

# The ODM and Define.xml

## PhUSE

11<sup>th</sup> October 2005. Heidelberg, Germany.

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Setting the  
Global Standard  
for Clinical Data



## **ODM and Define.xml**

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

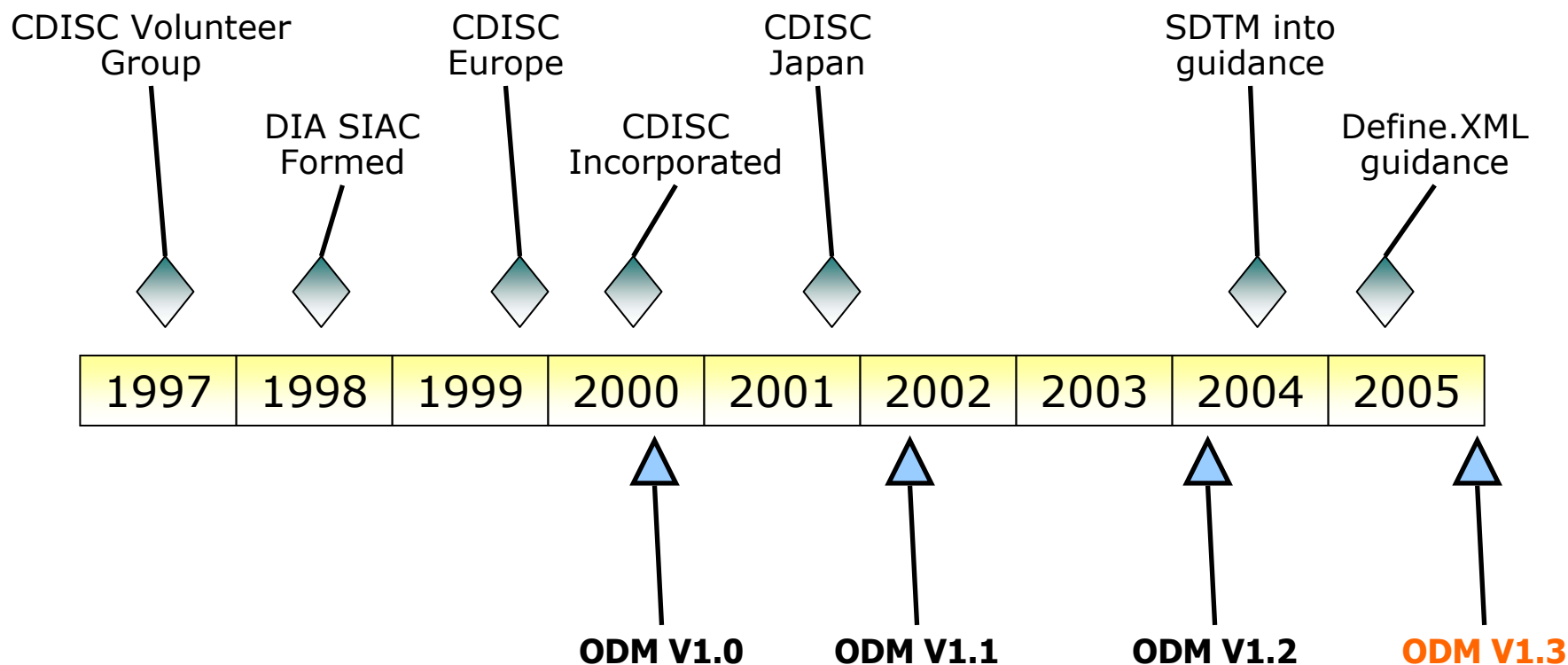


## ODM and Define.xml

- **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





## ODM and Define.xml

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

**Site Details**

Site No.: \_\_\_\_\_

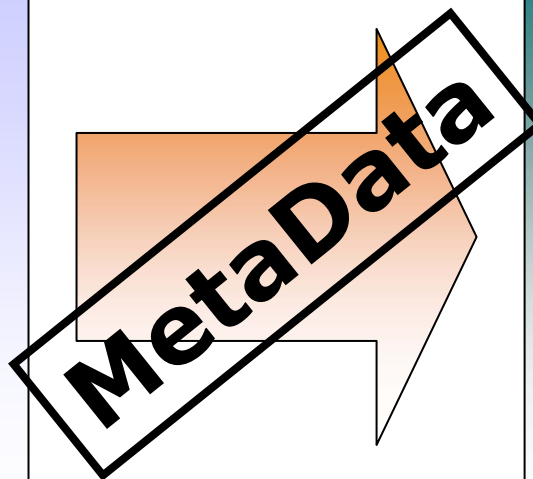
**Subject's Characteristics**

Number: \_\_\_\_\_

Sex:     M [ ]     F [ ]

Height: \_\_\_\_\_ cm

Weight: \_\_\_\_\_ kg

**MetaData****ODM  
XML**

**Site Details**

Site No.: \_\_\_\_5\_\_\_\_

**Subject's Characteristics**

Number: \_\_\_\_12\_\_\_\_

Sex:     M [Y]     F [ ]

