Legacy to SDTM Conversion Workshop: Tools and Techniques

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Legacy Data

- Old studies never die …
- Legacy studies are often required for submissions or pharmacovigilence.
- Often there are multiple Legacy systems, disparate from each other
- Problem: design an efficient method for converting legacy data to SDTM

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Legacy CDISC Implementation Goals

- Design a strategy such that:
  - No knowledge needed of system that originally produced the legacy data
  - Applicable to files from any system
  - Implementation is flexible enough to adapt to different study designs
  - Minimal programming support required for maintenance
  - Reasonable cost

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Study Scenarios

- Well-documented
  - Raw data available
  - Analysis data reliable
  - Study report, SAP, CRF available
  - Someone familiar with the study available to answer questions
- Less well-documented
  - Analysis data either not available, or not reliable
  - No SAP
  - Study report missing appendices
  - No one remembers the study
  - Requires a lot of “pre-work” before automated methods can be applied

Well–Documented Studies

- This presentation focuses on the best case
- These studies lend themselves to automated, non-expert driven solutions

The Other Ones, Briefly …

- Becomes a data management problem
- Problematic data may be excluded or imputed, so long as a reasonable, well-documented process can be defined
  - Replace unreliable lab normal ranges with published ranges
- Requires expert data manager to identify problems and propose solutions

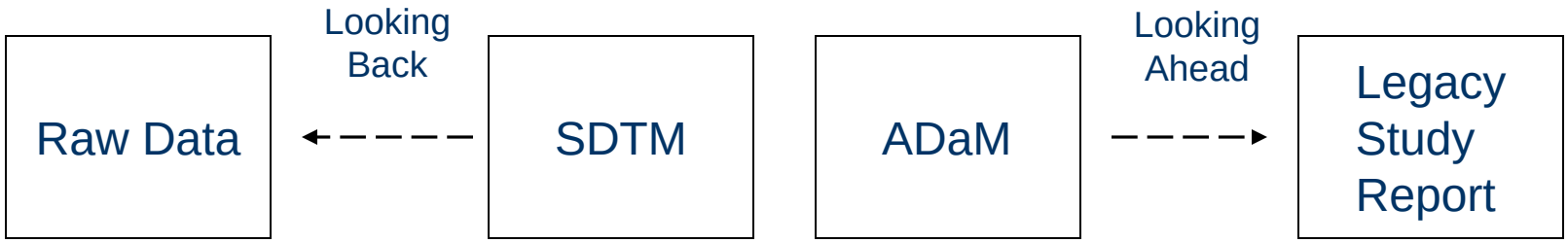
Well-Documented Studies

ETL Process

Our approach

- Start with the **analysis files**
  - Transform these to SDTM
  - Usually contain most of the data required for SDTM
  - Better ones tend to be self-documenting
- Compare the analysis files to the SDTM domains
  - Ensure that required and expected SDTM variables are available
  - Understand all derivations from SAP or study report

Issues



- Raw data, analysis data, or combination?
- SDTM is designed to represent raw data
  - raw data not included must be documented
- Must match results in legacy CSR
  - or explain why

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ETL Process

- Define how raw/analysis data fits into SDTM domains and variables
- Match data to required, permitted and expected SDTM data when possible
- Provide an automated mechanism for specifying the data sources and algorithms
- Basis for the FDA-mandated “DEFINE.PDF” documentation
- Provide the metadata for the SDTM files

Implementing an ETL Process

- Programs read table-driven metadata to translate the analysis data into SDTM formats
  - Tells the SAS code which analysis variables populate the SDTM variables
  - Indicates when specialized code is required
- All code is developed to be generic using the metadata to indicate when variations are required
- New studies only require changes to metadata

