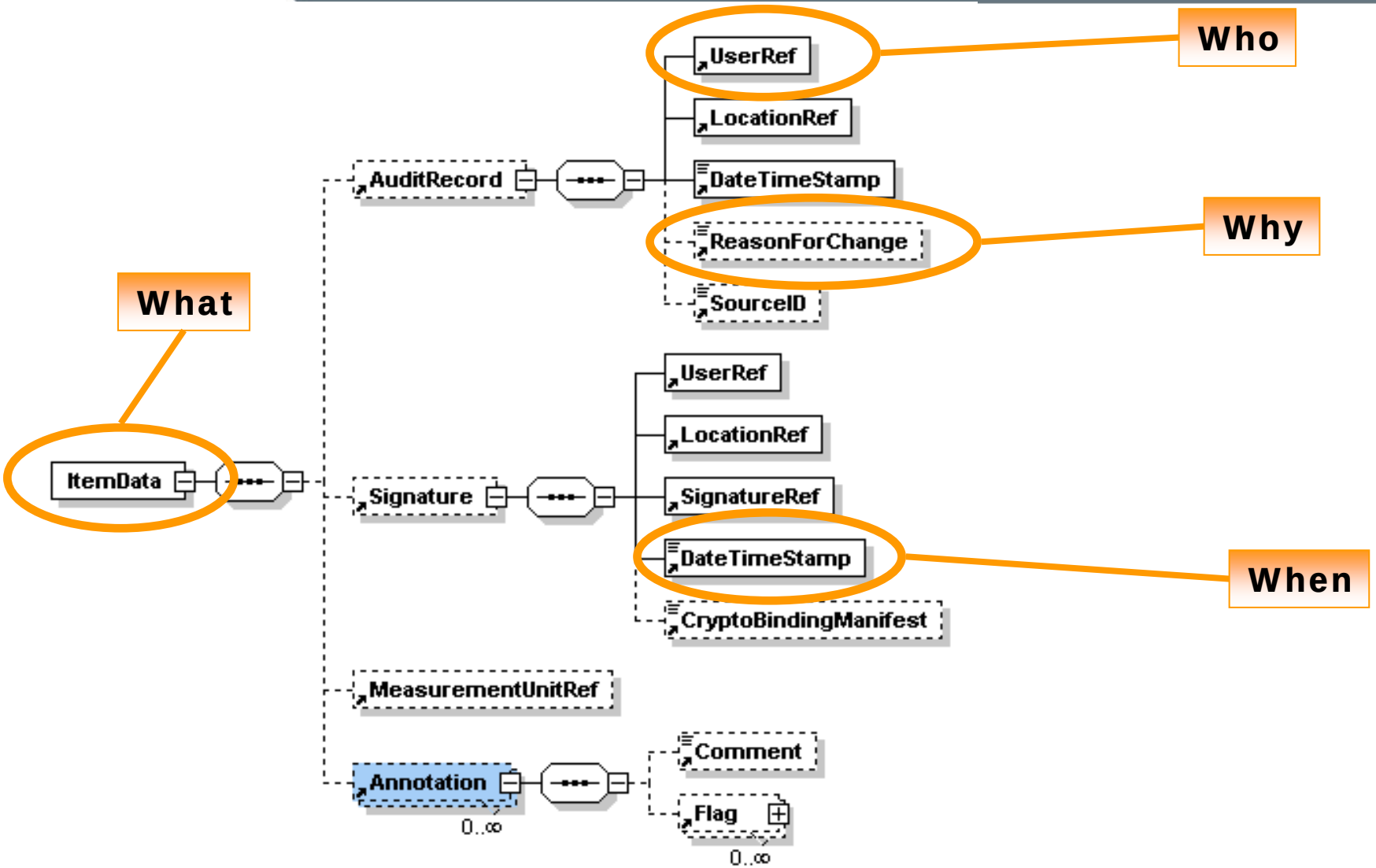
Submission


ODM
XML
MetaData
XSLT
Transformation
Data
ODM
XML
Audit
XSLT
Transformation
Subject: 10
Visit1
Demographics

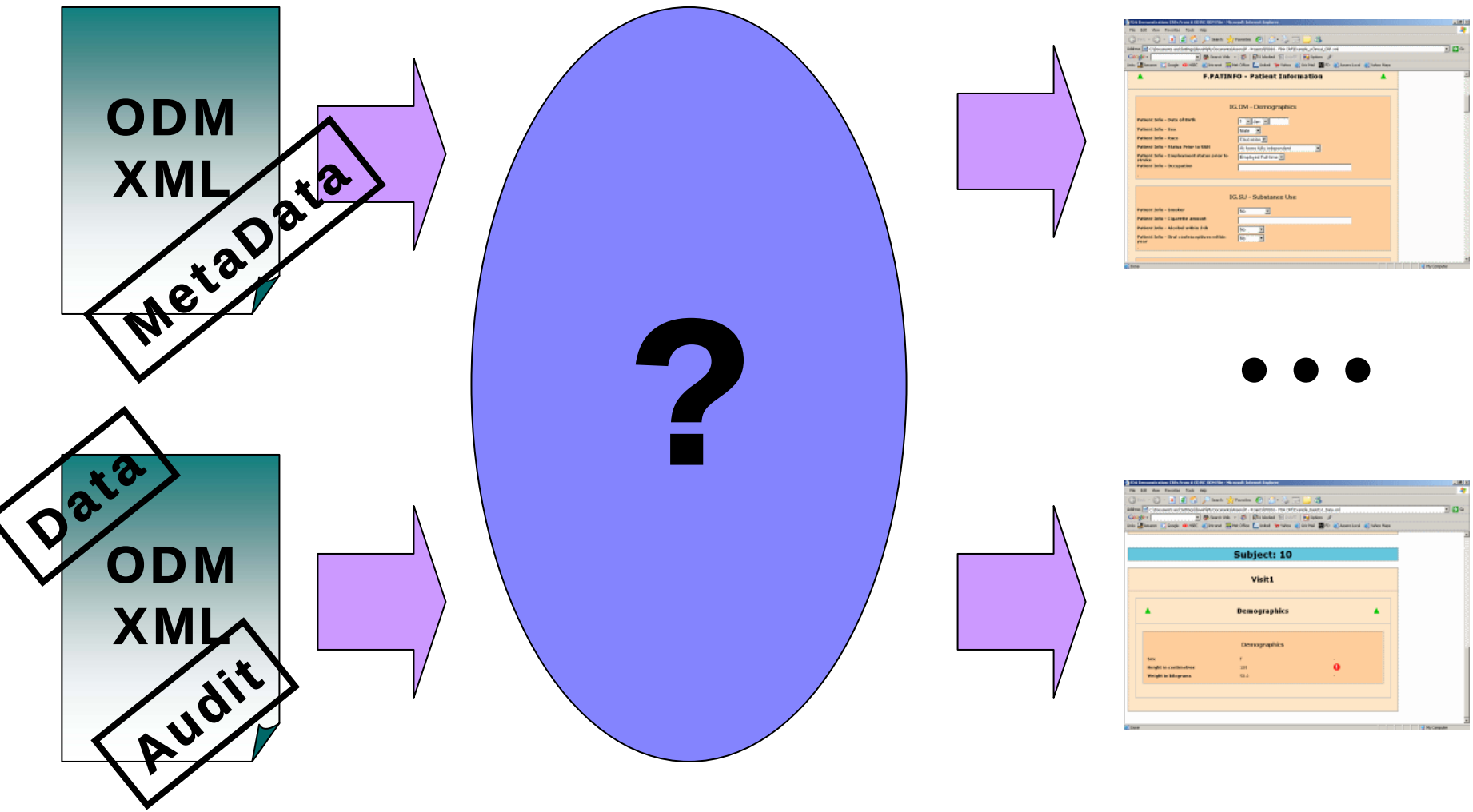
Submission

- Submission MetaData
  - Currently uses PDF mechanism – Define.PDF
  - ODM version – Define.XML
- Submission Datasets
  - Currently SAS XPORT Transport (XPT)
  - ODM support being developed
- CRF Data and Audit Trail
  - Currently paper or PDF
  - CDISC ODM?
- Annotated CRF
  - Currently PDF
  - CDISC ODM?

