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# CDISC SDTM
# &
# Standard Reporting

***One System***

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# Authors/Contributors

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# Merck Background

- Biostatistics and Statistical Information Systems (BASIS)
  - Statistics Organization in Clinical Development Programs
  - Provides statistical and programming support for the design, analysis, and reporting of clinical trials data for approved drugs
  - Results used in publications and promotions
    - Some support for Registration (sNDAs)

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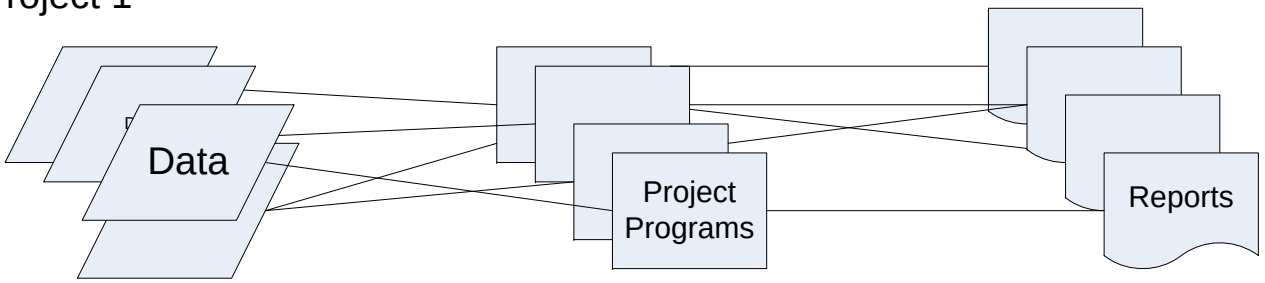
# Legacy Process

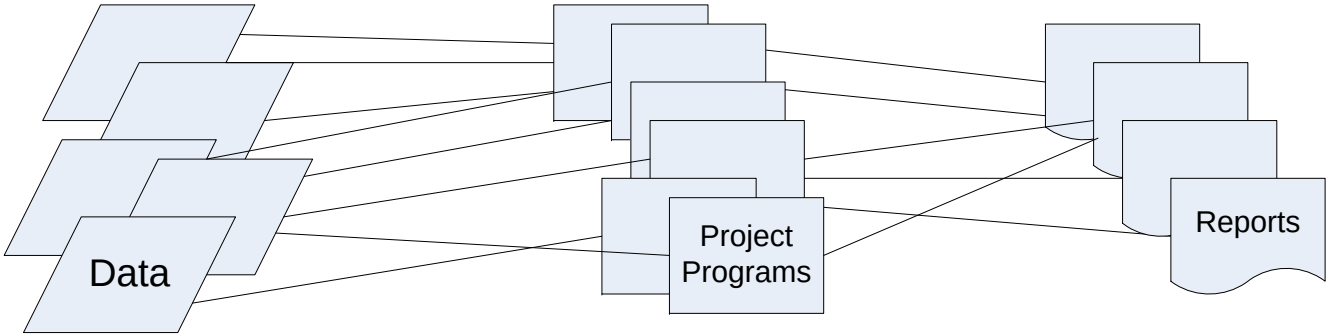
- Data in disparate databases and structures
- Multiple versions/sets of programs to generate Tables and Listings (T&Ls)
- Distinct processes for Analysis & Reporting (A&R)

# Legacy Process

Project 1




Project 2




… etc.

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# Legacy Process (continued)

- Challenges:
  - Combining and reporting data across studies
  - Inefficient Process:
    - Resource burden of maintaining multiple reporting tools, programs, validation, etc.
    - Sub-optimal process for response to requests for additional Strategic Analyses
      - e.g. sub group analyses with classifications and covariates

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# BASIS A&R Vision

- "One-step away from knowledge" statistical analysis and reporting process

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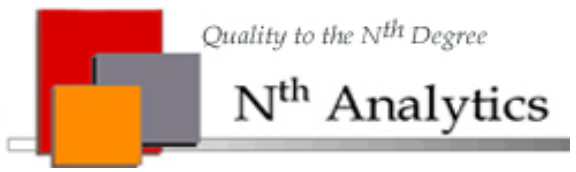
# BASIS A&R Strategic Goal

- A common (SAS-based) platform
- A Structured Data Model
- Access to all clinical trial data independent of time, place, database, or compound
- One-step away access to data for statistical analysis and reporting to any level of complexity