Height:   \_\_\_\_1560\_\_\_\_ cm

Weight:   \_\_\_\_87.2\_\_\_\_ kg

**ODM  
XML**

## 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**



**Site Yellow**



**Doctor Green**

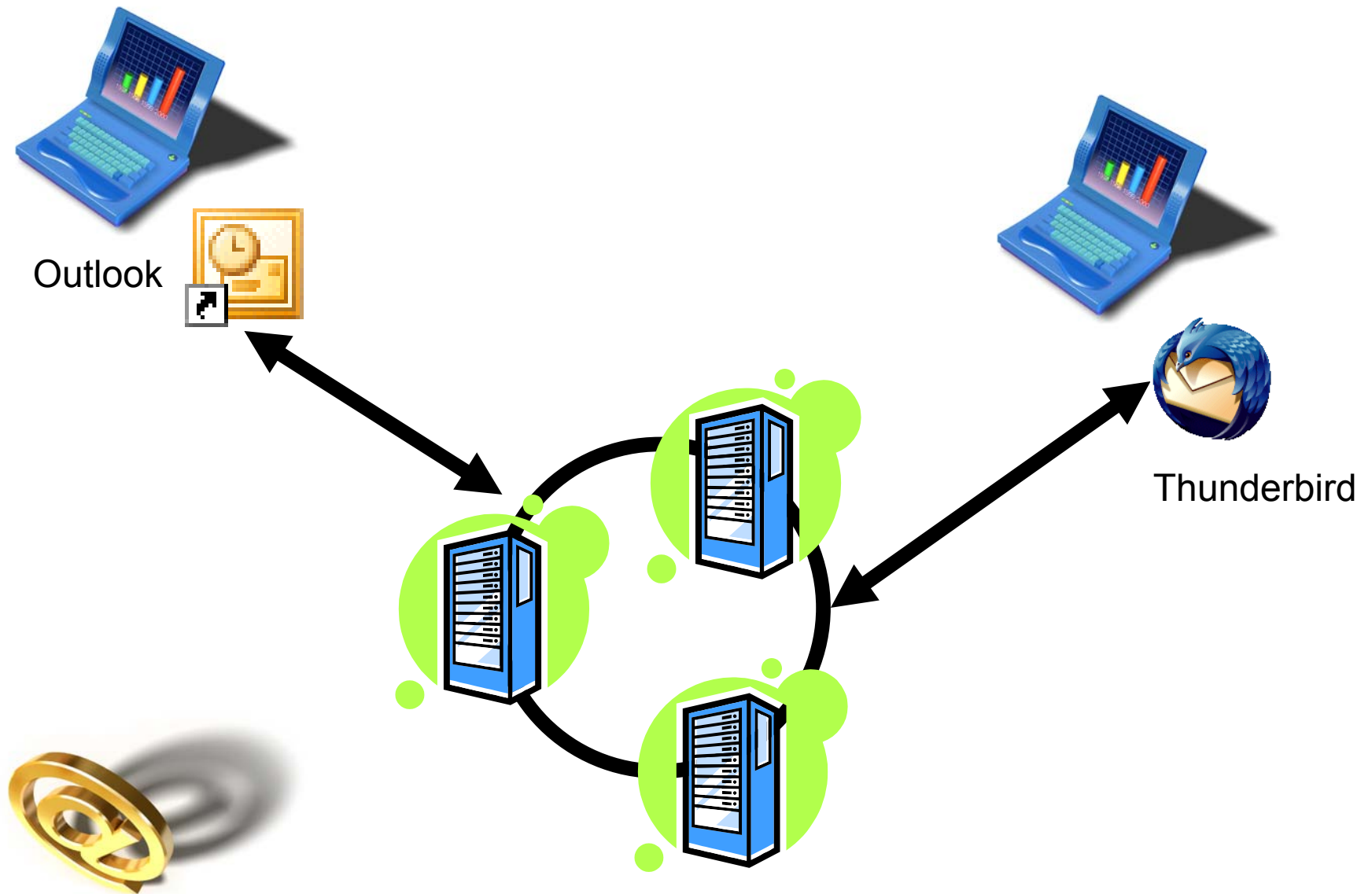


**ODM  
XML**



## ODM and Define.xml

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



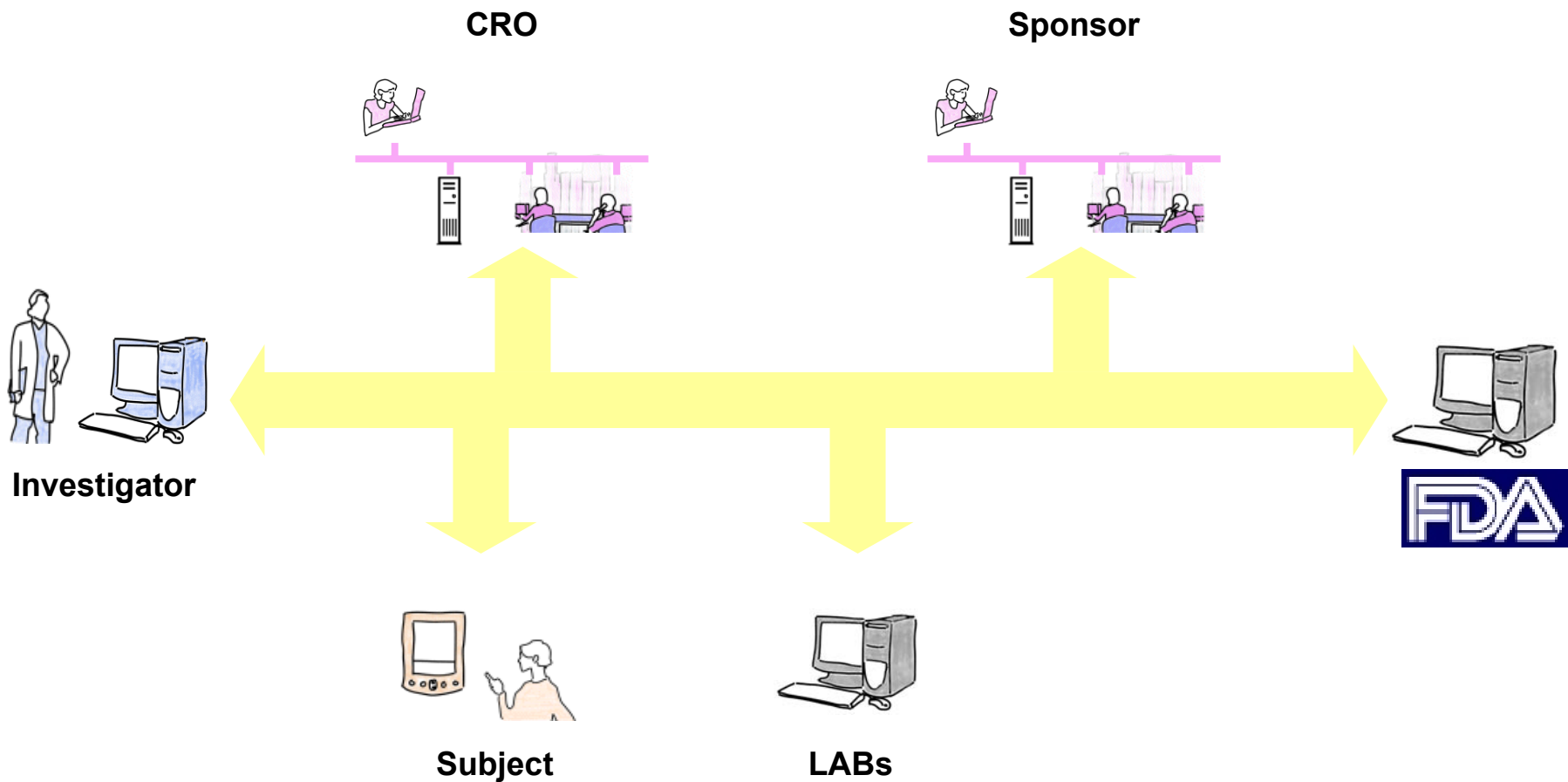


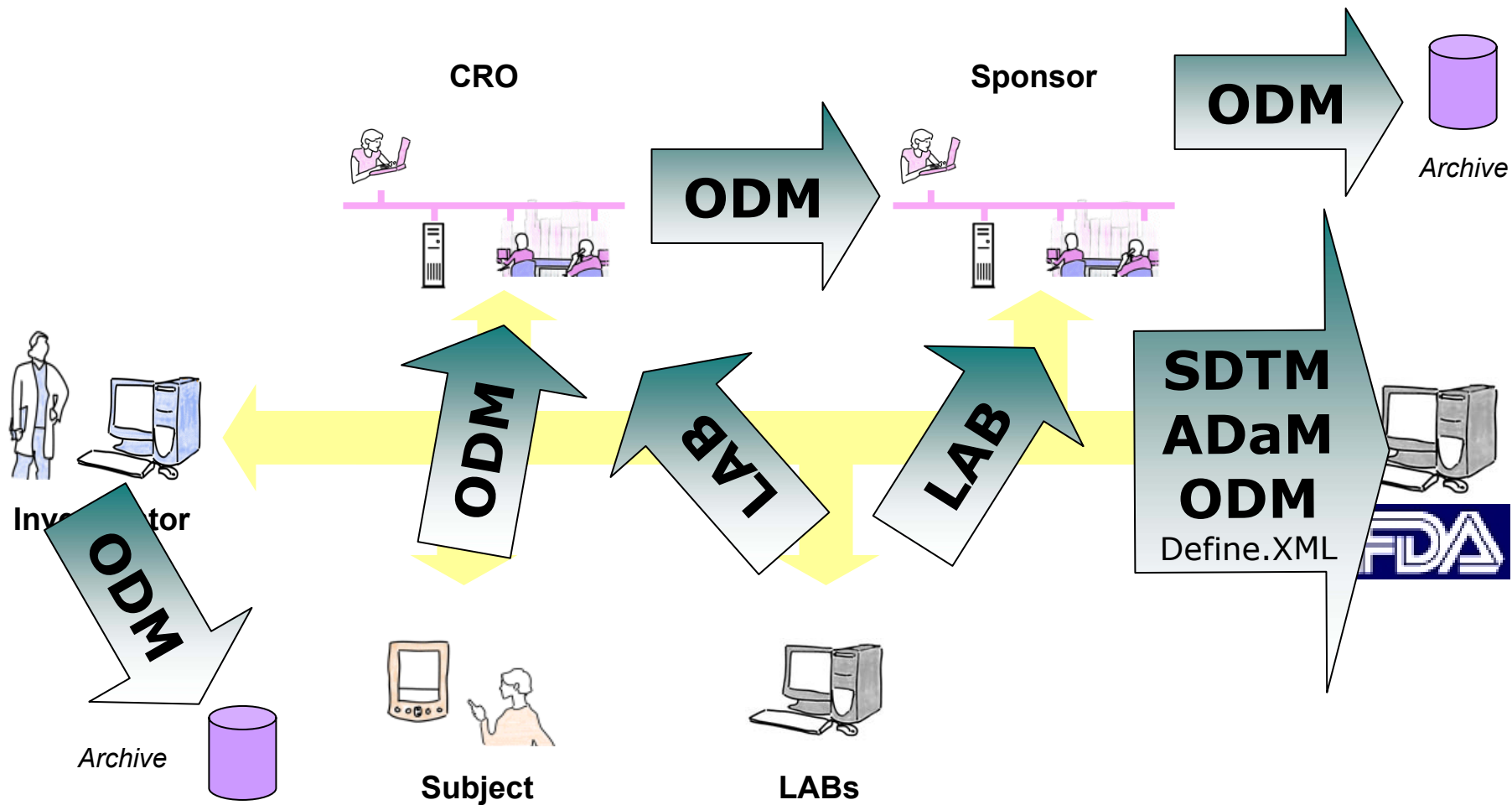
- Email Content
  - From
  - To
  - Subject
  - Body
- Standards
  - SMTP & POP3

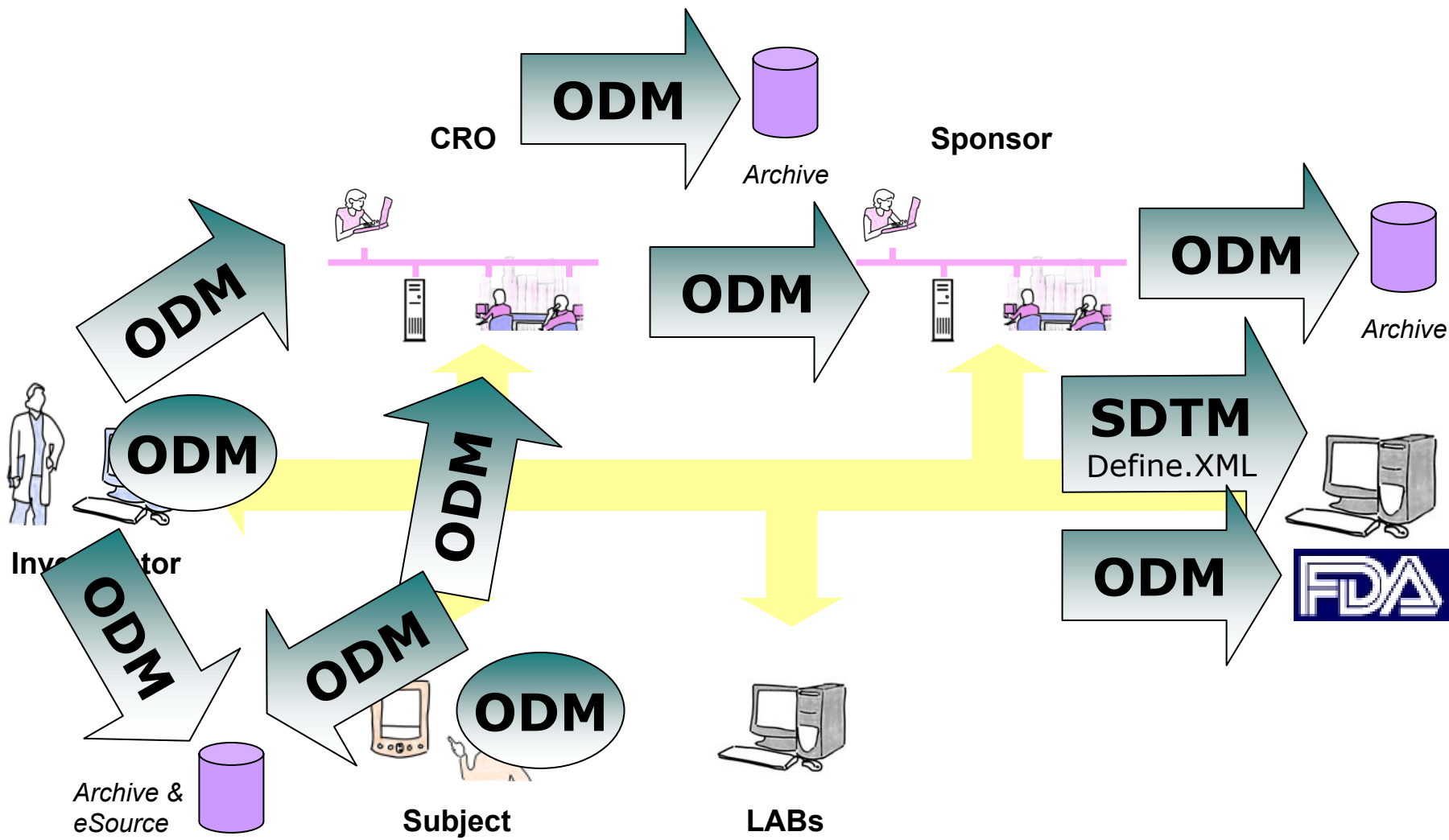


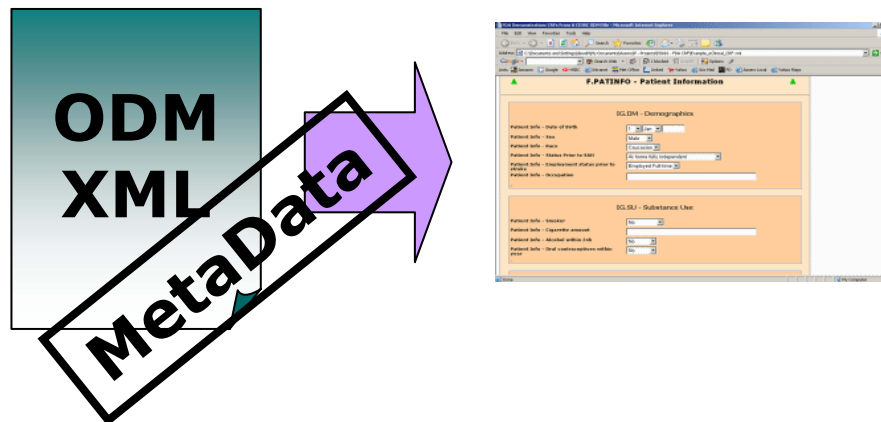
- Standards exist at varying levels within a hierarchy
- We do not necessarily need to understand the inner workings to benefit from them
- The CDISC Models sits at different levels
  - SDTM & ADaM are about “content”, ways of organising
  - LAB and ODM have a physical form, they are based on XML

| CRF Forms<br>& Data | Lab<br>Data | Tabulations | Analysis<br>Datasets |
|---------------------|-------------|-------------|----------------------|
| <b>ODM</b>          | <b>LAB</b>  | <b>SDTM</b> | <b>ADaM</b>          |
| <b>XML</b>          |             |             |                      |









- 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

## SPONSOR NAME

|              |                                                                |                                                                |                                                                |
|--------------|----------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------|
| Protocol No. | Investigator No.                                               | Subject No.                                                    | Subject Initials                                               |
| ABC123       | <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> |

### ADVERSE EVENTS

Has the subject experienced any adverse events?

1 ☐ Yes 0 ☐ No

If Yes, describe below.

| Event No. | Adverse Event                    | Start Date<br>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) | <div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> </div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> | <div> <div>Mark only 1 response</div> <div>0 - No</div> <div>1 - Yes</div> </div> | <div> <div>Mark only 1 response</div> <div>1 - Mild</div> <div>2 - Moderate</div> <div>3 - Severe</div> </div>                                                       | <div> <div>Mark only 1 response</div> <div>0 - No</div> <div>1 - Yes</div> </div>         | <div> <div>Mark only 1 response</div> <div>0 - None</div> <div>1 - Study drug regimen changed</div> <div>2 - Temporarily stopped study drug</div> <div>3 - Study drug discontinued</div> </div> | <div> <div>Mark only 1 response</div> <div>0 - Subject remains in study</div> <div>1 - Withdrawn from study</div> <div>2 - Lost to follow-up</div> <div>3 - Death</div> </div> |
|           |                                  | <div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> </div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> | <div> <div>1 <input type="checkbox"/></div> </div>                                | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div> | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> </div>  | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div>                            | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div>           |
|           |                                  | <div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> </div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> | <div> <div>1 <input type="checkbox"/></div> </div>                                | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div> | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> </div>  | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div>                            | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div>           |
|           |                                  | <div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> </div> <div> <div><input type="text"/></div> <div><input type="text"/></div> <div><input type="text"/></div> </div> <div> <div>day</div> <div>month</div> <div>year</div> </div> | <div> <div>1 <input type="checkbox"/></div> </div>                                | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div> | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> </div>  | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div>                            | <div> <div>0 <input type="checkbox"/></div> <div>1 <input type="checkbox"/></div> <div>2 <input type="checkbox"/></div> <div>3 <input type="checkbox"/></div> </div>           |

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

## Adverse Event Form (ACRO)

Visit: Adverse Event

Subject ID: 00011:SAW



### Common

Site #  Subject ID #  Visit Date  11

### Adverse Events Occurred

Has the subject experienced any adverse events ☐ No ☐ Yes

### Adverse Event

Event No.