Archive


Who
What
Why
When
UserRef
LocationRef
AuditRecord
DateTimeStamp
ReasonForChange
SourceID
ItemData
UserRef
LocationRef
Signature
SignatureRef
DateTimeStamp
CryptoBindingManifest
MeasurementUnitRef
Comment
Annotation
Flag
0..∞
0..∞

Archive


ODM
XML
MetaData
Data
ODM
XML
Audit
?
F.PATINFO - Patient Information
IG.DM - Demographics
IG.SU - Substance Use
Subject: 10
Visit1
Demographics
Demographics

Archive Success Factors (1)

- Data should be archived in an electronic form
- The archive should contain the trial metadata
- The archive should permit the data to be used in trial reconstruction
- The archive mechanism should allow for both sponsor (full) and investigator (subset) archives
- The data archive should be supportable for periods of 20 years or more

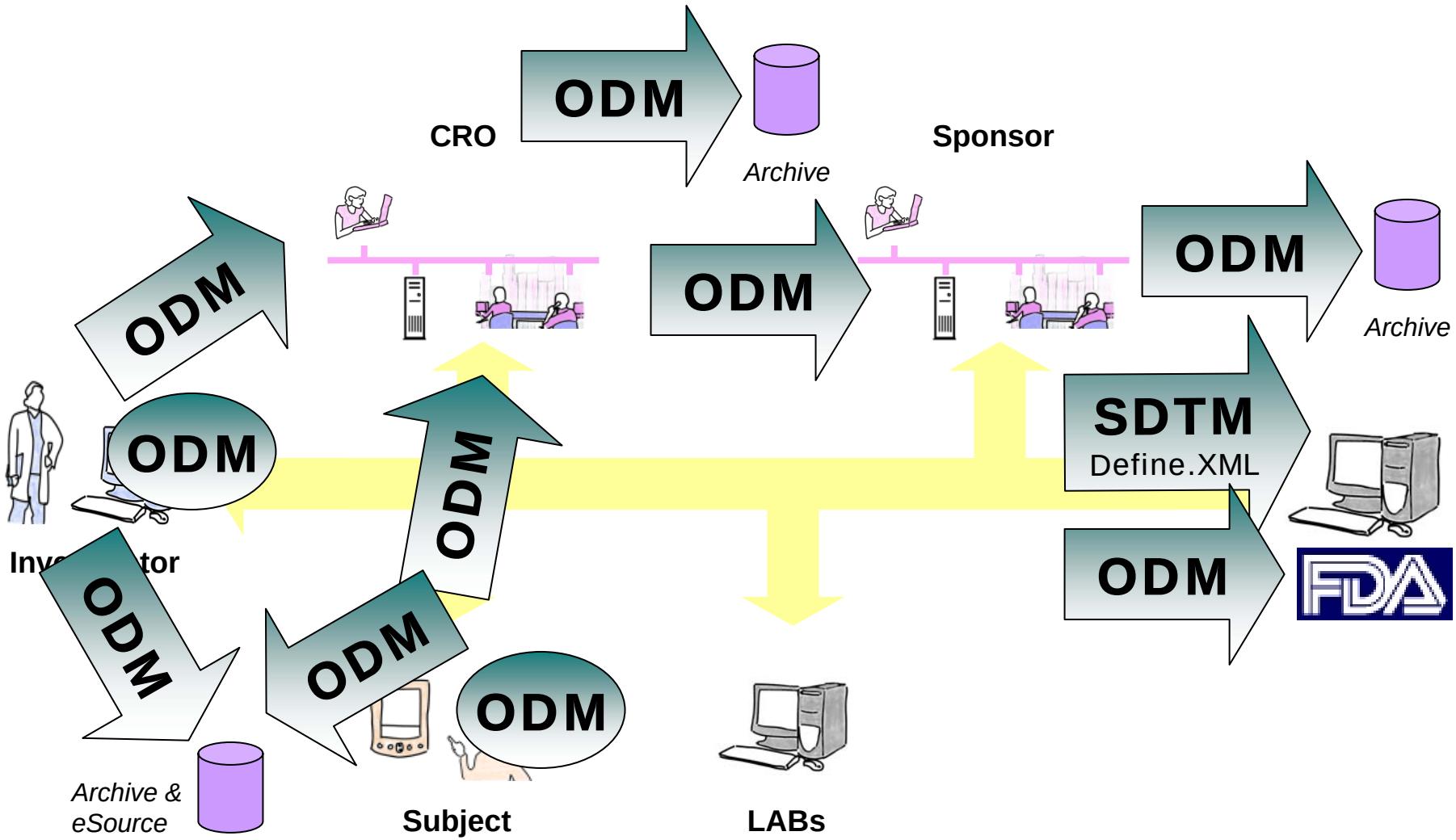
Archive Success Factors (2)

- The data archive should prevent unauthorised access
- The data archive should prevent changes being made to the data
- The data archive should contain the audit trail
- The data migration process should preserve the quality and integrity of the data
- The data archive should permit the regulatory authorities to inspect the data