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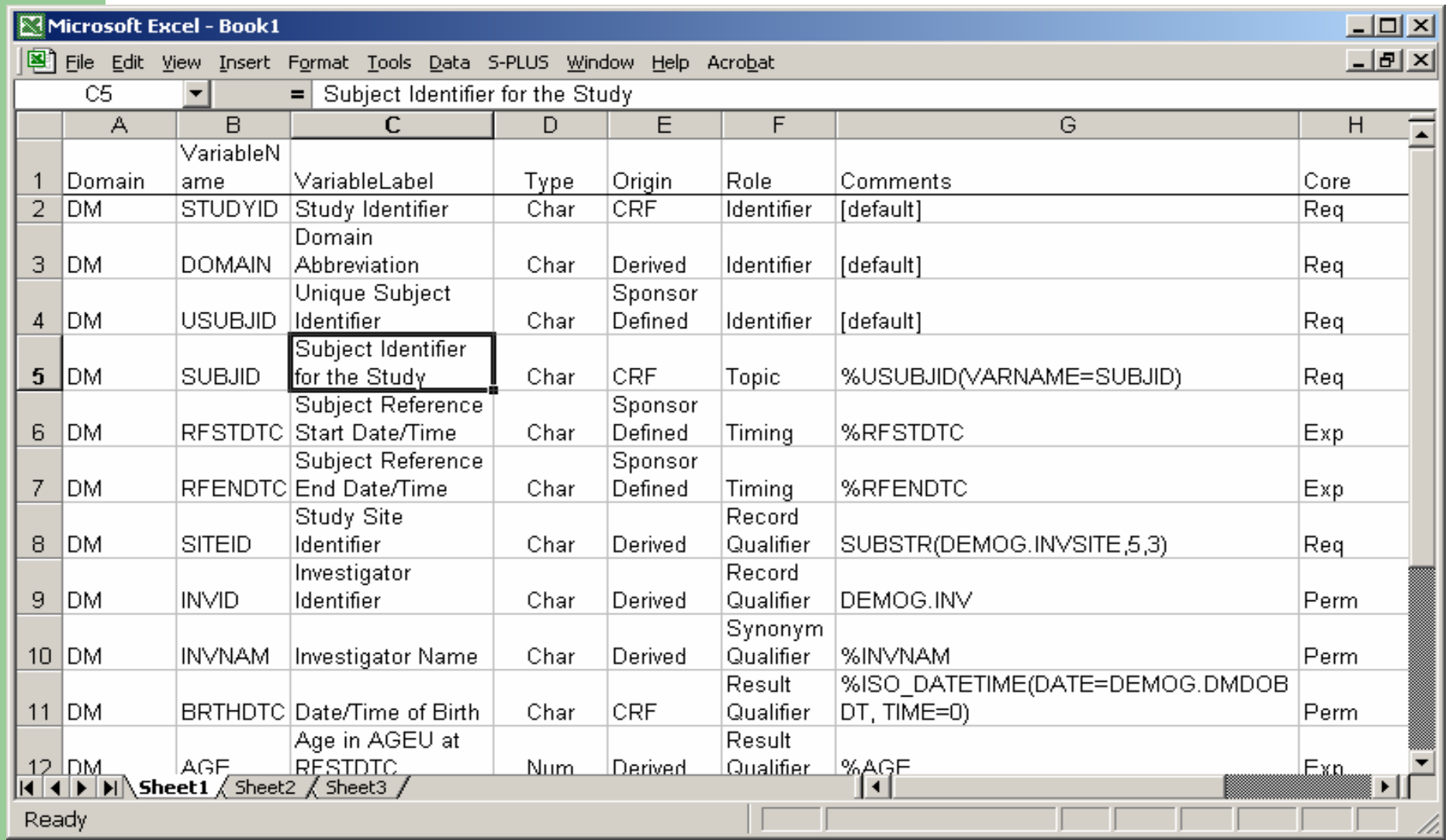
Sample Mapping Spreadsheet