Adverse event

Start Date  11

Stop Date  11

Mark if event is still continuing ☐ No ☐ Yes

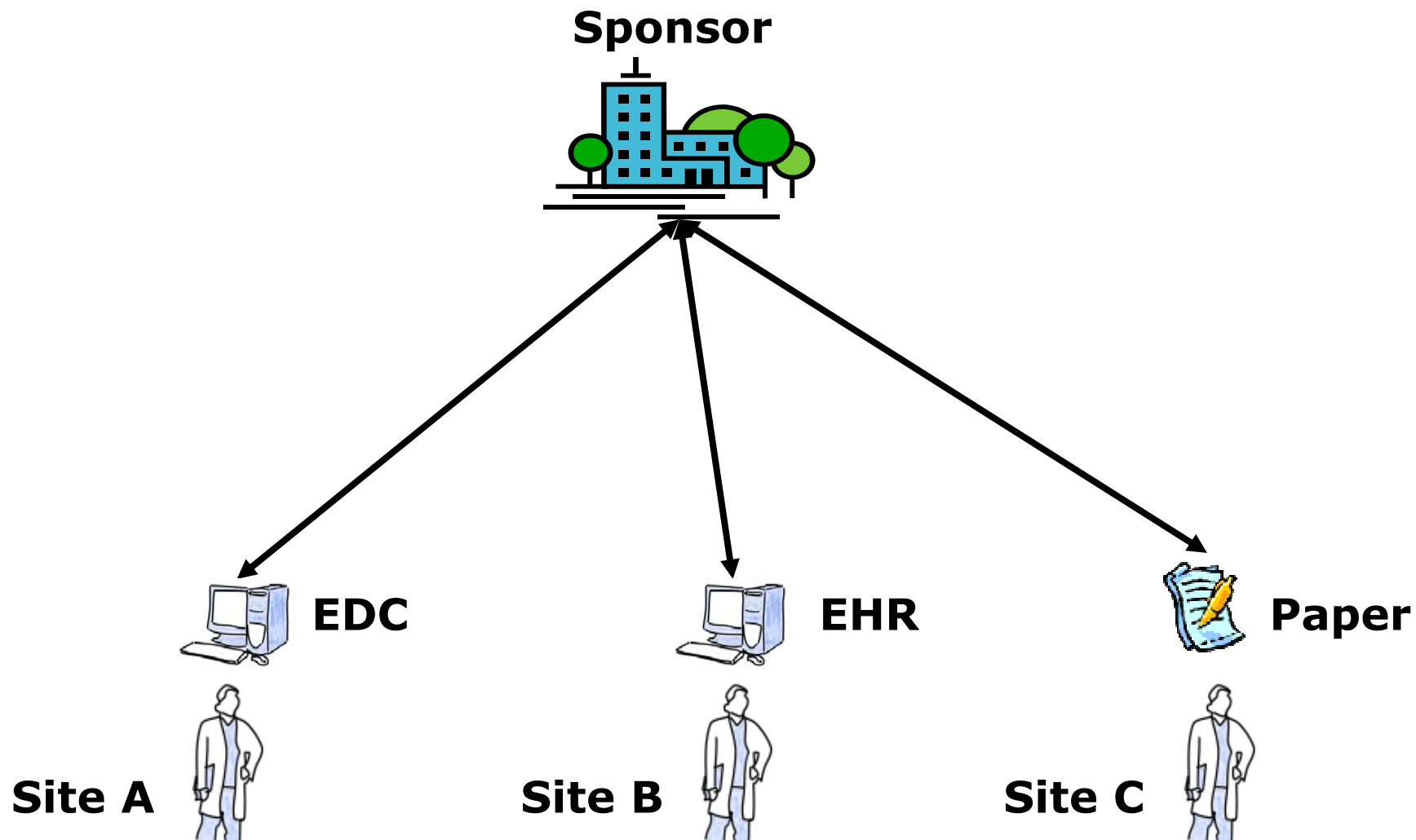
Was event serious ☐ No ☐ Yes

Severity ☐ Mild ☐ Moderate ☐ Severe

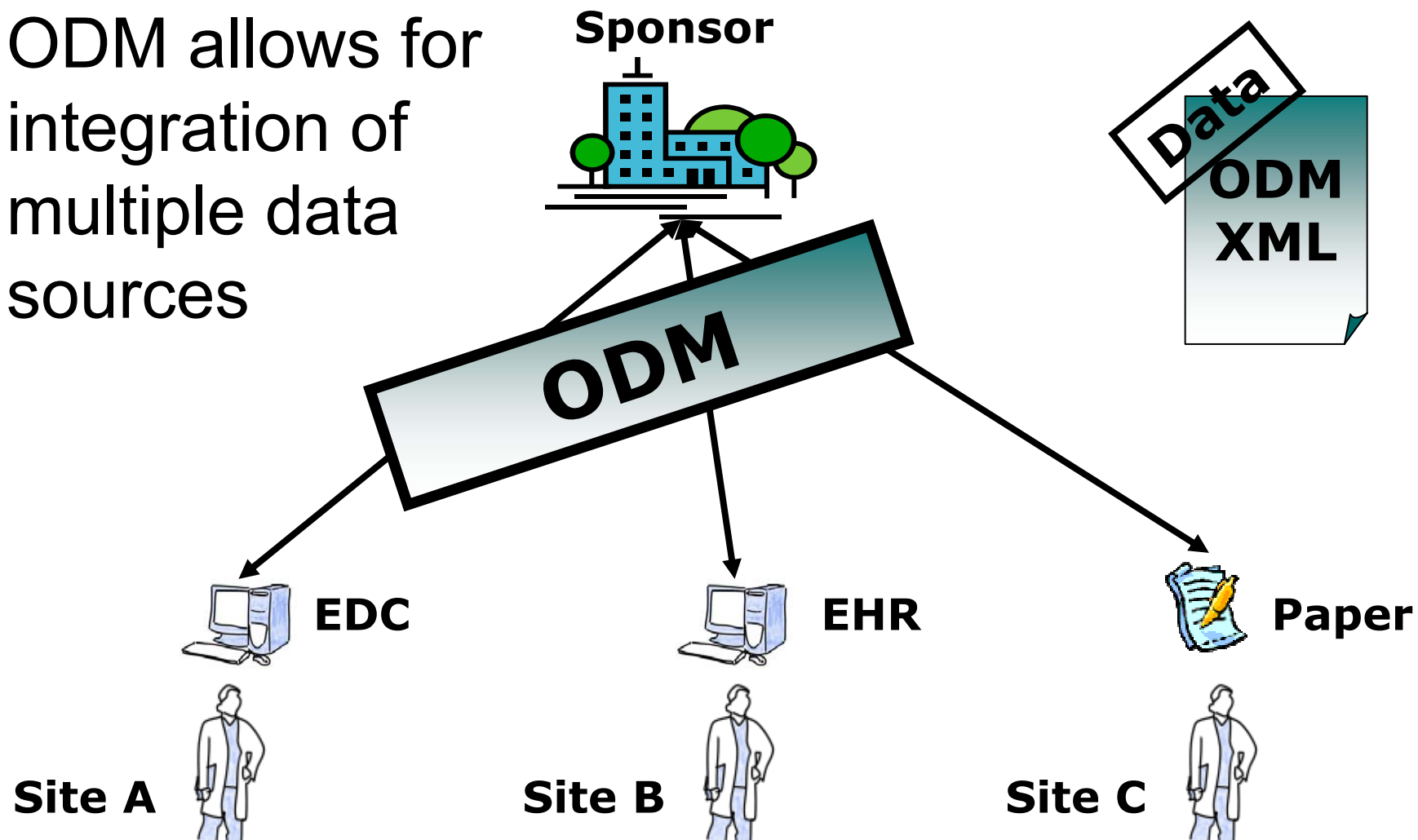
Is there a reasonable possibility that the AE may have been caused by the study drug ☐ No ☐ Yes

Action taken with study drug ☐ None  
☐ Study drug regimen changed  
☐ Temporarily stopped study drug  
☐ Study drug discontinued

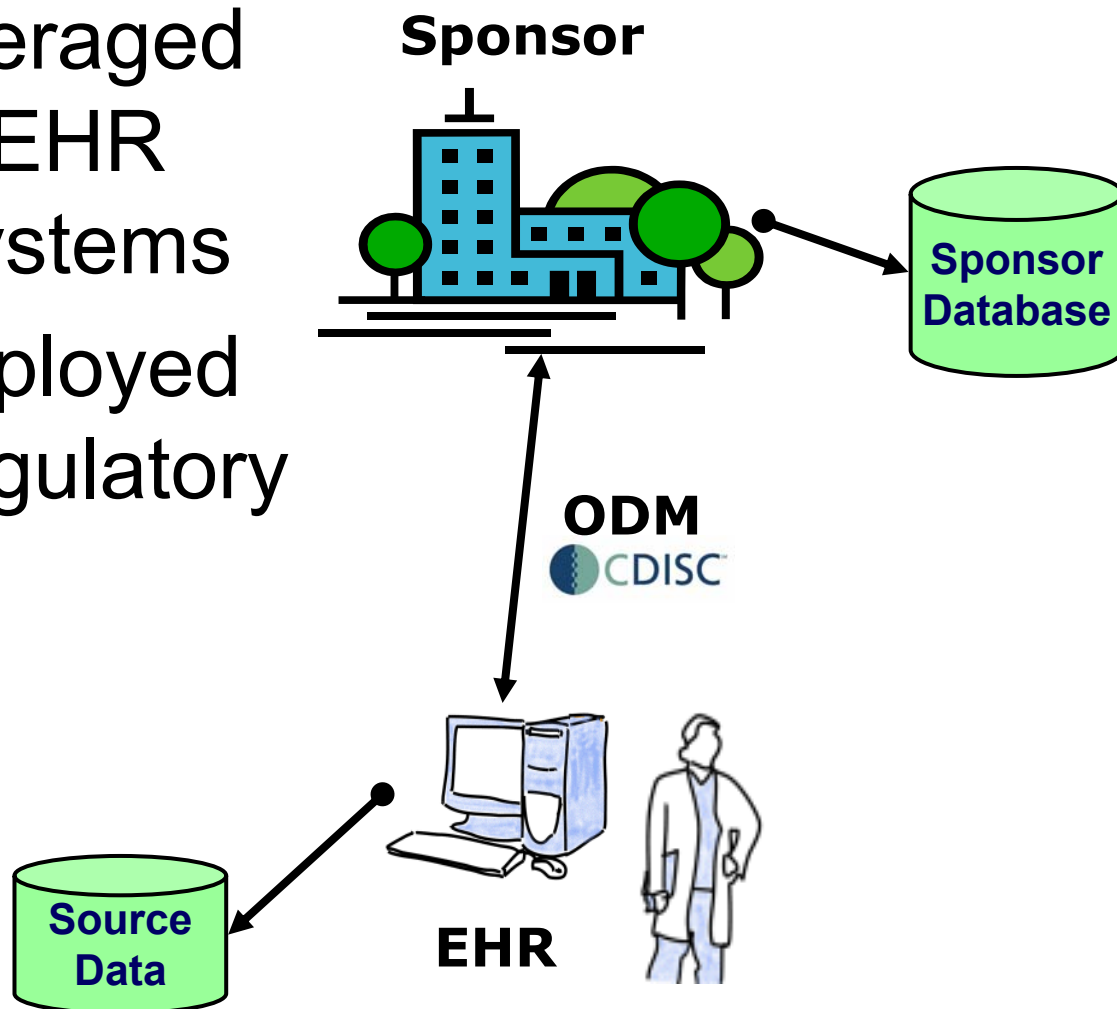
Subject outcome ☐ Subject remains in study  
☐ Withdrawn from study  
☐ Lost to follow-up  
☐ Death