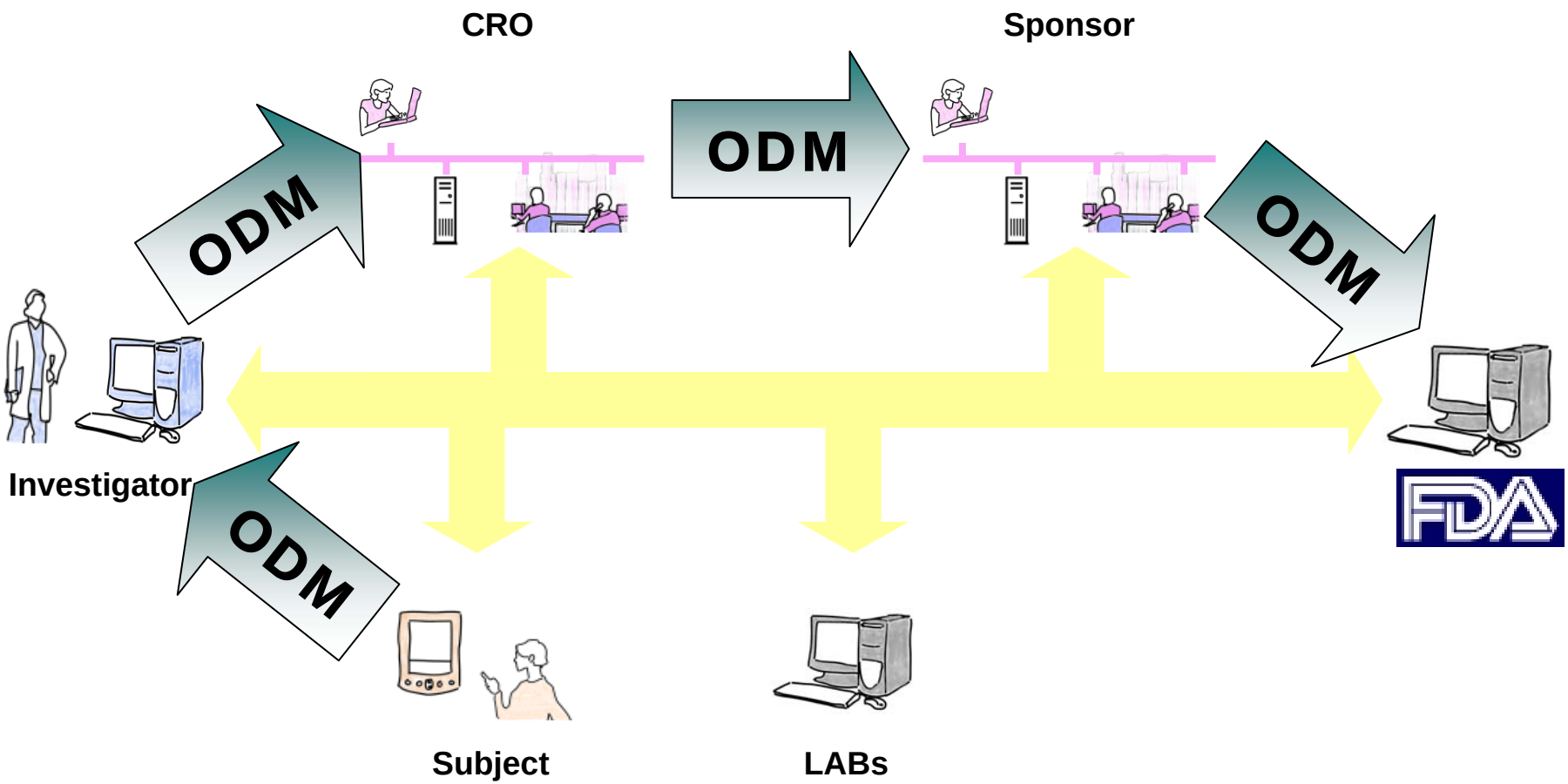
ODM & Archive

- ✓ Electronic
- ✓ MetaData
- ✓ Reconstruction
- ✓ Full and Partial Archives
- ✓ Long-term
- ✗ Unauthorised Access
- ✓ Changes
- ✓ Audit
- ✓ Quality & Integrity
- ✓ Inspection

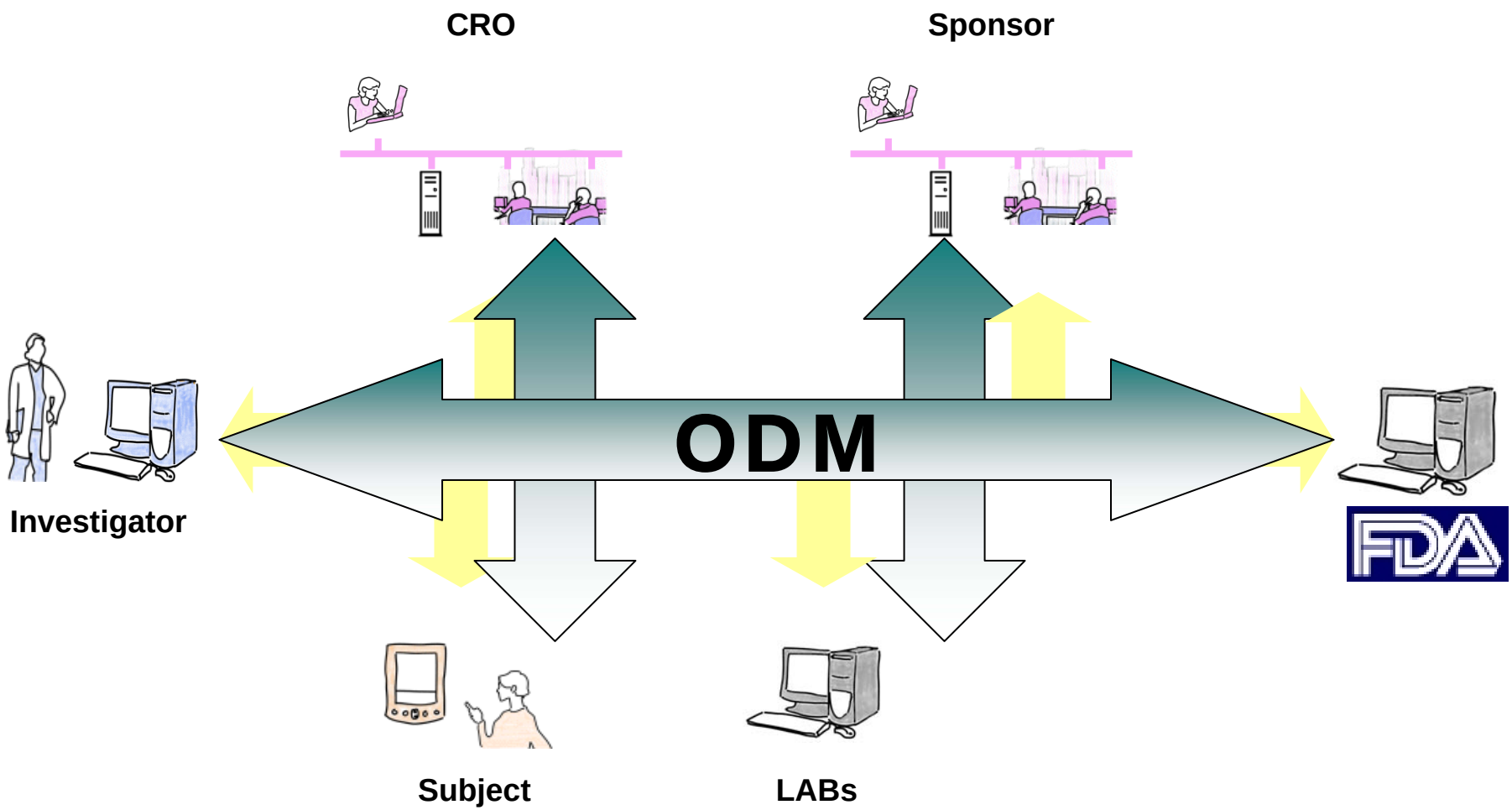
ODM Touch Points



ODM Flow



ODM as the Backbone



ODM and Define.xml

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Case Report Tabulation Data Definition Specification (define.xml)

This document specifies the standard for providing Case Report Tabulations Data Definitions in an XML format for submission to a regulatory authority such as the U.S. Food and Drug Administration (FDA).

Sponsor – Submission

- Sponsor needs to submit
  - Metadata
  - Data
  - FDA's Electronic Common Technical Document (eCTD)
- Metadata can employ
  - The Case Report Tabulation – Data Definition Specification (Define.XML), standard
  - The ODM as the transport mechanism
- Data will employ
  - The SDTM standard
  - Currently use SAS transport files as the transport mechanism

SDTM, ODM and Define.XML

- For the wine connoisseur, it is all about the wine.
- The bottle and the glass are means of transporting the wine from the vine yard to the table.
- The wine label provides important information about the wine, the contents of the bottle.

SDTM, ODM and Define.XML

- SDTM is our wine, the important content.