Microsoft Excel - Book1

File Edit View Insert Format Tools Data S-PLUS Window Help Acrobat

C5 = Subject Identifier for the Study

	A	B	C	D	E	F	G	H
1	Domain	VariableName	VariableLabel	Type	Origin	Role	Comments	Core
2	DM	STUDYID	Study Identifier	Char	CRF	Identifier	[default]	Req
3	DM	DOMAIN	Domain Abbreviation	Char	Derived	Identifier	[default]	Req
4	DM	USUBJID	Unique Subject Identifier	Char	Sponsor Defined	Identifier	[default]	Req
5	DM	SUBJID	Subject Identifier for the Study	Char	CRF	Topic	%USUBJID(VARNAME=SUBJID)	Req
6	DM	RFSTDTC	Subject Reference Start Date/Time	Char	Sponsor Defined	Timing	%RFSTDTC	Exp
7	DM	RFENDTC	Subject Reference End Date/Time	Char	Sponsor Defined	Timing	%RFENDTC	Exp
8	DM	SITEID	Study Site Identifier	Char	Derived	Record Qualifier	SUBSTR(DEMOG.INVSITE,5,3)	Req
9	DM	INVID	Investigator Identifier	Char	Derived	Record Qualifier	DEMOG.INV	Perm
10	DM	INVNAM	Investigator Name	Char	Derived	Synonym Qualifier	%INVNAM	Perm
11	DM	BRTHDTC	Date/Time of Birth	Char	CRF	Result Qualifier	%ISO_DATETIME(DATE=DEMOG.DMDOBDT, TIME=0)	Perm
12	DM	AGE	Age in AGEU at RFSTDTC	Num	Derived	Result Qualifier	%AGE	Exp