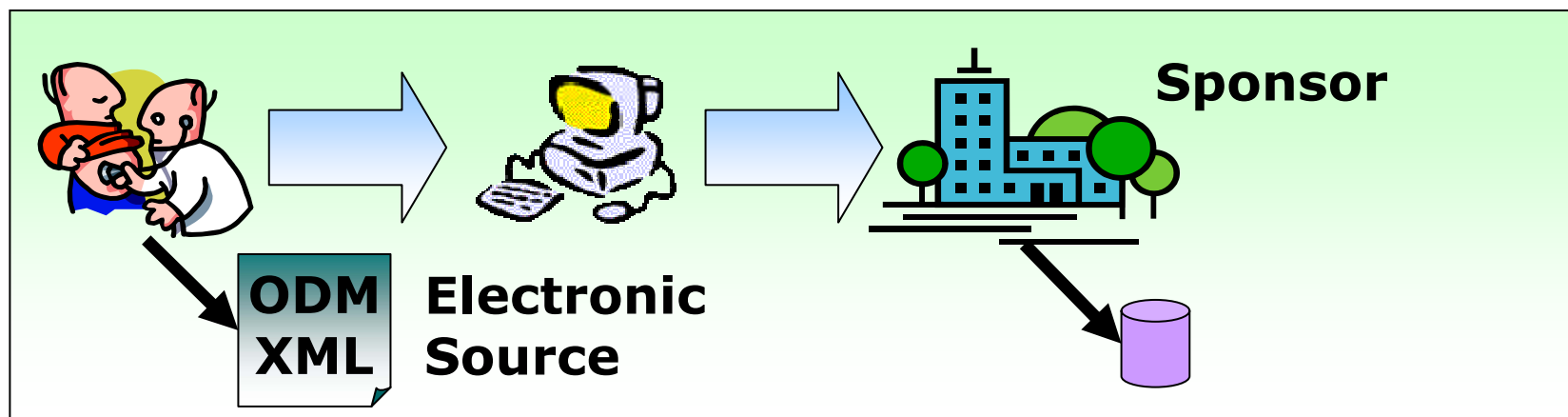
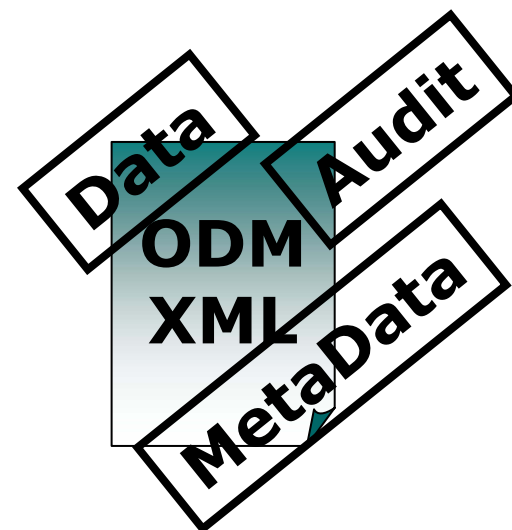
- ODM allows for integration of multiple data sources

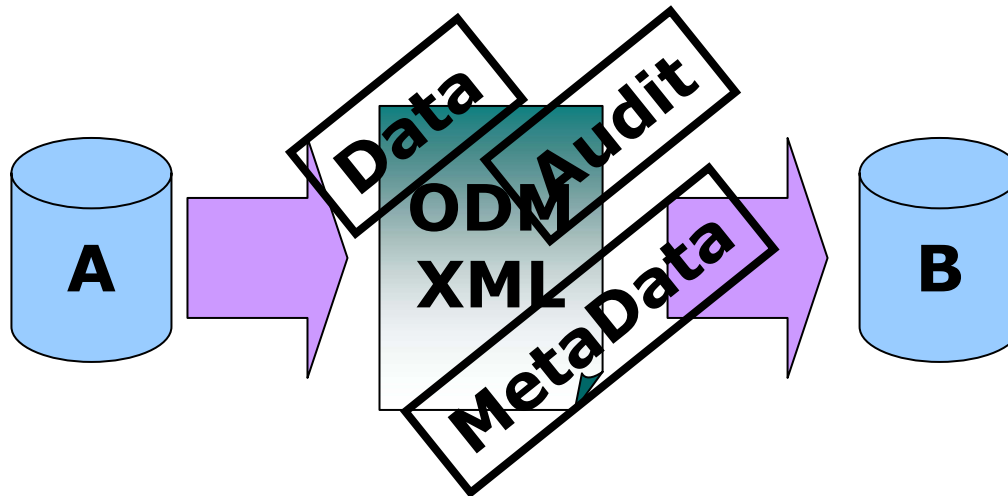


- ODM being leveraged to integrate an EHR with sponsor systems
- ODM being employed to help meet regulatory requirements

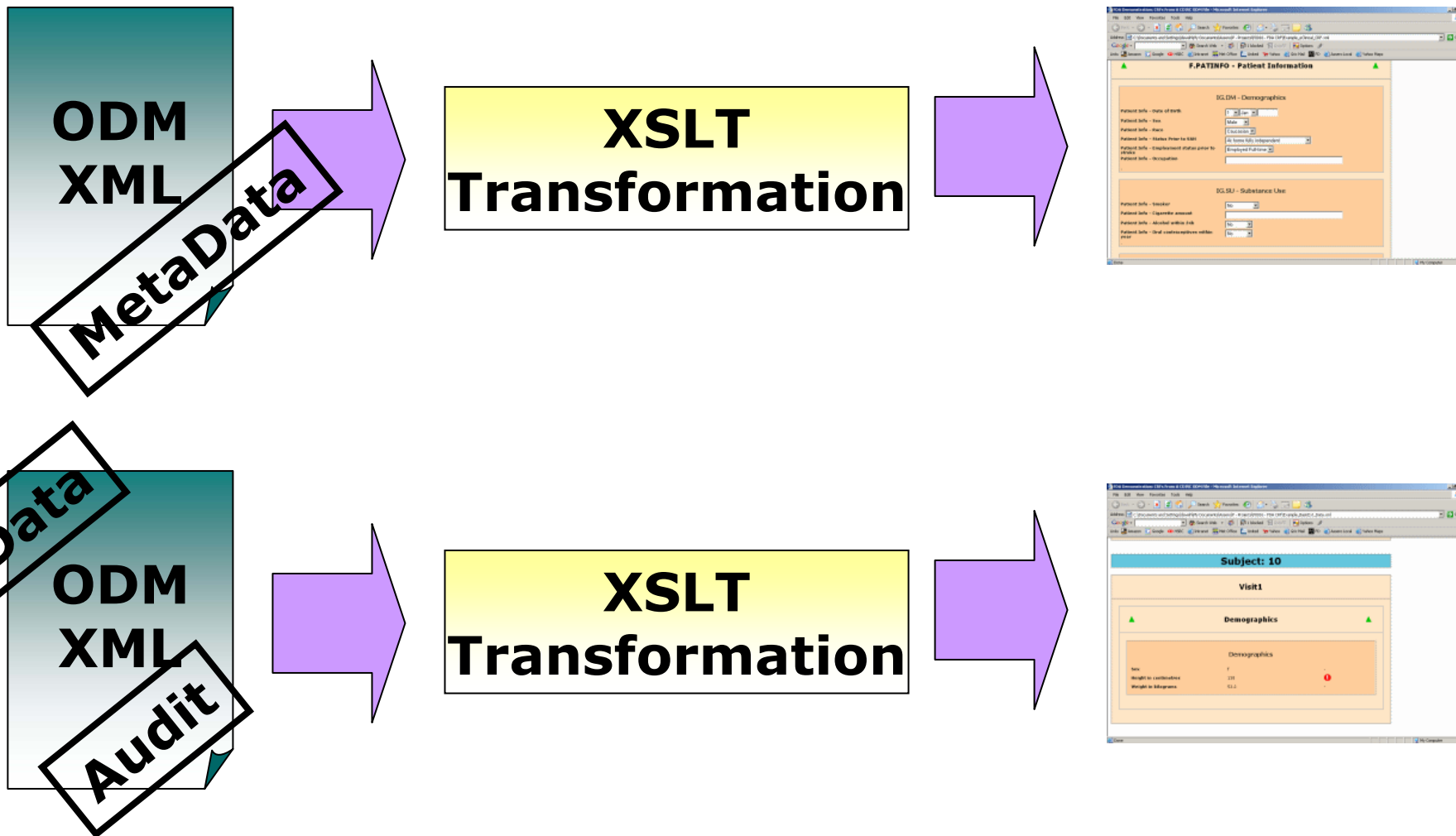


- Investigator is obliged to
  - Maintain source data (accurate)
  - Retain source data
  - Prevent its destruction
  - Allow access to inspectors