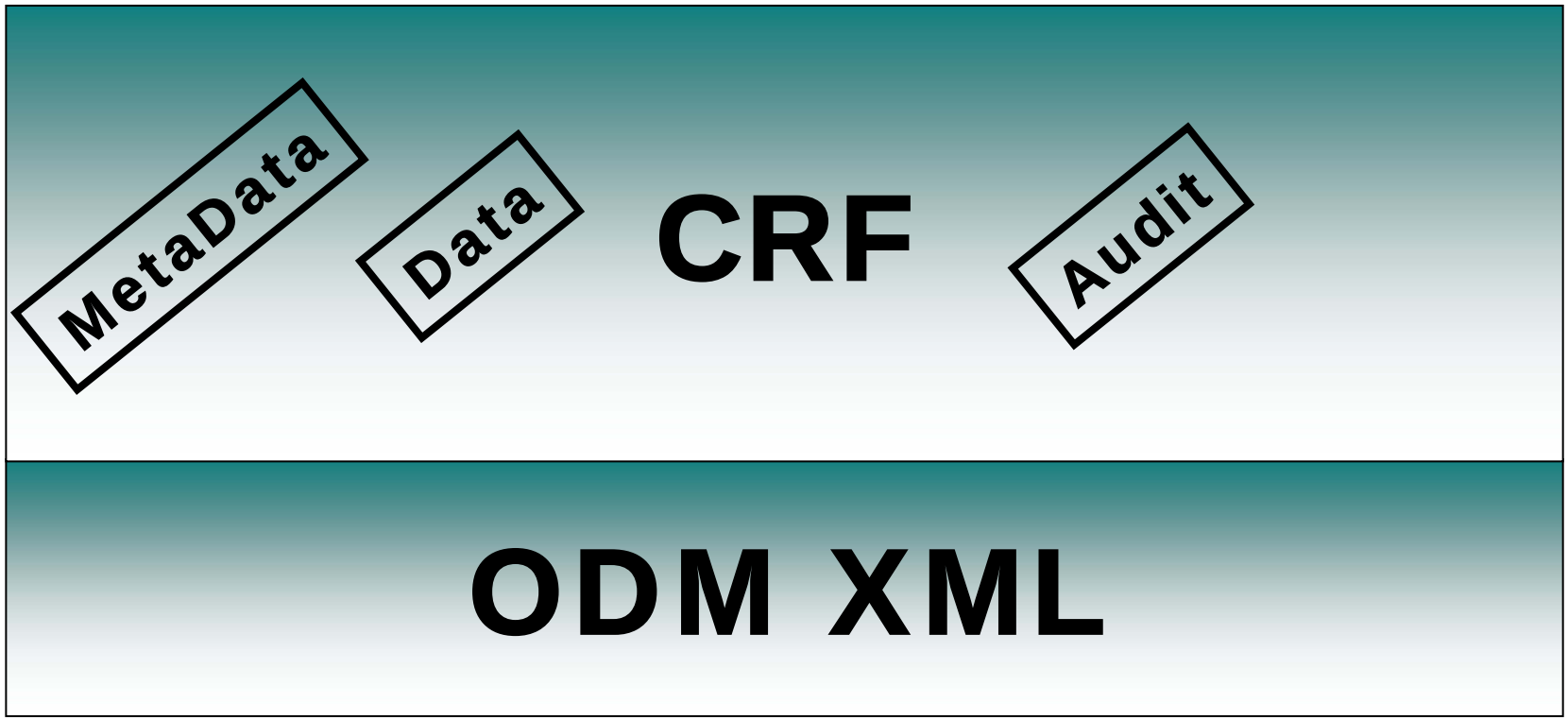
- ODM is the bottle, containing the SDTM data. Currently SAS transport files are used

- Define.XML is our label, telling us what SDTM we have. A machine-readable format that replaces Define.PDF for transmitting submission metadata.

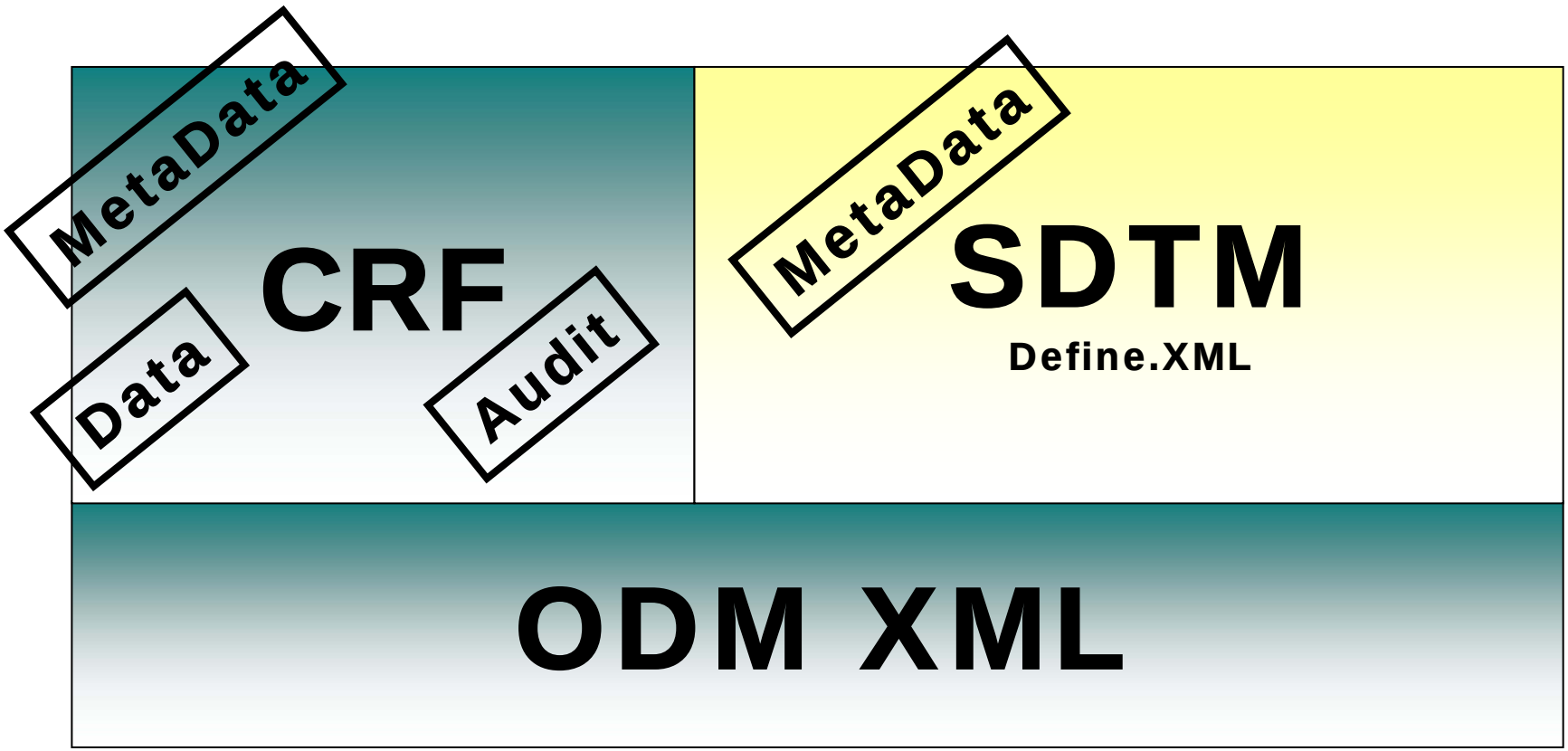
Submission

- Submissions Data Tabulation Model (SDTM)
  - Referenced in FDA Guidance as of 21 July 04
- Federal Register announcement
  - Department of Health and Human Services, Semiannual Regulatory Agenda (26818 Federal Register / Vol. 70, No. 93 / Monday, May 16, 2005 / Unified Agenda)
  - *"The proposal would revise our regulations to require that CSD [Clinical Study Data] submitted for NDAs, ANDAs, BLAs, and their supplements and amendments be provided in electronic format and require the use of standard data structure, terminology, and code sets."*
- Define.XML
  - Referenced in FDA Guidance as of 18 March 05