Sheet1 Sheet2 Sheet3

Ready

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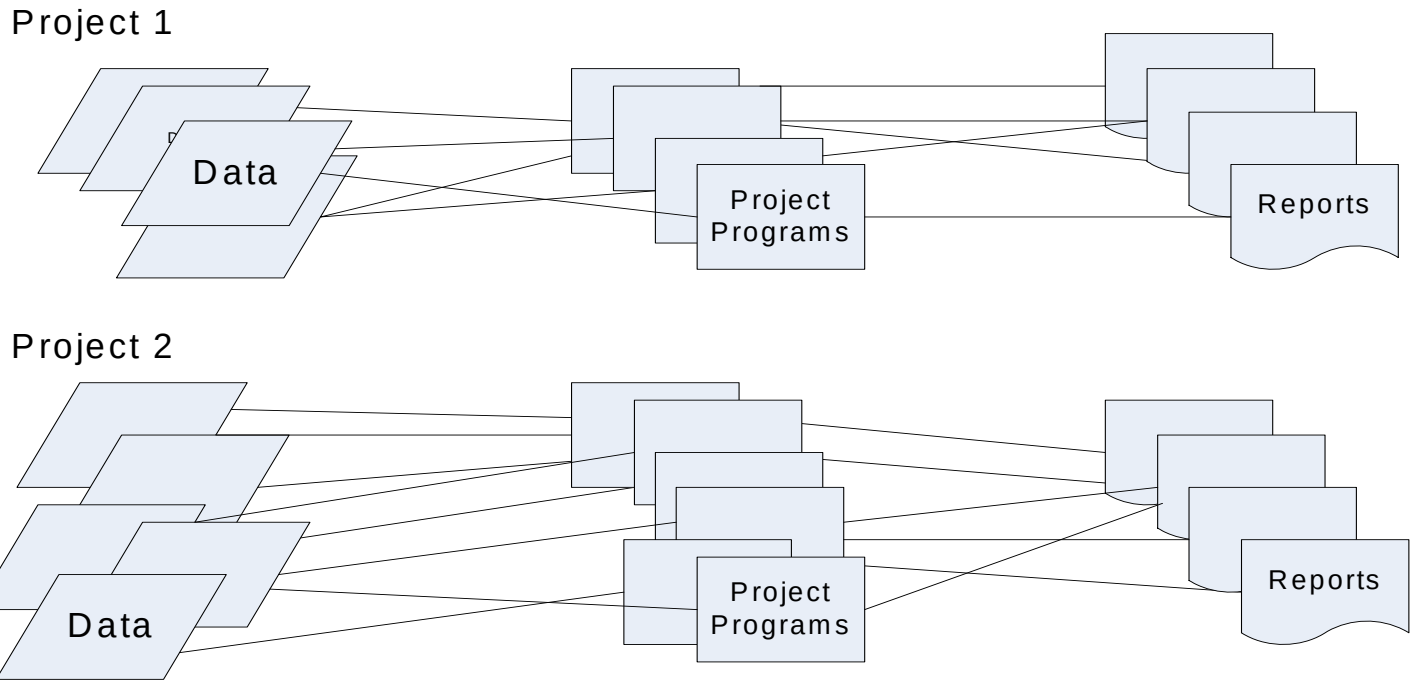
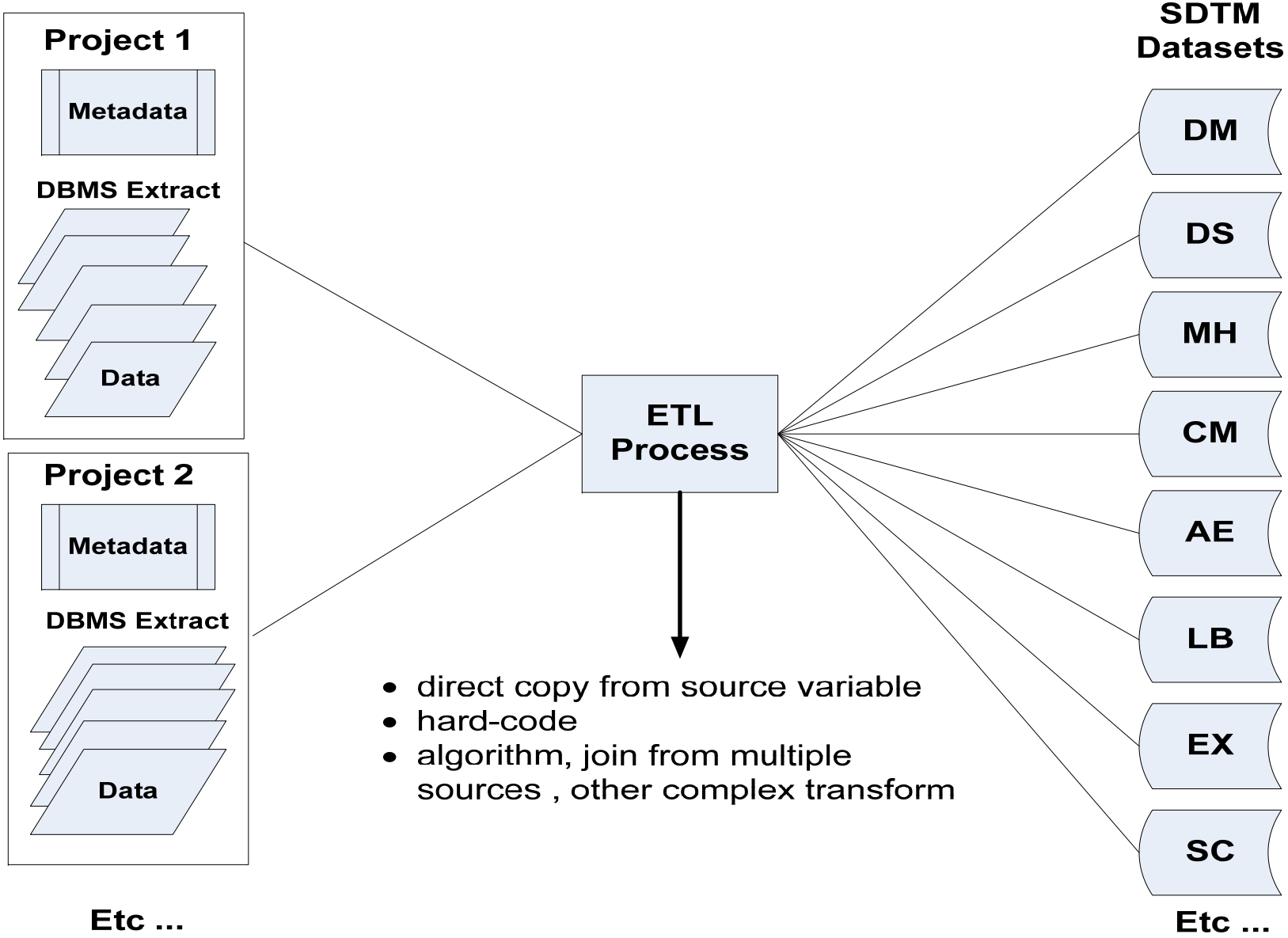
Process Without Automation