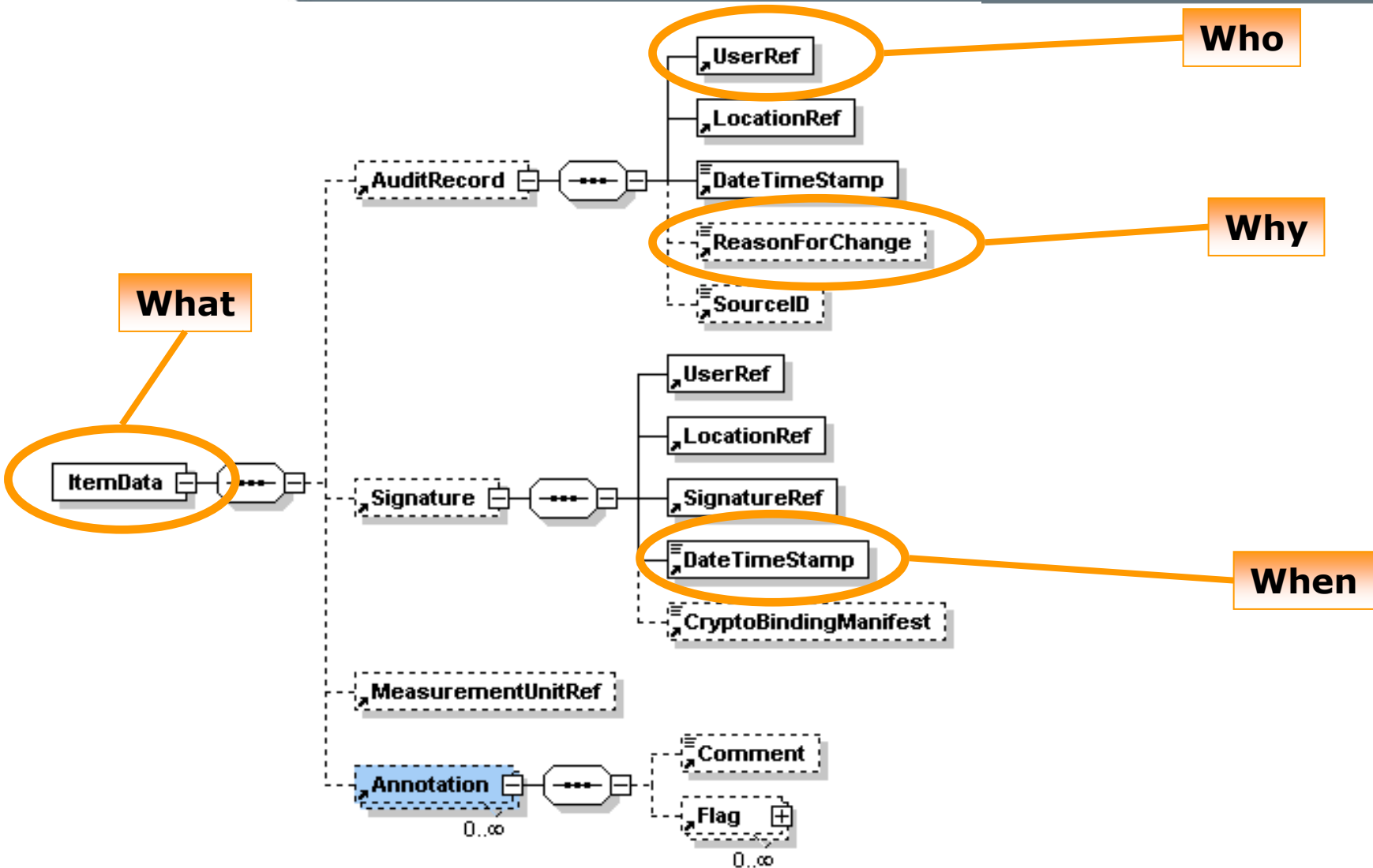


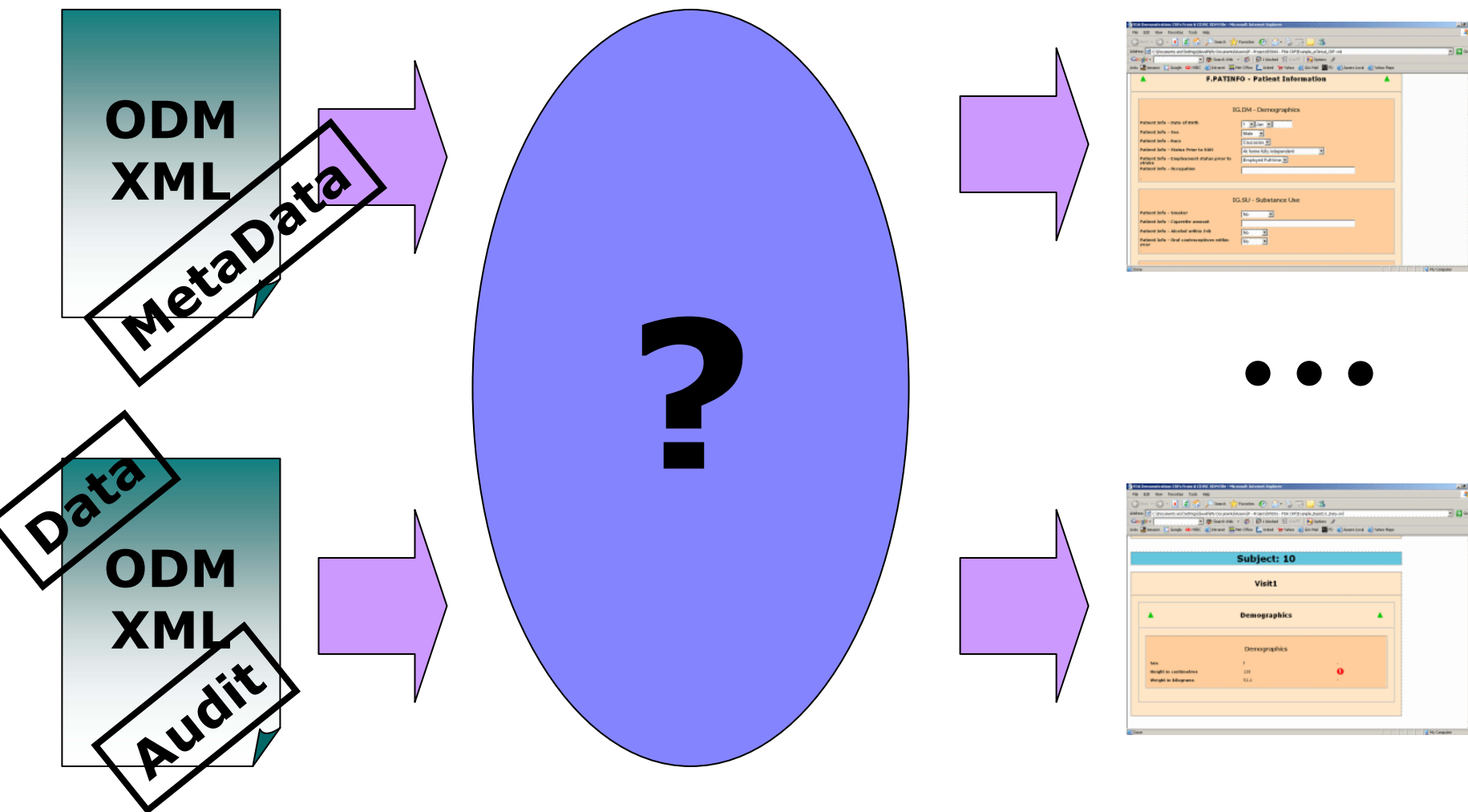


- One of the original use cases for the model
- Ability to interchange Metadata and / or Clinical Data



- 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?

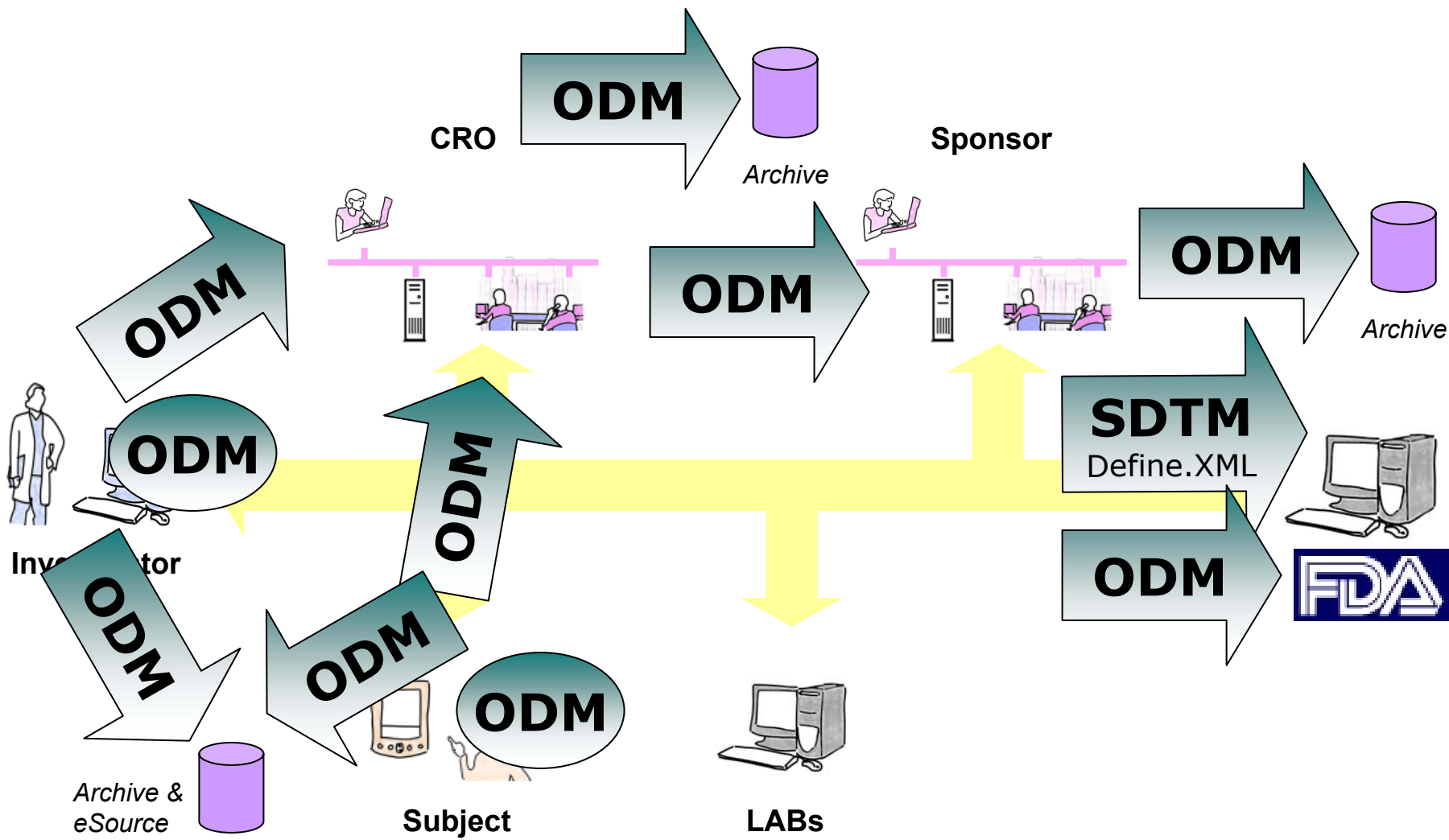


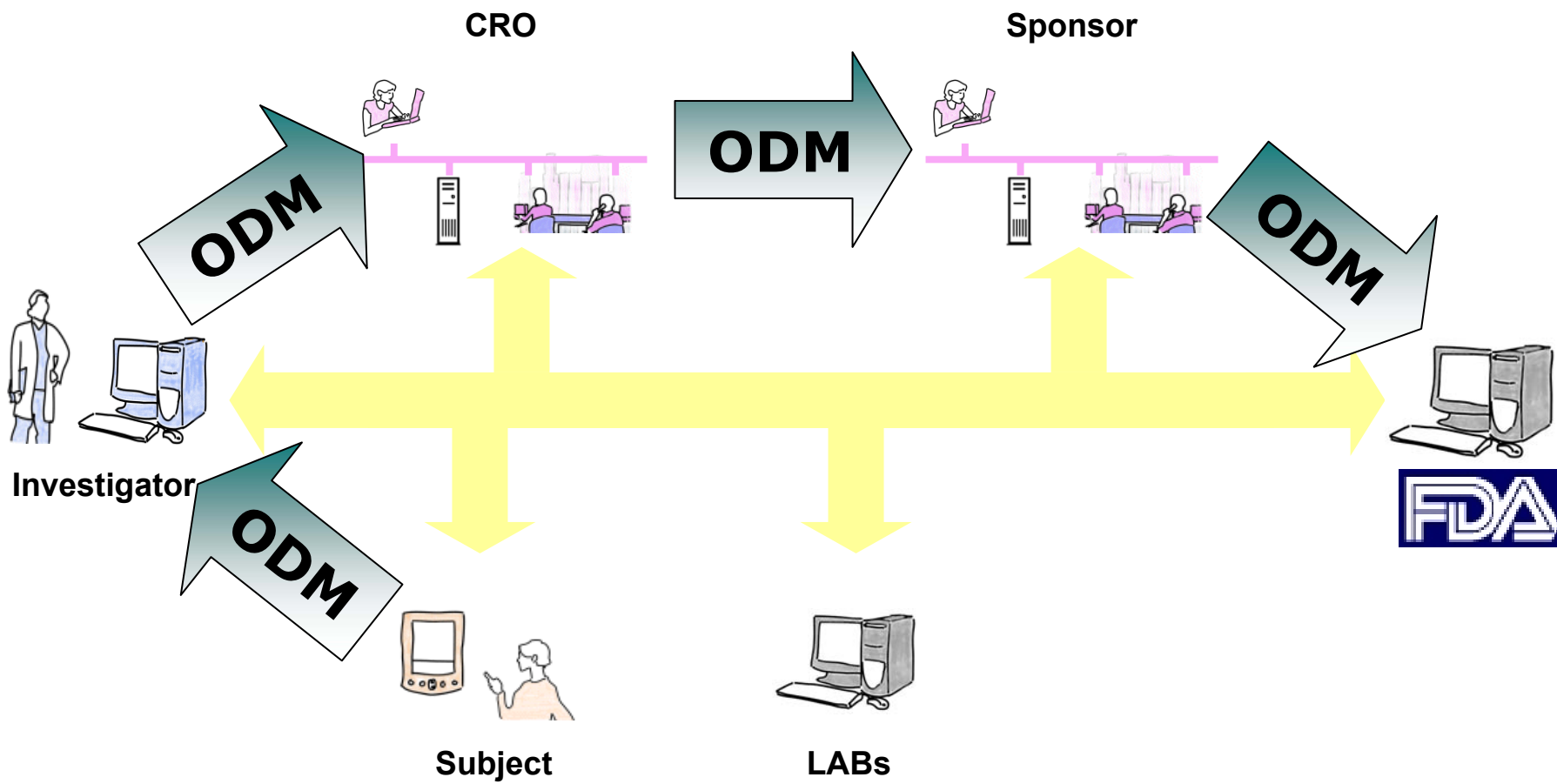


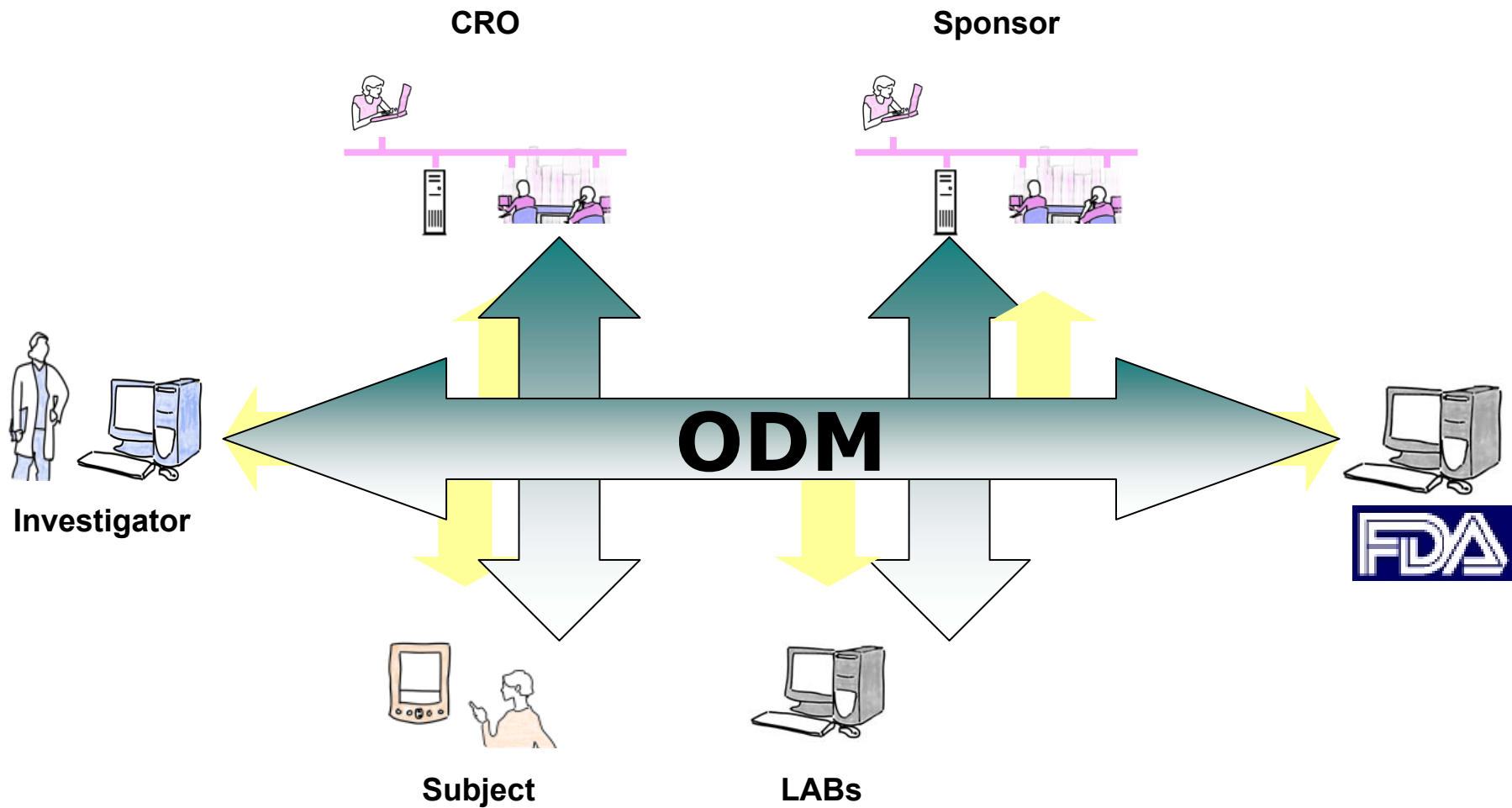
- Data should be archived in an electronic form
- The archive should contain the trial metadata
- The archive should permit the data to be used in trial reconstruction
- The archive mechanism should allow for both sponsor (full) and investigator (subset) archives
- The data archive should be supportable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

- 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

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









## ODM and Define.xml

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

# 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 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



- 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 is our wine, the important content.