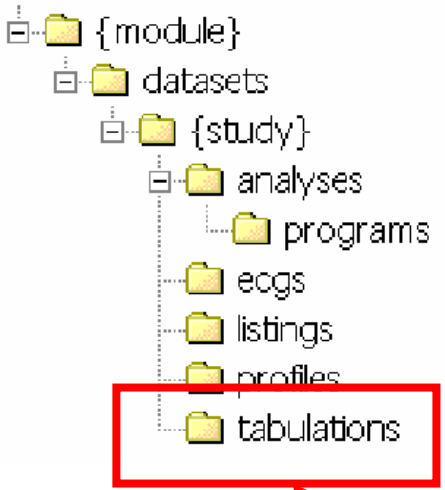
ODM Transport



Define.XML leveraged the ODM



Study Data Specifications



Replace with module name, e.g., m5

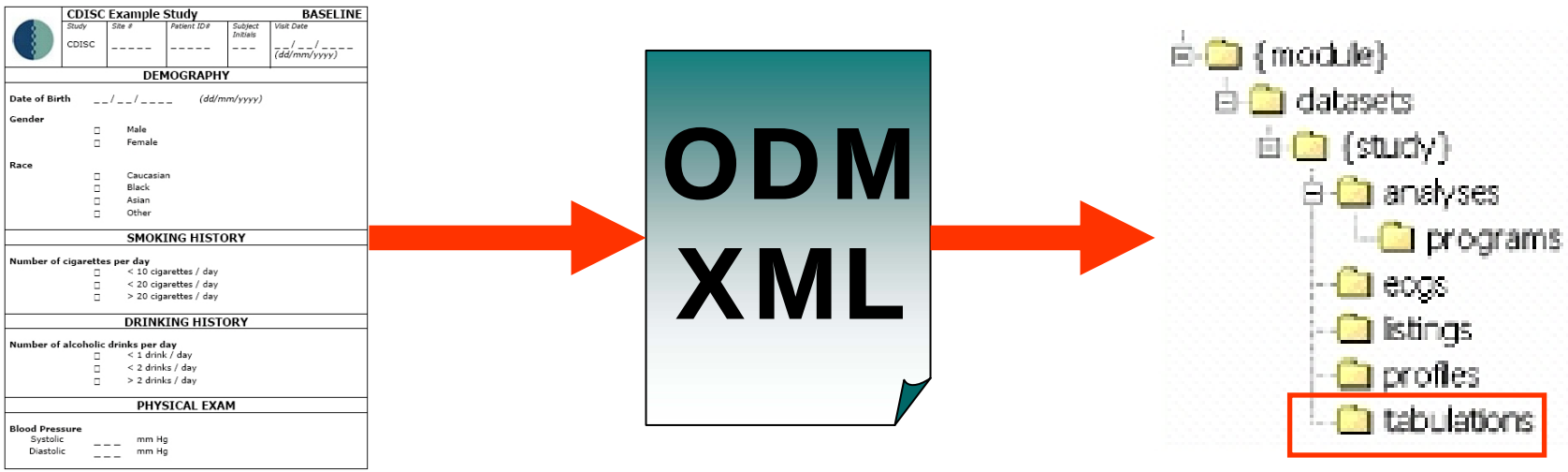
Replace with study identifier, e.g., 123-070
Contains analysis datasets, annotated CRF, data definition
Contains program files
Contains annotated ECG waveform datasets
Contains data listing datasets, annotated CRF, data definition
Contains subject profiles
Contains data tabulation datasets, annotated CRF, data definition

Define.xml would be supplied in support of the Data Tabulations

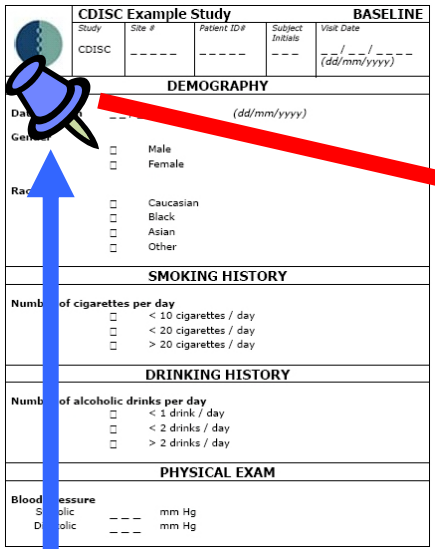
Slide taken from “ODM and Electronic Submissions”. William J. Qubeck, IV. Pfizer. DIA Annual Meeting 2005

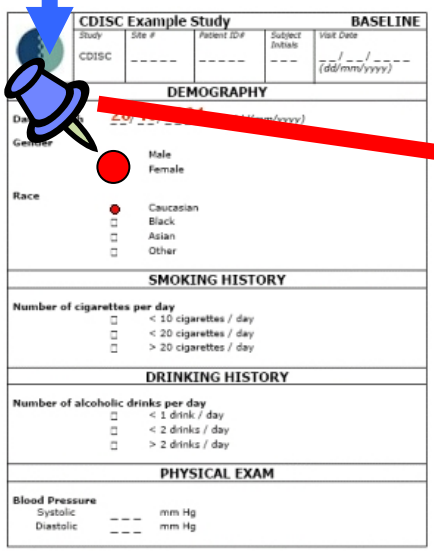
The Big Question

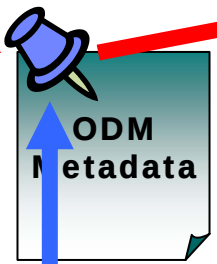
- How do we “link” the data from collection through to the submission by the sponsor?