... etc.

ETL Process


Project 1
Metadata
DBMS Extract
Data
Project 2
Metadata
DBMS Extract
Data
Etc ...
ETL Process
direct copy from source variable
hard-code
algorithm, join from multiple sources , other complex transform
SDTM Datasets
DM
DS
MH
CM
AE
LB
EX
SC
Etc ...

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Software

- Market leader : SAS Data Integration Studio
  - Formerly ETL Studio
  - $80K per server
- “Off-the-Shelf ETL“
  - Metadata: Excel and Access work very well
    - Converts easily to DEFINE.PDF
  - SAS macros read metadata, generate custom SAS code to create SDTM domains from source data
  - Generates standalone, submission-ready programs

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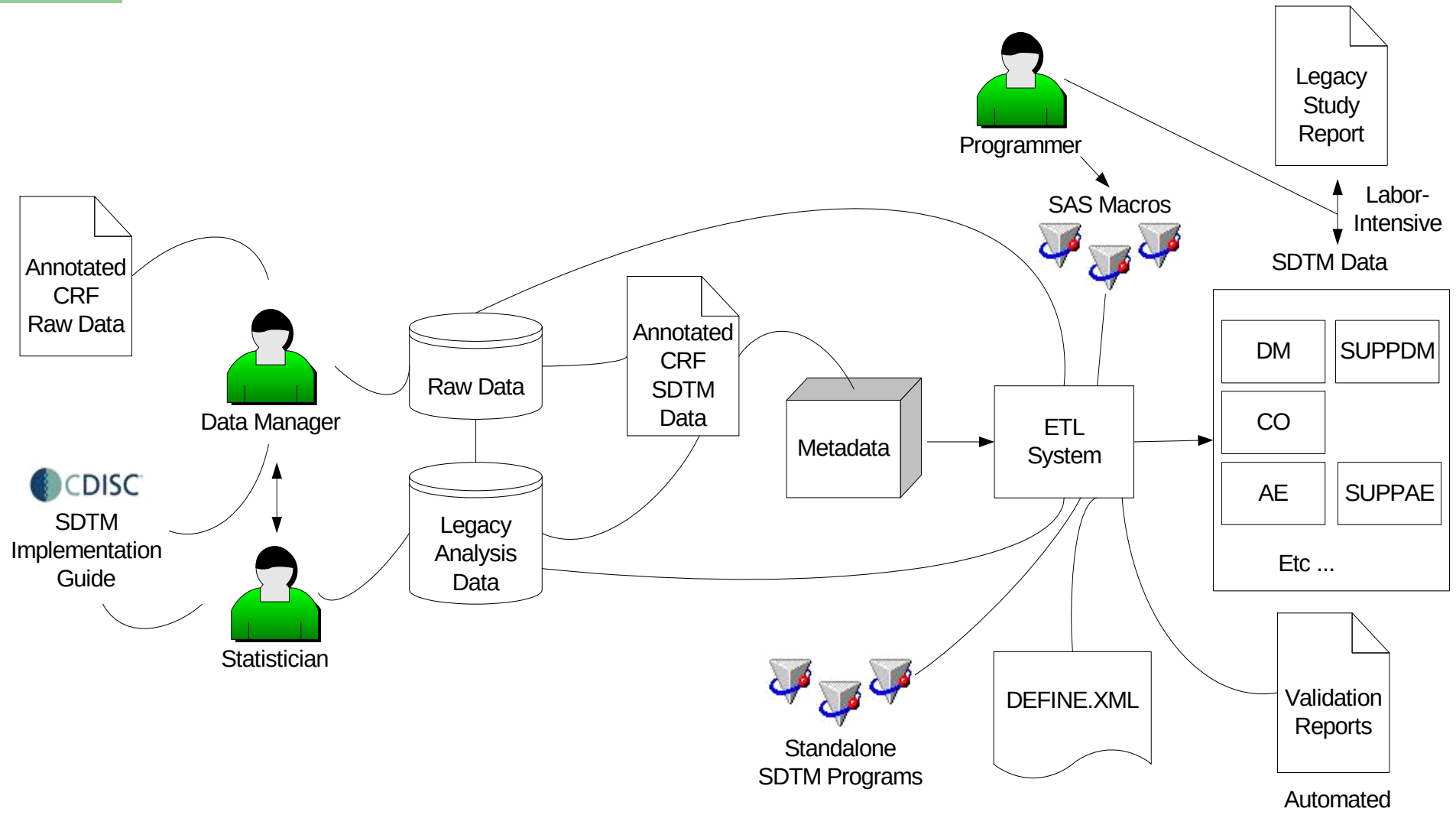
Data Flow Process