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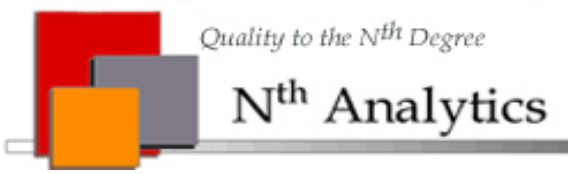
# Vision & Strategic Goal Implementation

- Unified A&R Environment
- Standard SAS Dataset Model
  - Independent of Data Source/System
  - Define a structured analysis data model
  - Metadata-driven
    - All derivations at dataset level
  - Standardized by Therapeutic Area
    - but allows for customization
  - Standard Code and Template Library to generate datasets, T&Ls



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# New A&R Process Advantages

- Easy to combine data across studies
- Unified (integrated) A&R process
- Reusable, standard code for datasets and T&Ls
- Easy to maintain, validate, and update

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# New A&R Process Advantages

- Optimal process for addressing additional requests for strategic analyses
- Proactively anticipate and plan for additional requests
- Easily respond to unanticipated requests

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# Nth Analytics Solution

- Part I - An ETL Process to generate CDISC SDTM+ datasets
- Part II – A Generic Table System to generate standard Merck reports from the SDTM+ datasets

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# Nth Analytics Solution

- ETL procedure to create CDISC SDTM datasets
  - Maps source data into SDTM domains
  - Provides an automated method for specifying data sources and algorithms
  - Provides all information required for the FDA-mandated “DEFINE.PDF”

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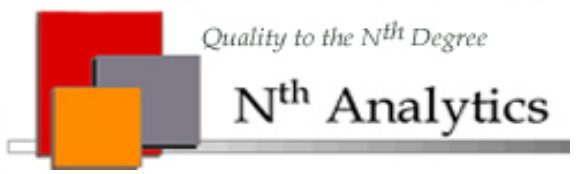
# Why Choose SDTM?

- SDTM adoption approaching critical mass
- Standard data structure simplifies reporting
- Merck is adopting CDISC standards
- Issues:
  - SDTM structures exclude derived variables
  - ADaM not finalized
  - Need to include all variables collected



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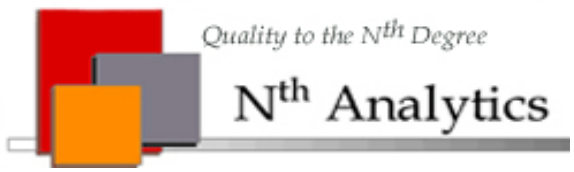
# What About ADaM?

- ADaM is an evolving standard
  - not finalized in Aug 2004
  - adoption would have been premature
- Some ADaM principles were applied:
  - Build on SDTM structures
  - One PROC away
  - SAS dates, not ISO dates
  - Numeric codes for sorting