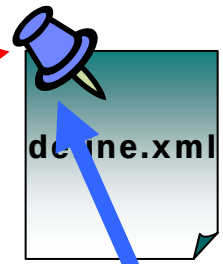


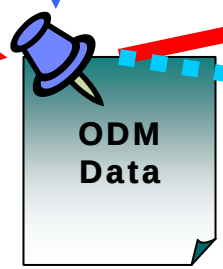
The Flow

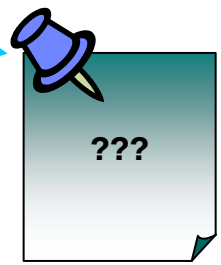






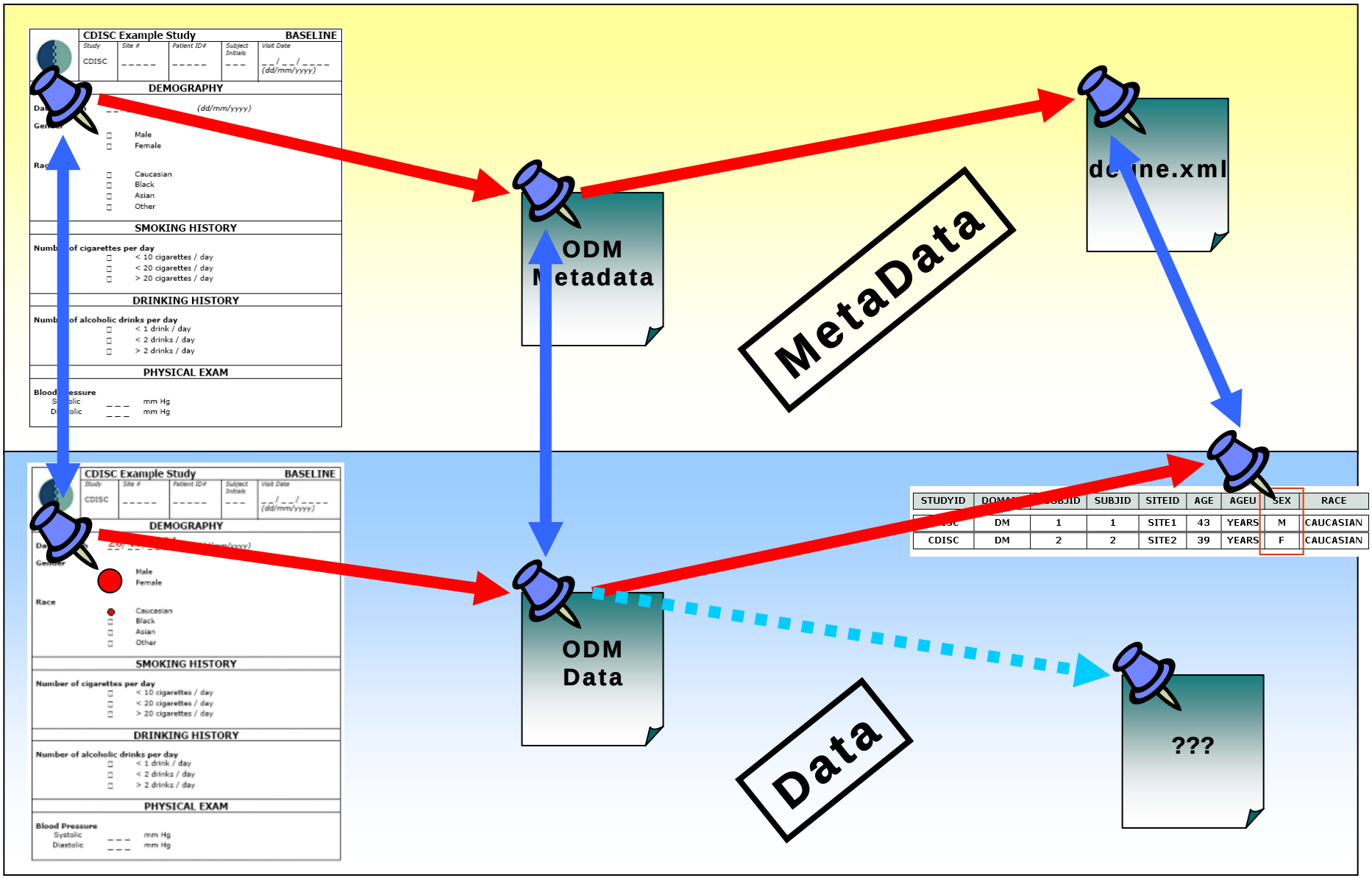






STUDYID	DOMAIN	USUBJID	SUBJID	SITEID	AGE	AGEU	SEX	RACE
CDISC	DM	1	1	SITE1	43	YEARS	M	CAUCASIAN
CDISC	DM	2	2	SITE2	39	YEARS	F	CAUCASIAN

The Flow


CDISC Example Study
BASELINE
DEMOGRAPHY
SMOKING HISTORY
DRINKING HISTORY
PHYSICAL EXAM
ODM Metadata
MetaData
define.xml
ODM Data
Data
???
STUDYID | DOMAIN | USUBJID | SUBJID | SITEID | AGE | AGEU | SEX | RACE
CDISC | DM | 1 | 1 | SITE1 | 43 | YEARS | M | CAUCASIAN
CDISC | DM | 2 | 2 | SITE2 | 39 | YEARS | F | CAUCASIAN