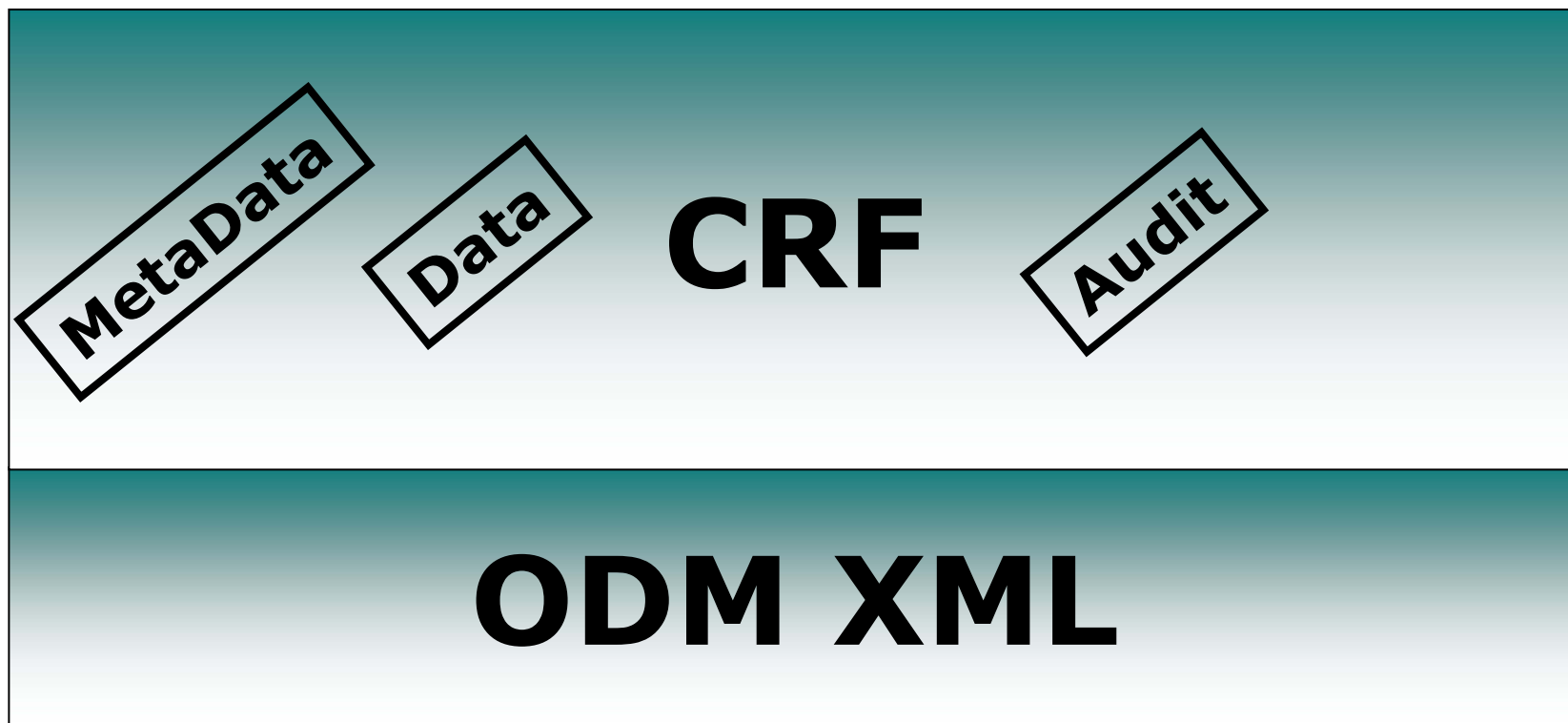


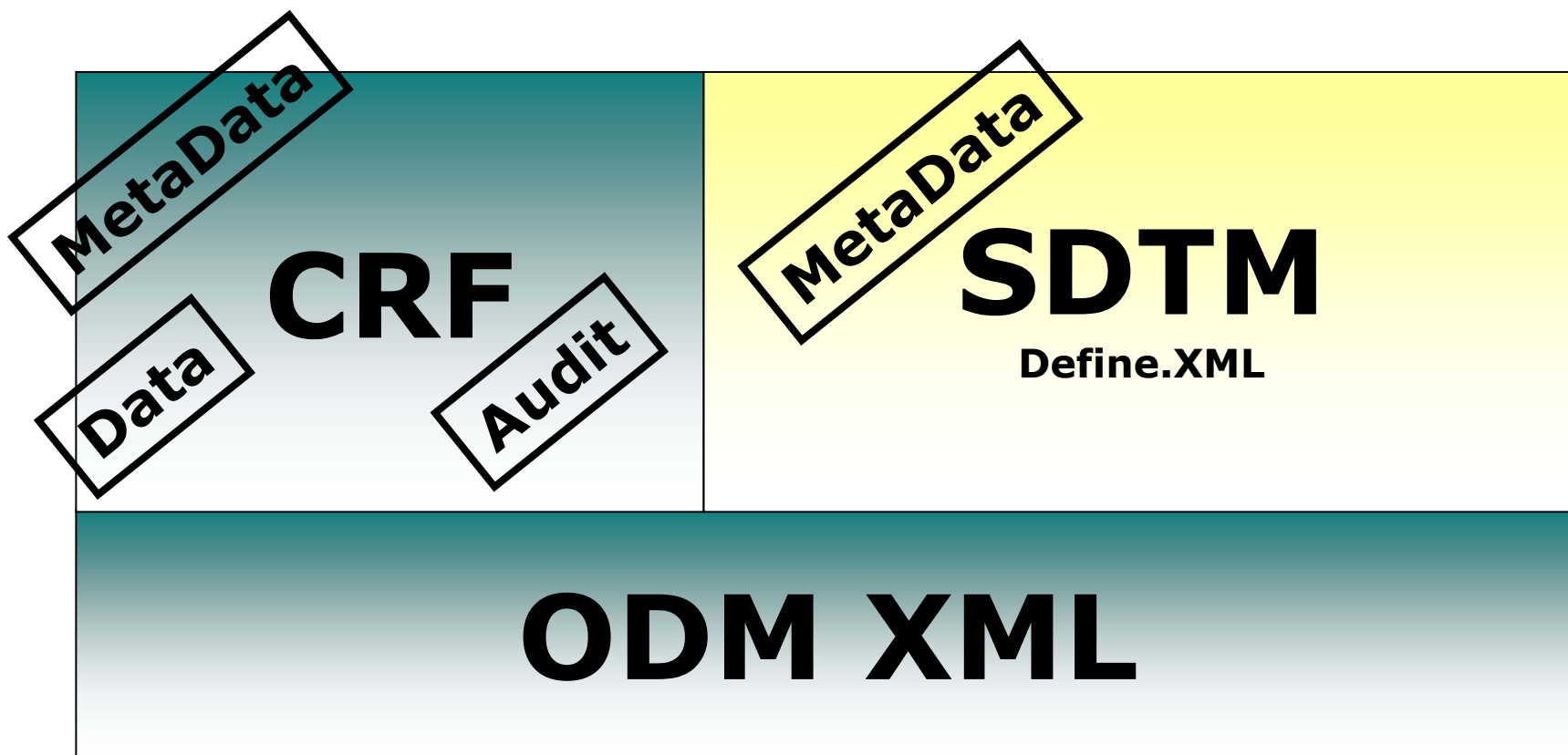
- ODM is the bottle, containing the SDTM data. Currently SAS transport files are used

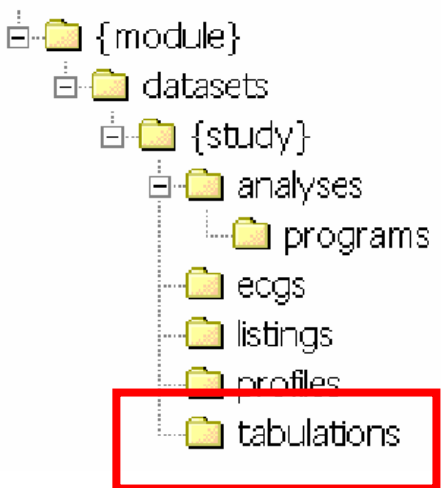


- Define.XML is our label, telling us what SDTM we have. A machine-readable format that replaces Define.PDF for transmitting submission metadata.

- 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







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

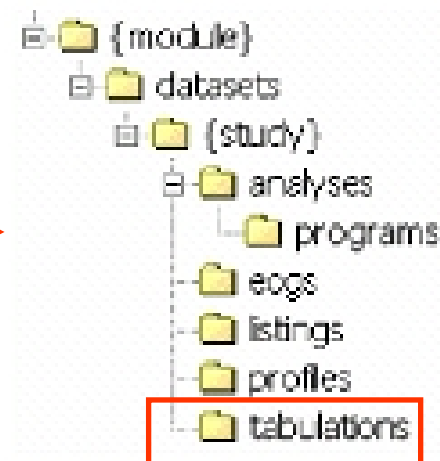
Contains data tabulation datasets, annotated CRF, data definition