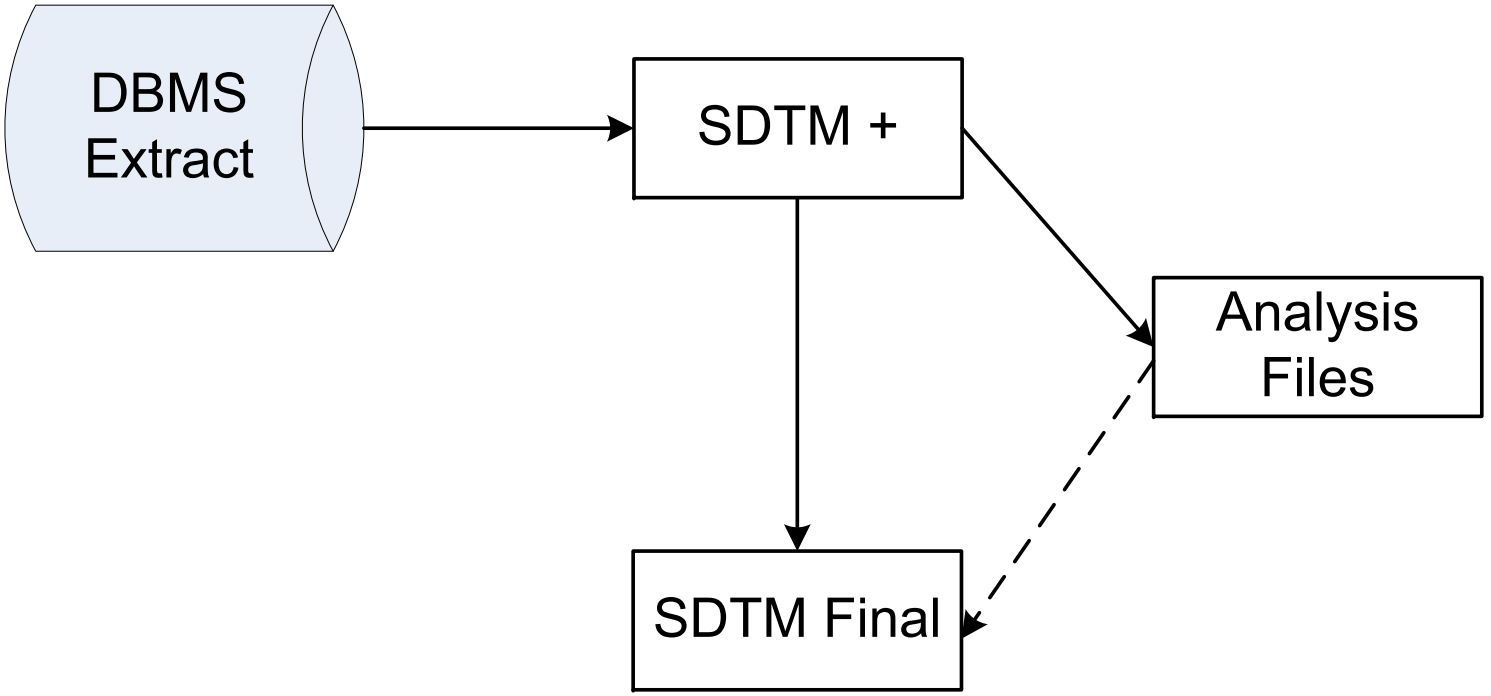
# Special Considerations

- In determining a solution, there were some special considerations:
  - Studies not intended for submission
  - Full CDISC compliance not critical
    - Unless studies are included in a submission
  - Focused reporting objectives

# Possible Implementation Strategies

- Parallel method
  - develop SDTM and analysis data simultaneously
- Retrospective method
  - develop analysis data first, then derive SDTM from the analysis data
- Linear method
  - develop SDTM first, then create analysis data from SDTM

# Hybrid Method



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# Hybrid Method - Advantages

- Analysis file programs are useful to reviewer and as documentation
- Encourages standardization of analysis datasets
- Variables or records in SDTM that need statistical input can be obtained from analysis files
- Derived records or supplemental variables can be easily added to SDTM if needed or desired
  - Disposition events
  - Population flags

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# Possible Implementation Strategies (cont.)

- Hybrid method
  - "SDTM+ conforms to standards but may not be complete with respect to variables or records that need clinical or statistical input or other permitted variables"
  - "May contain non-SDTM variables needed for analysis"

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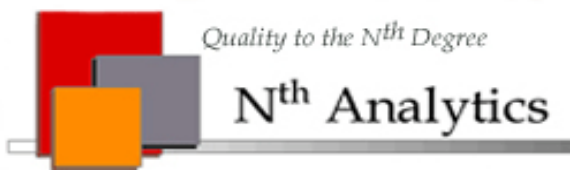
# SDTM+ to SDTM Final – Submission Ready

- Changes related to submission:
  - Drop non-SDTM variables
    - automated process because these variables are flagged in metadata
  - Create trial design datasets
  - Create RELREC, SC, SUPPQUAL
  - Create ISO dates/times
    - SAS formats make this easy to automate



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# Preparing for Submission

- The SDTM+ datasets are the source for ADaM datasets
- Easily convert SDTM+ to submission-ready SDTM datasets
- Documentation = mapping table
- Standalone submission-ready programs built-in

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# Nth Analytics Solution - Reporting

- STDM+ simplifies reporting
- Generic Table System
  - Calling programs use SAS Macros to generate standard reports from SDTM+
  - Achieves standardization, and is easy for programmers to use