Outline

ODM and Define.xml

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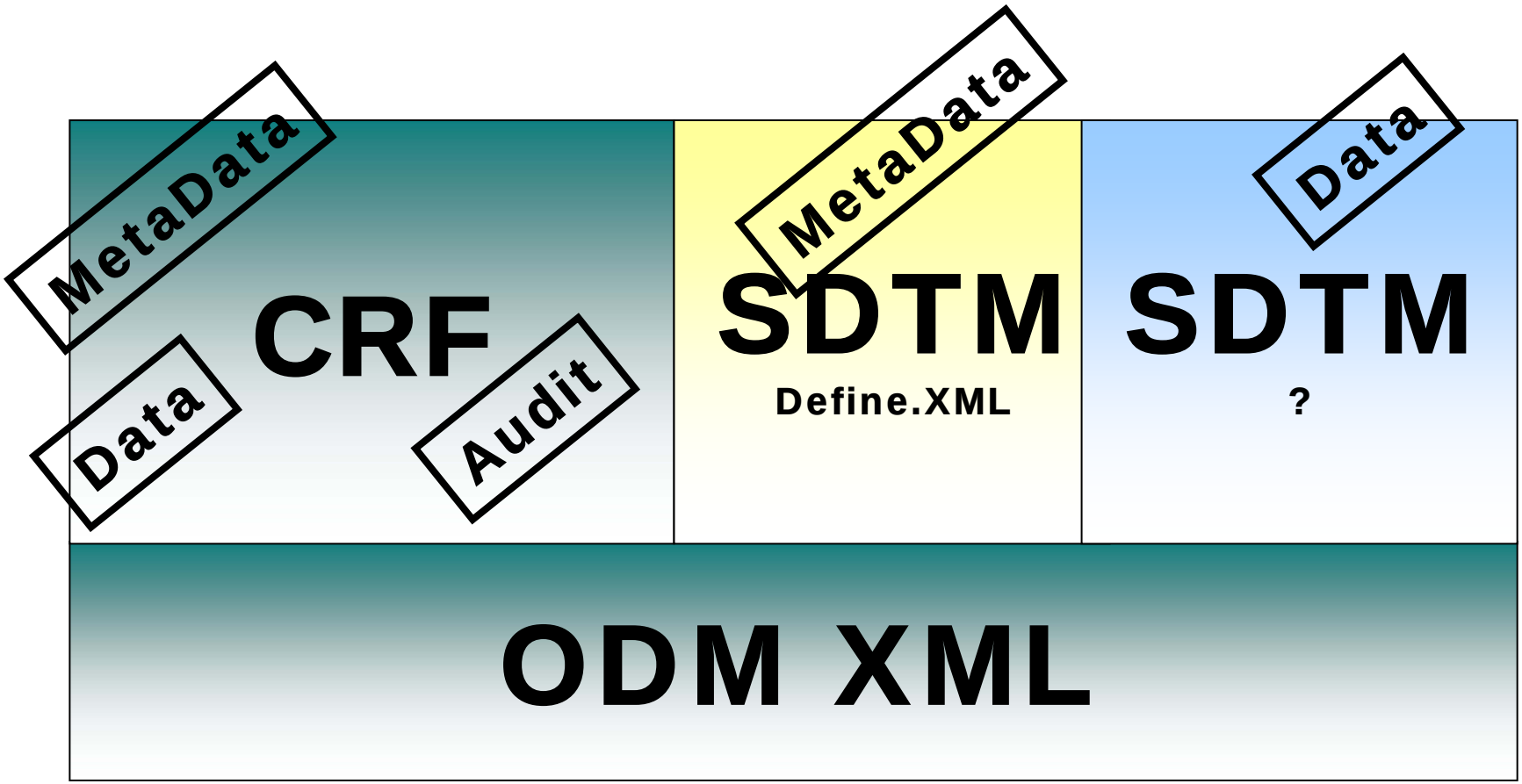
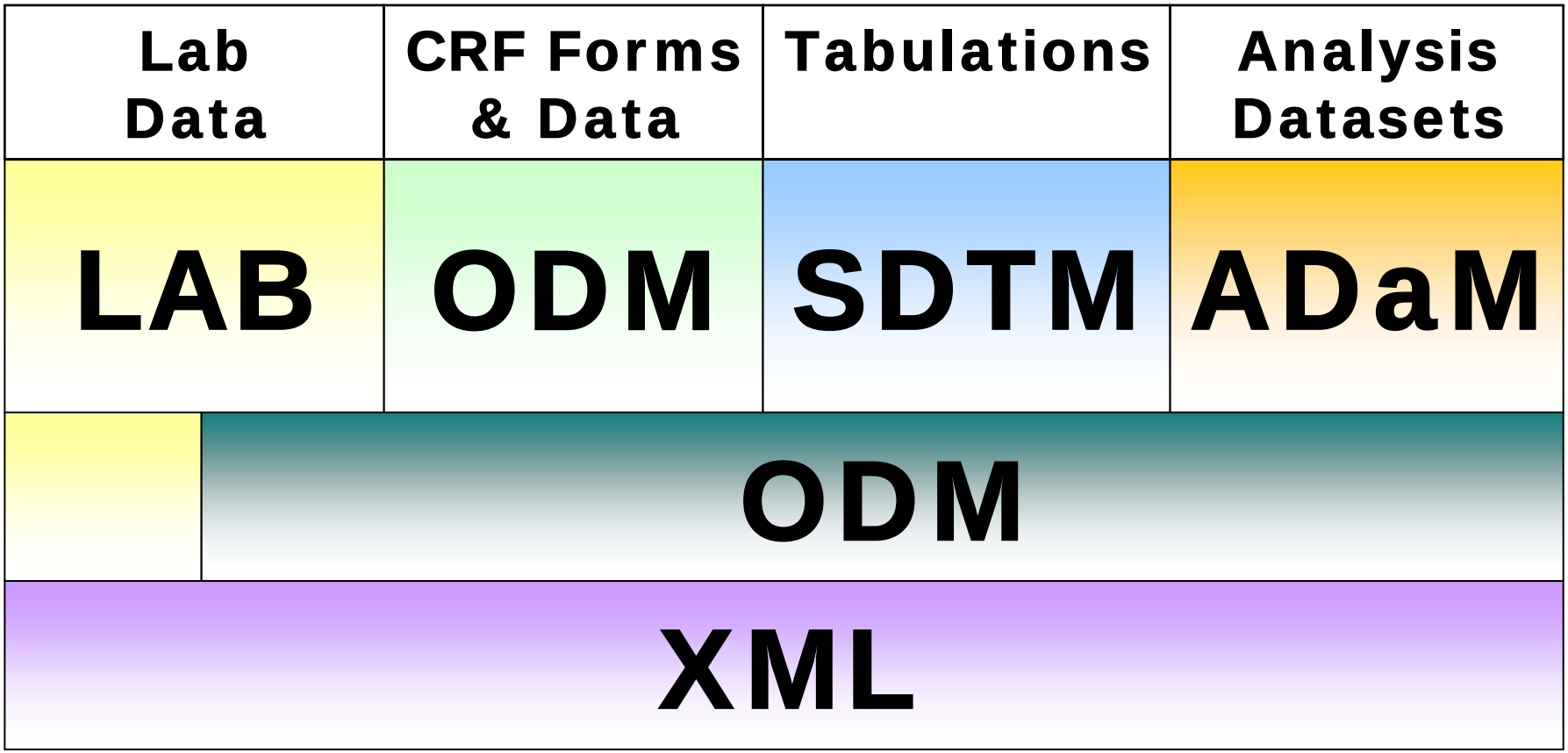
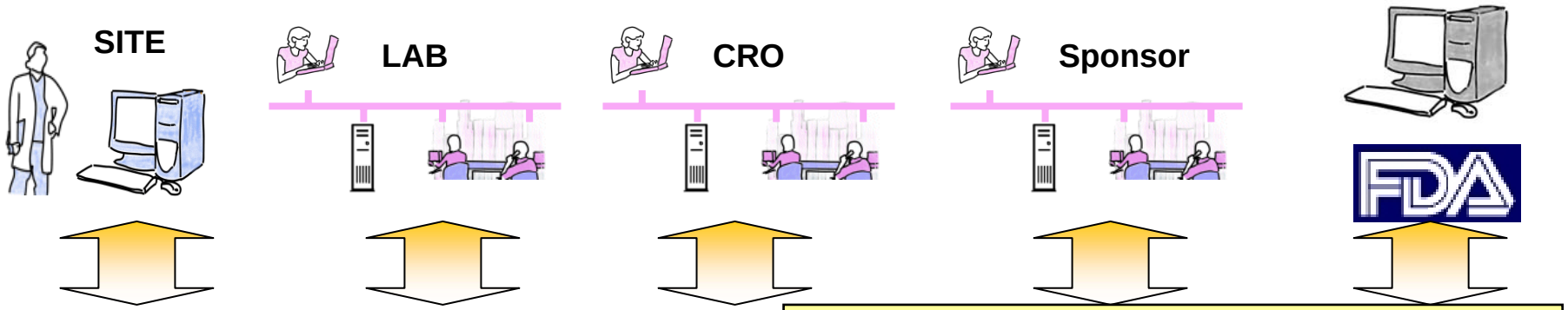
The Next Step