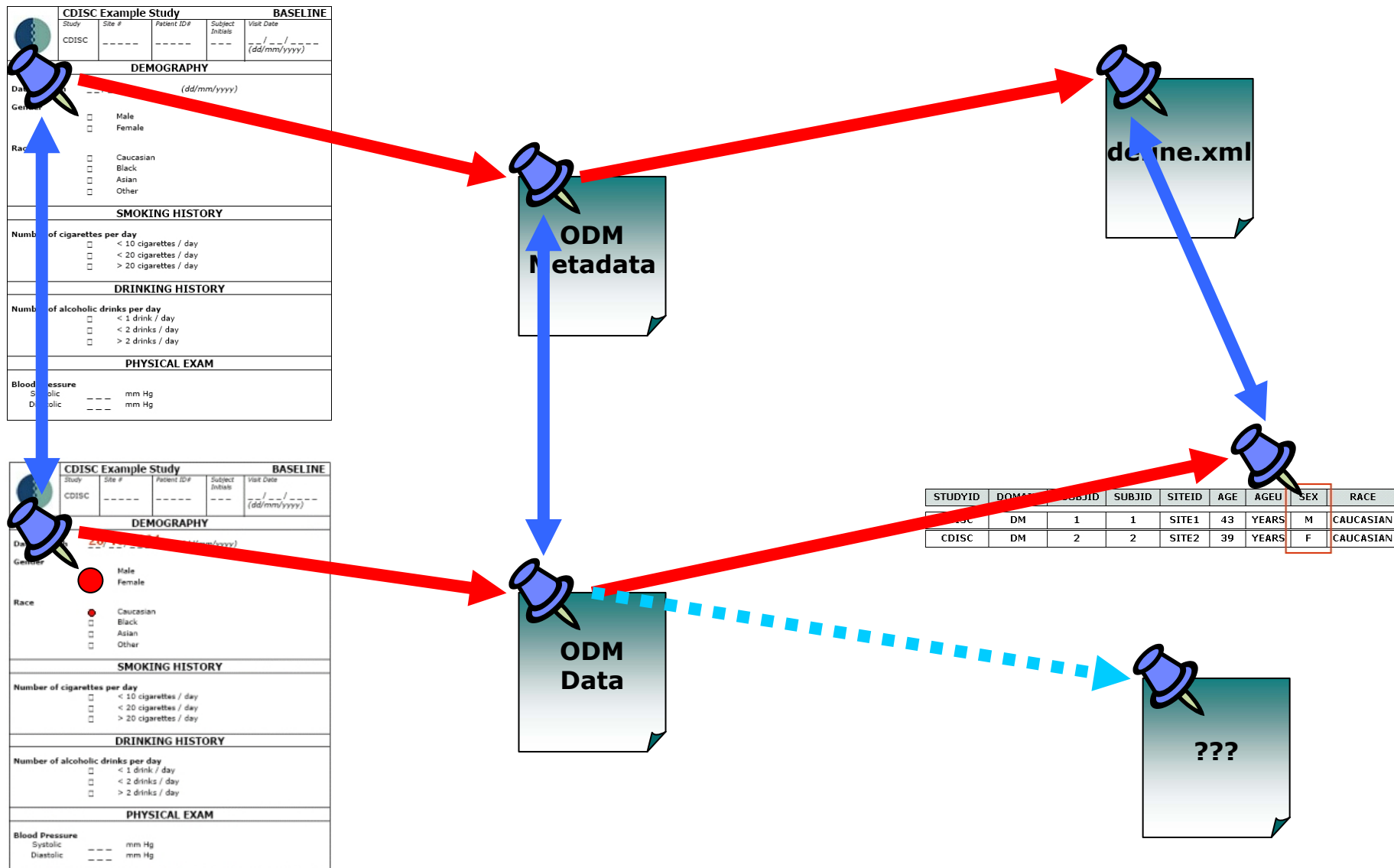
Define.xml would be supplied  
in support of the Data  
Tabulations

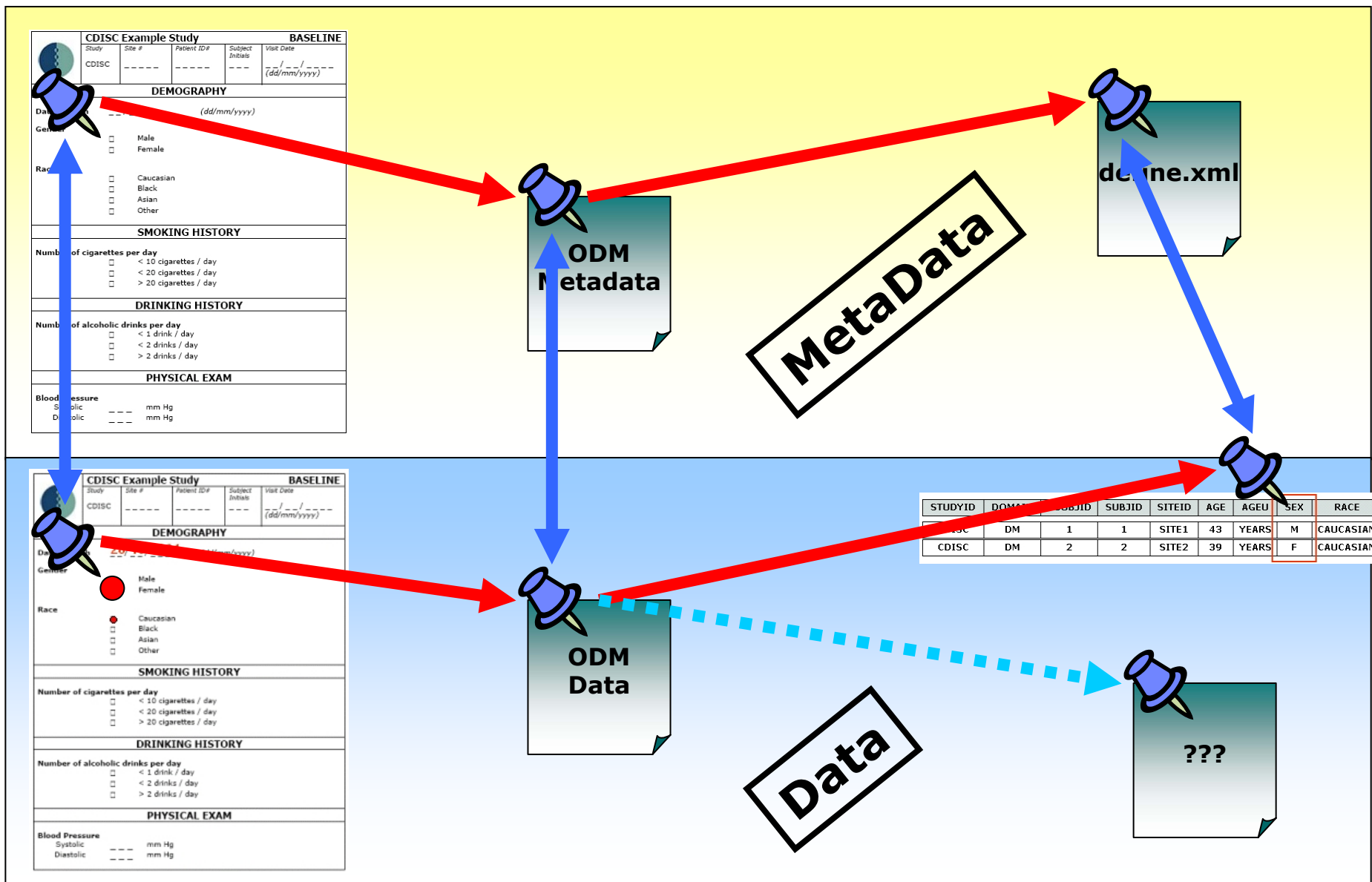
- How do we “link” the data from collection through to the submission by the sponsor?

| CDISC Example Study                            |        | BASELINE    |                  |
|------------------------------------------------|--------|-------------|------------------|
| Study                                          | Site # | Patient ID# | Subject Initials |
| CDISC                                          | -----  | -----       | ---              |
| Visit Date<br>(dd/mm/yyyy)                     |        |             |                  |
| -----                                          |        |             |                  |
| DEMOGRAPHY                                     |        |             |                  |
| Date of Birth    -- / -- / --    (dd/mm/yyyy)  |        |             |                  |
| Gender                                         |        |             |                  |
| <input type="checkbox"/> Male                  |        |             |                  |
| <input type="checkbox"/> Female                |        |             |                  |
| Race                                           |        |             |                  |
| <input type="checkbox"/> Caucasian             |        |             |                  |
| <input type="checkbox"/> Black                 |        |             |                  |
| <input type="checkbox"/> Asian                 |        |             |                  |
| <input type="checkbox"/> Other                 |        |             |                  |
| SMOKING HISTORY                                |        |             |                  |
| Number of cigarettes per day                   |        |             |                  |
| <input type="checkbox"/> < 10 cigarettes / day |        |             |                  |
| <input type="checkbox"/> < 20 cigarettes / day |        |             |                  |
| <input type="checkbox"/> > 20 cigarettes / day |        |             |                  |
| DRINKING HISTORY                               |        |             |                  |
| Number of alcoholic drinks per day             |        |             |                  |
| <input type="checkbox"/> < 1 drink / day       |        |             |                  |
| <input type="checkbox"/> < 2 drinks / day      |        |             |                  |
| <input type="checkbox"/> > 2 drinks / day      |        |             |                  |
| PHYSICAL EXAM                                  |        |             |                  |
| Blood Pressure                                 |        |             |                  |
| Systolic    ---    mm Hg                       |        |             |                  |
| Diastolic    ---    mm Hg                      |        |             |                  |