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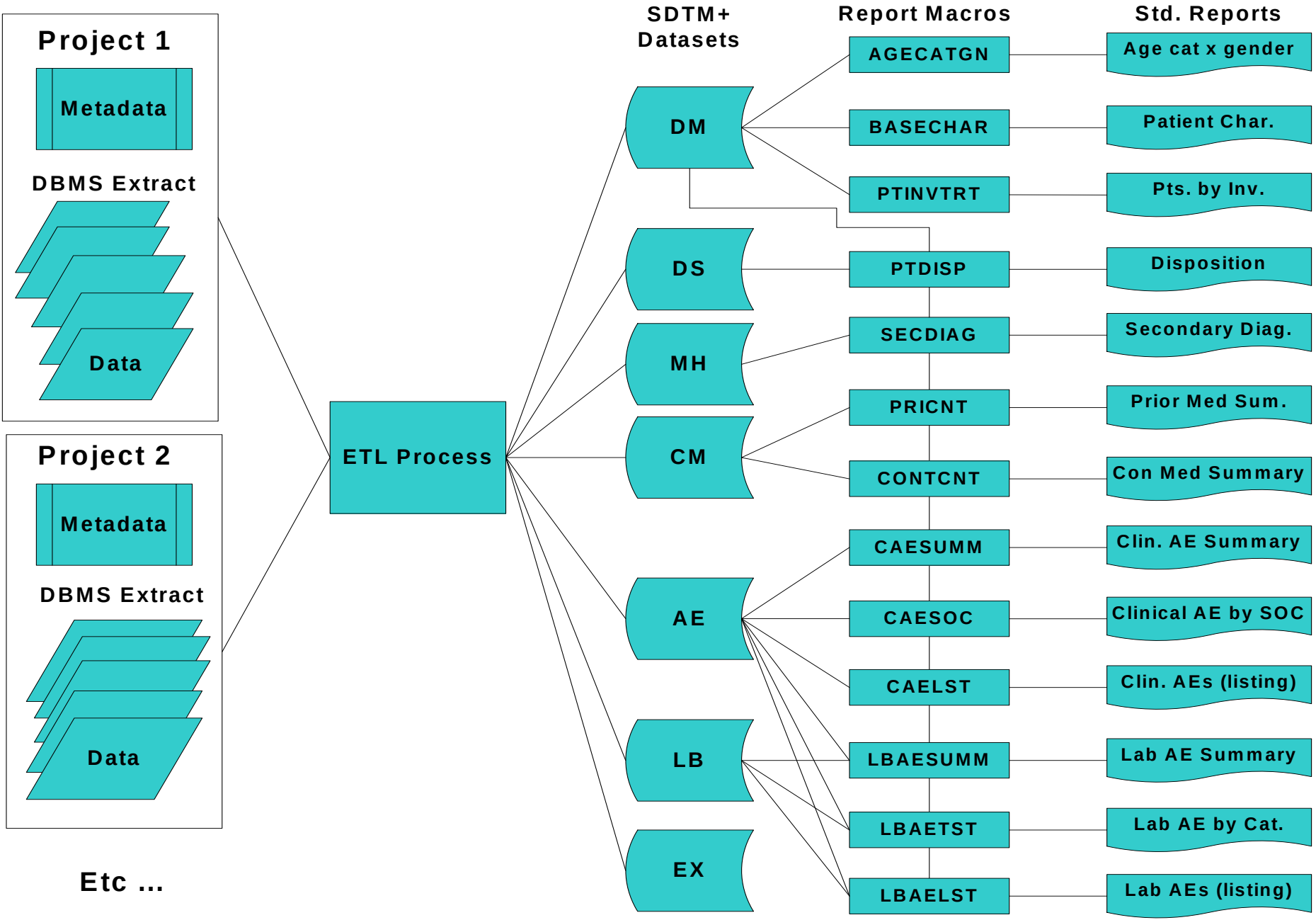
# Implementation Methodology



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# Nth Analytics Solution

- Why this approach worked for Merck
  - Did not disrupt existing clinical trial systems
  - It can be applied to legacy data
  - Minimal rework
    - only metadata will change for each study

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# Nth Analytics Solution

- Why this approach worked for Merck (cont.)
  - Table driven metadata provides automatic documentation
  - Effort to produce subsequent SDTM files is minimized
    - only study-specific situations require additional coding

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# Merck - Implementation

- Tool has been installed and used for 8 studies in 3 Therapeutic Areas
  - Multiple eDC versions with different structures
- Currently being used in 5 ongoing studies
  - 2 CRO studies
  - 2 eDC systems

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# Adoption with New Studies

- Minor customization for new studies
  - Mapping table process
  - Macros
  - Preprocessing code allows for further customization

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# Merck - Benefits

- Increased efficiency by over 50%
  - Reduced programming time, resources
  - Limited validation effort
    - standards
    - single reporting system
- All T&Ls delivered within 5-10 days from DB lock

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# Merck Benefits - (continued)

- Consistency in A&R ground rules
- Standard data exchange protocol
  - transparent and portable
- Timely response for Strategic Analyses and *ad hoc* requests

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