Validation: SDTM Structure

- SDTM compliance checks
  - Conformance with Implementation Guide rules can be automated
    - Variable names, labels, type etc. are correct
    - All required variables have values, etc.

Validation: Source Data Validation

- Verify metadata
  - Data manager/statistician
  - Manual review process
- Possible approaches
  - independent programming
  - for each raw dataset, verify raw to SDTM conversion for a random sample of subjects

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Validation: All Raw Data Mapped?

- Leverage metadata
- Use metadata to query raw data structure and determine differences
  - List of raw data variables not mapped
  - Raw datasets vs. domains
  - Raw data variables to SDTM variables

Validation: New SDTM/ADaM Match Legacy Study Report?

- Demonstrate that programs using SDTM (or ADaM) data can reproduce results in the legacy study report
- Nasty – no shortcuts
- Tasks can split among multiple programmers
  - they will be needed!

Advantages

- Does not disrupt existing clinical trial systems
- It works for all legacy data
- Reduces cost since only metadata changes for each new study
- Only new study specific situations cause additional coding
- Changes to CDISC standards are made to the metadata avoiding costly programming revisions

Advantages (continued)

- Self-documenting
- Metadata easily converted to DEFINE.PDF
  - If you follow the system, metadata are guaranteed to provide complete and accurate documentation
- Generates submission-ready SAS programs
  - System macros create standalone code
  - Code looks good because it is machine-written
  - Use PROC COMPARE to verify that standalone programs accuracy create the SDTM datasets

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Challenges

- Incomplete Analysis Data
  - Have to go back to raw data for domains/variables not covered by analysis data
    - Example: Inclusion/Exclusion
- Incomplete Raw Data
  - If annotated CRF is unavailable, it may be difficult to determine what certain raw data actually represent.
  - Data quality issues:
    - was the data cleaned?

Challenges (continued)

- Trial Design and Subject domains
  - Trial Design and Subject domains have to be created manually
- ADaM
  - Ideally, ADaM data are created from SDTM data
  - For derived variables already in analysis datasets, recreate them, then use original variables for validation

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Summary

- Messy legacy studies require a lot of data management expertise before automated methods can be used
- Metadata is the key for successful automation
- Off-the-shelf tools can provide a powerful ETL solution