ODM  
XML



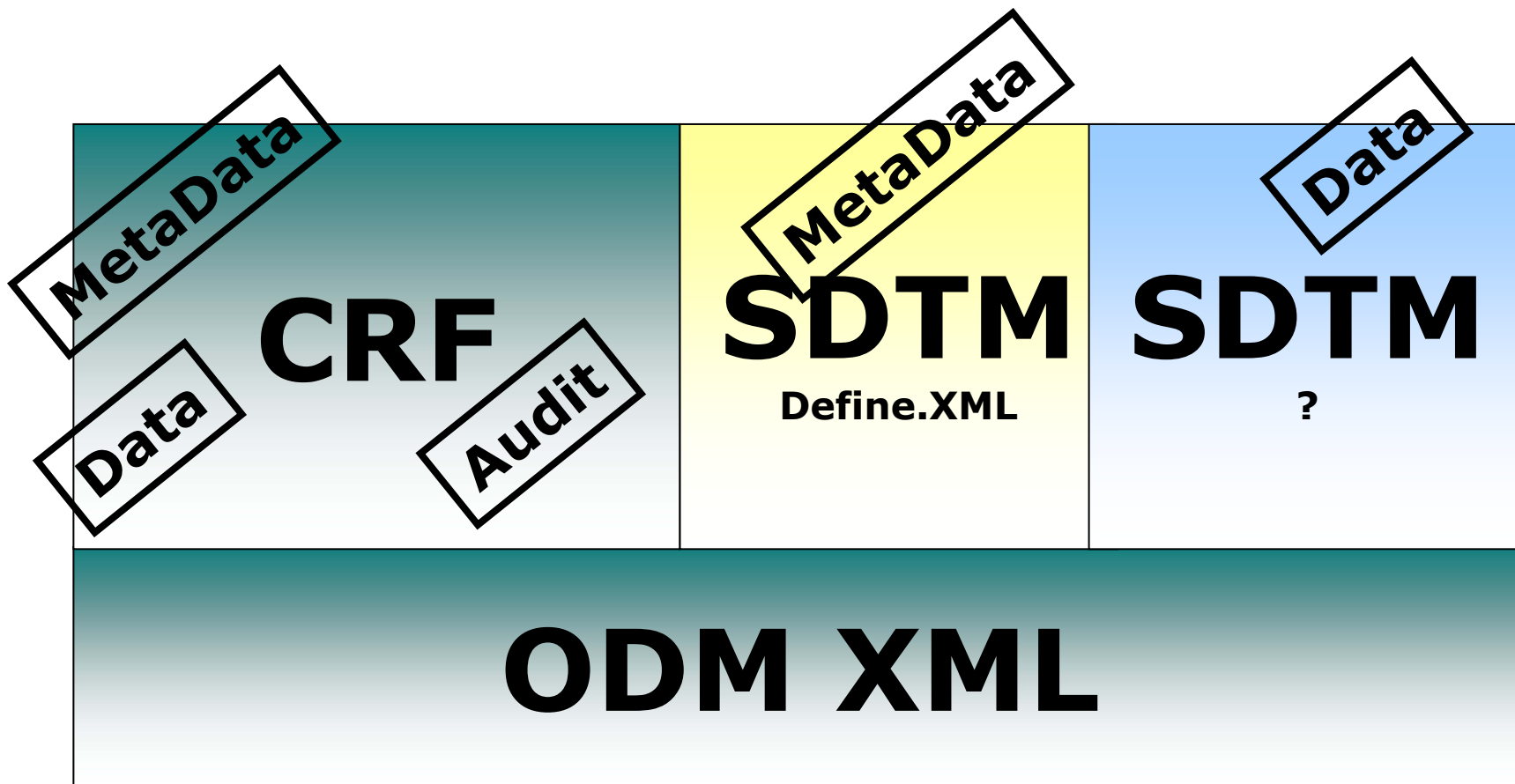




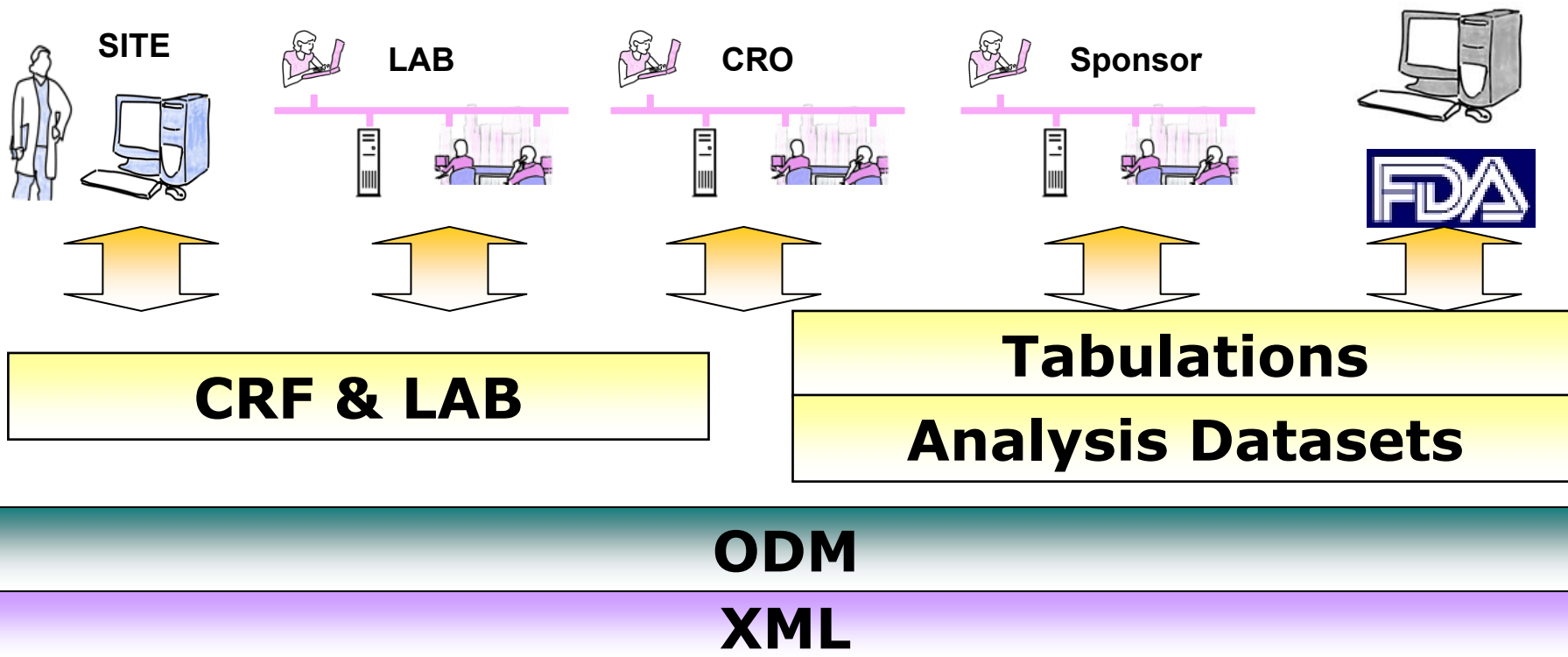


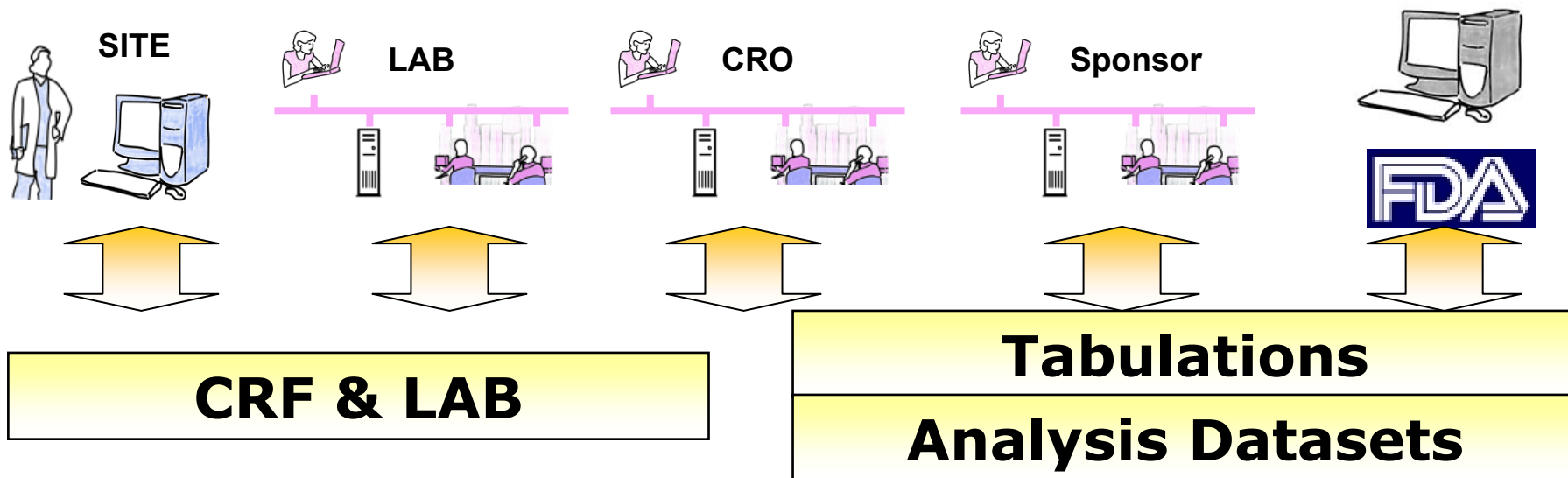
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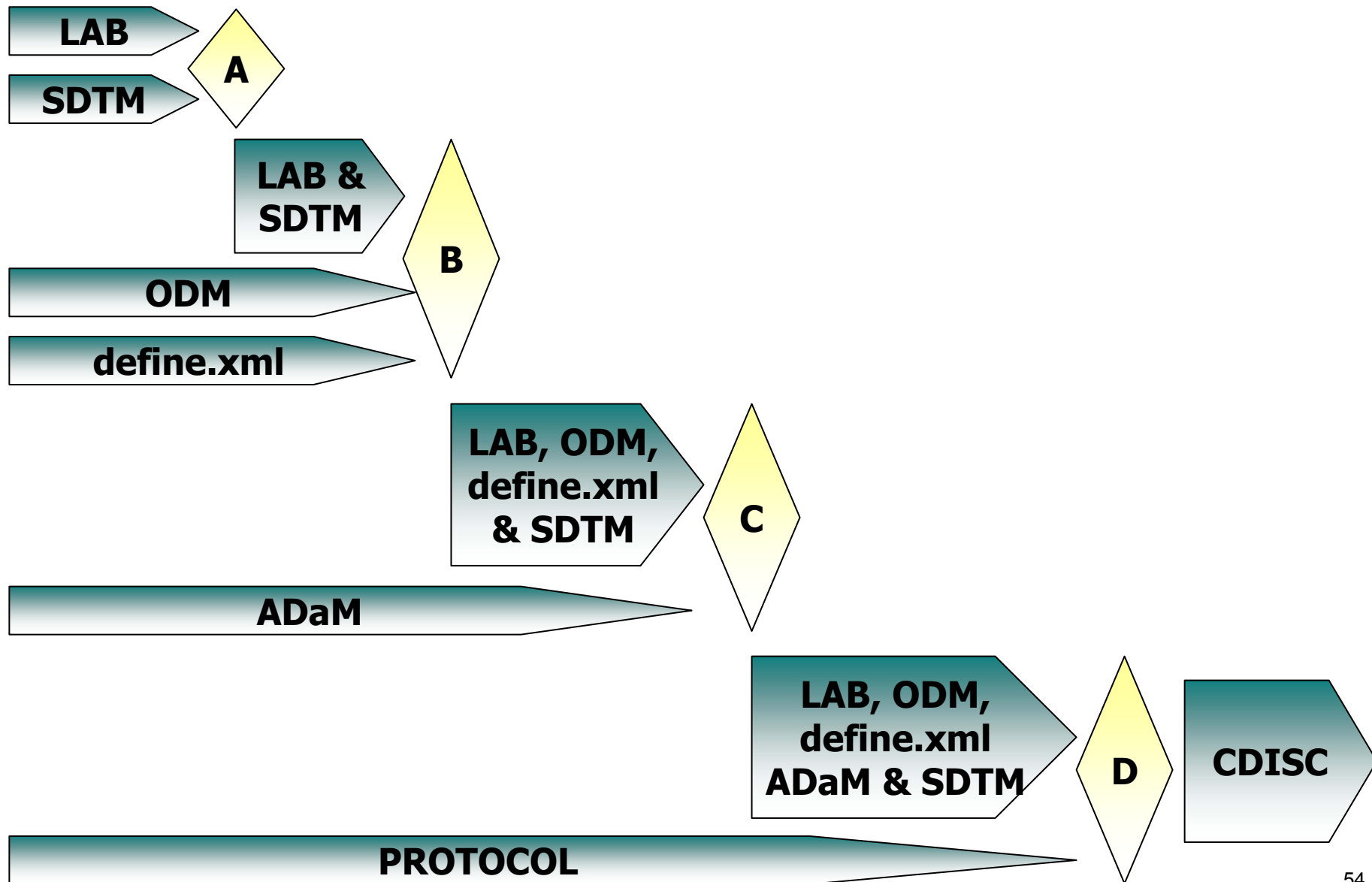


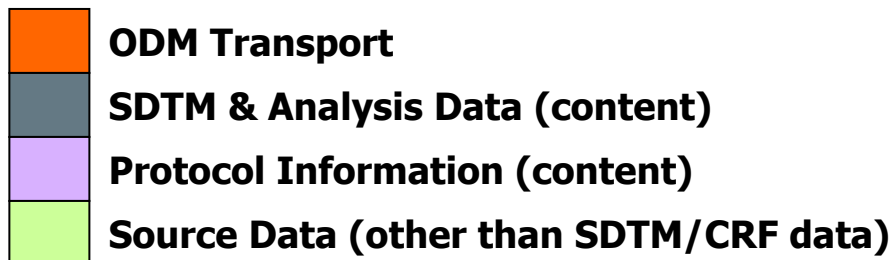
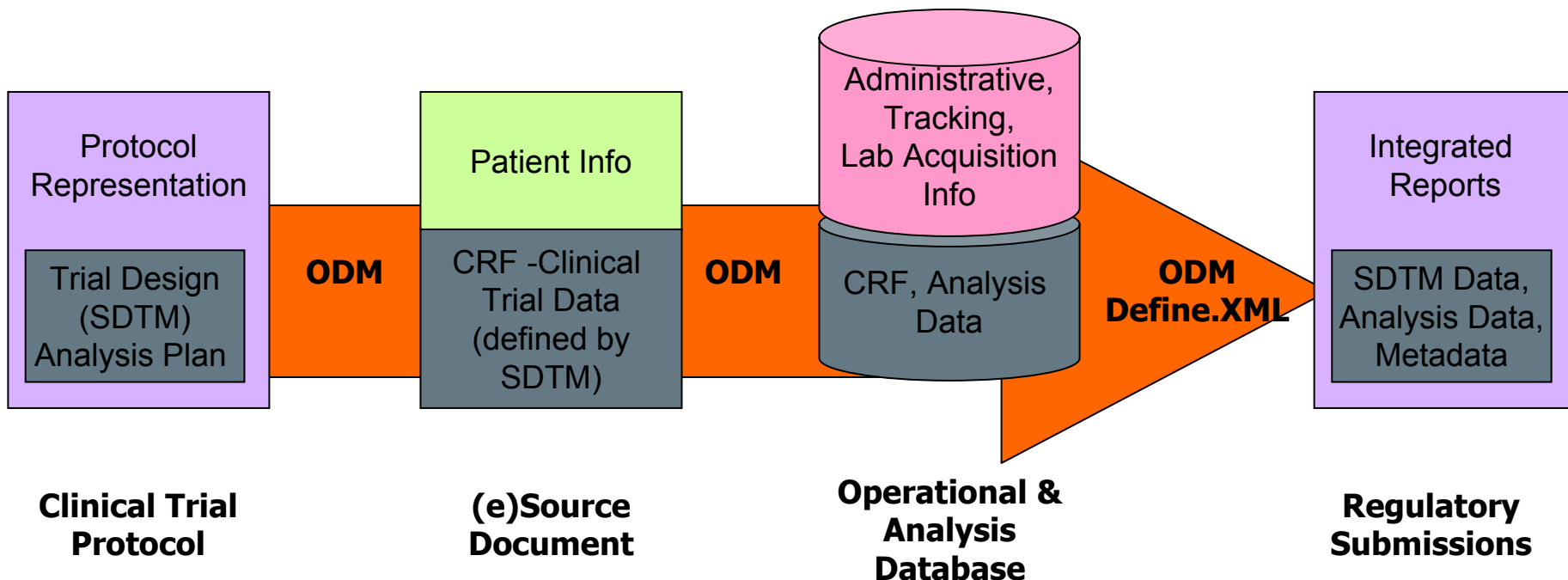
| Lab Data | CRF Forms & Data | Tabulations | Analysis Datasets |
|----------|------------------|-------------|-------------------|
| LAB      | ODM              | SDTM        | ADaM              |
|          | ODM              |             |                   |
| XML      |                  |             |                   |





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





**NEW**



## ODM and Define.xml

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- **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