CDISC Models In Unison



CDISC Models In Unison



CRF & LAB

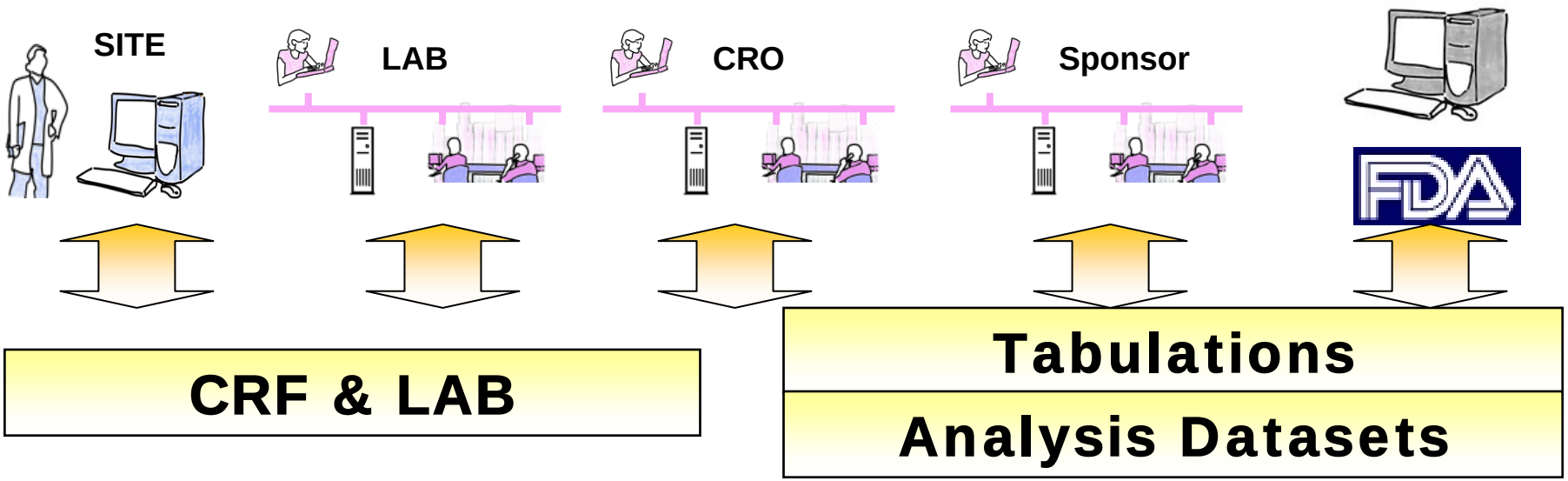
Tabulations

Analysis Datasets

ODM

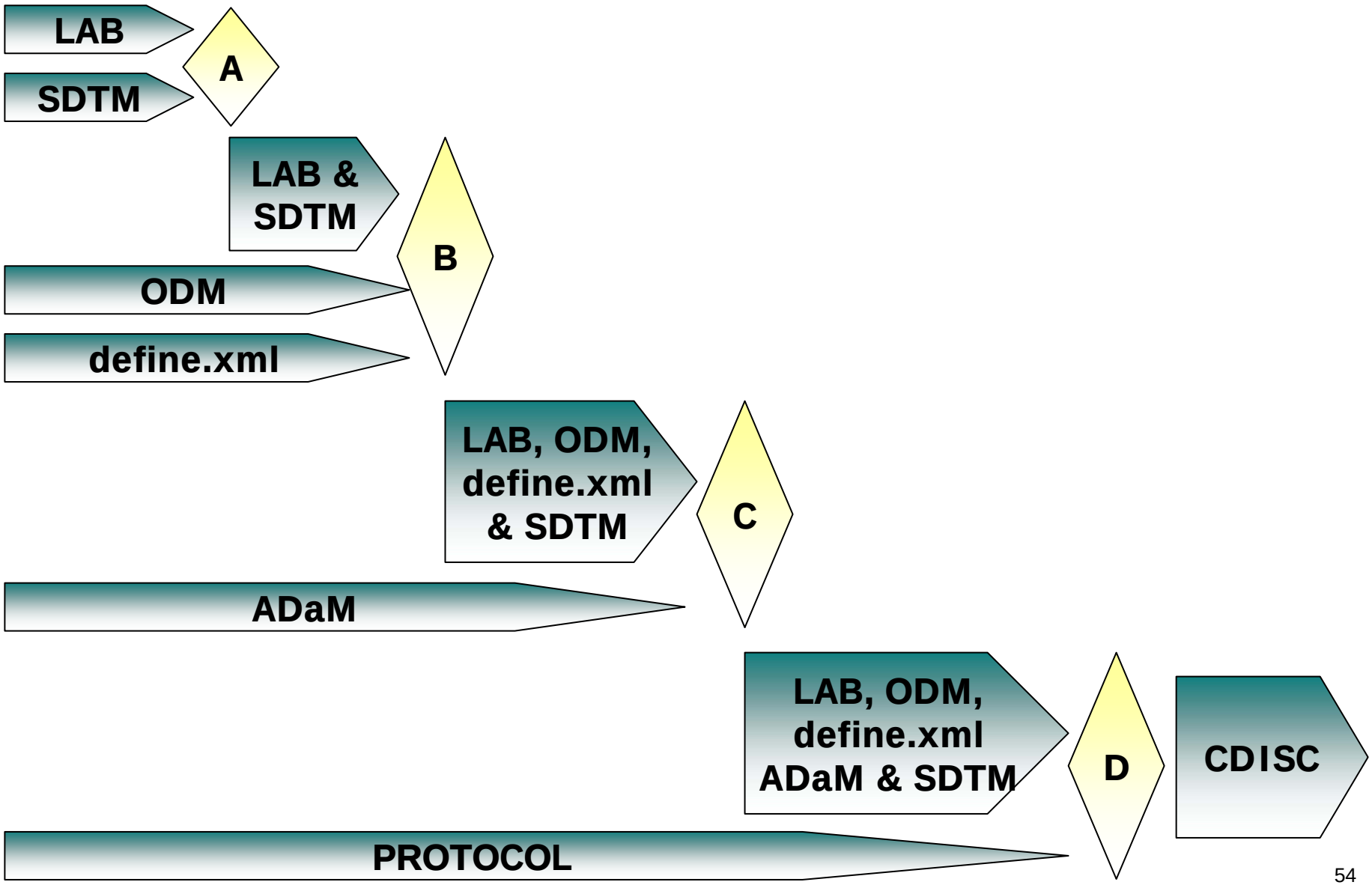
XML

CDISC Models In Unison

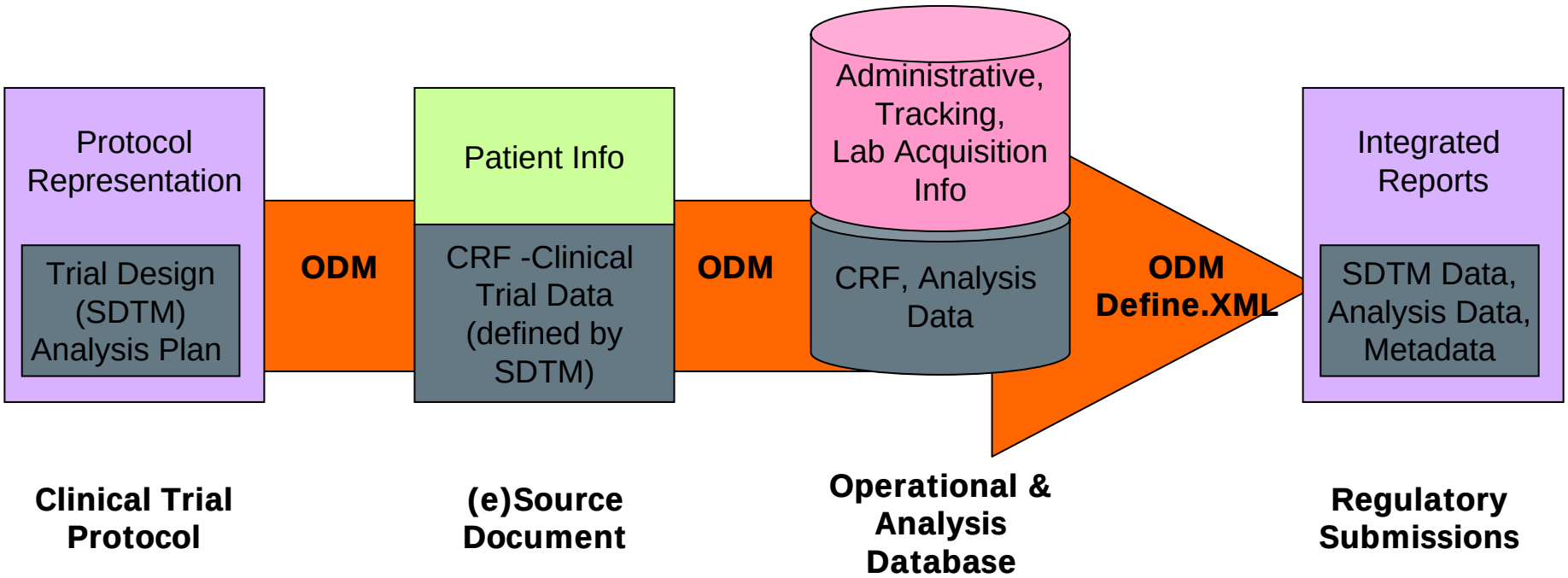


- Content
  - CRF & LAB Data
  - Tabulations & Analysis Datasets
- Standards
  - SDTM, ADaM, ODM, LAB

Road Map


LAB
SDTM
A
LAB & SDTM
ODM
define.xml
B
LAB, ODM, define.xml & SDTM
ADaM
C
LAB, ODM, define.xml ADaM & SDTM
PROTOCOL
D
CDISC

Data Flow using the CDISC Std



- ODM Transport
- SDTM & Analysis Data (content)
- Protocol Information (content)
- Source Data (other than SDTM/CRF data)

NEW

Outline

ODM and Define.xml

- History
- The ODM
- ODM Touch Points
- Define.xml
- The Future
- **Summary**

Summary

- ODM and define.xml are important components in the FDA's move to an XML world
- The ODM is the transport backbone for the CDISC standard

Questions