

One Model to Rule Them All... and in the Trial Bind Them

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Agenda

- One Model...?
- Considerations
- Implementation Approach
 - SDTM
 - ADaM
- Conclusion, Learnings and Reflections

Challenges in implementation and governance

- External
 - Multiple operational data model / implementation guide versions
 - SDTM 1.3 + SDTM IG 3.1.3
 - SDTM 1.4 + SDTM IG 3.2
 - [SDTM 1.7 + SDTM IG 3.3](#)
 - ADaM 2.1 + ADaM IG 1.1 + ADaM OCCDS 1.0
 - Define-XML 1.0 / 2.0 / [2.1](#)
 - Controlled Terminologies
 - CDISC SDTM/ADaM CT
 - MedDRA / WHODrug / WHODrug Global / UNII / SNOMED / MED-RT / LOINC
 - Conformance Guide / Rules
 - FDA Technical Conformance Guide / Technical Rejection Criteria for Study Data
 - PMDA Technical Conformance Guide on Electronic Study Data Submissions

Challenges in implementation and governance

- Internal
 - Cross organisational process chain
 - SDTM is governed in Data Management
 - ADaM is anchored in Biostatistics
 - Diverse project and trial specific needs across therapeutic areas
 - Diabetes
 - Haemophilia
 - Growth disorders
 - Obesity



Considerations – data models

'Rigid' SDTM



- Explicitly defined
- Complete definition – domains and variables
- Operational implementation guide
- Designed to streamline processes in managing and use of collected data

'Elusive' ADaM



- Room for interpretation
- Only provided with core building blocks
- Limited operational information
- Designed to be flexible in response to hypotheses defined in protocol

Considerations - organisational structure

Data Management handles SDTM

- domain definitions
- mapping rules
- controlled terminology
- CRFs

Biostatistics handles ADaM

- dataset definitions
- controlled terminology for analysis datasets

One Model to rule them all...

Is it achievable?

One Model approach

- NN SDTM Master Model / NN ADaM Master Model
 - Ensure end-to-end implementation throughout the organisation
 - Contain **maximum allowed contents** as a result of thorough end-to-end assessment for **SDTM – core contents** for **ADaM**
 - CDISC compliance
 - Authorities requirements
 - Traceability
 - Operationality

Master Model Change Log											
Change ID	Title	Impact Analysis									Other
		SDTMIG/TAUG reference	Controlled Terminology	Topic Code Linkage	Global Annotation	Global Mapping	NNIG	SDRG	Standard Program	P21 Config File	
MM-058	Update keys for TI										
MM-059	add nn_internal variables to support										
MM-060	Update label of RS domain	SDTM IG 3.3 (draft)						standard explanation required			

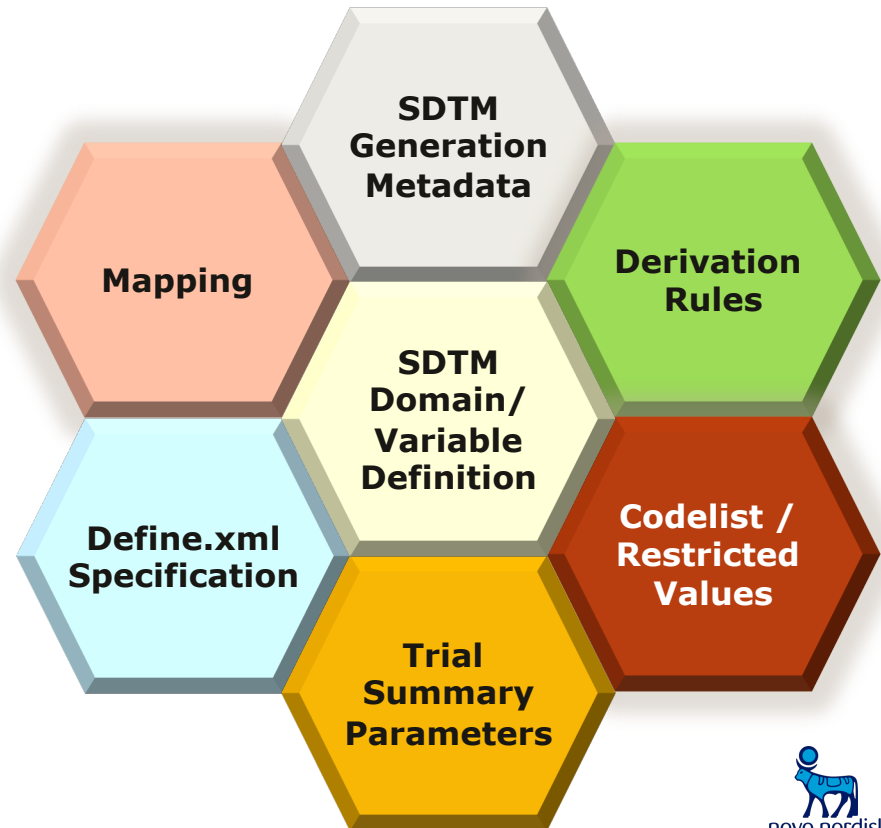
One Model approach

- NN SDTM Master Model / NN ADaM Master Model
 - Aligned with SDTM / ADaM Implementation Guide versions
 - Version-controlled: capture changes in requirement and usage over time
 - Maintain only one active version of an NN Master Model at a time
 - Reduce maintenance effort and complexity of use
 - Retired versions of NN Master Models remain functional

- ▼ cdisc-adam-2.1
 - cdisc-adam-2.1-nn06p
 - cdisc-adam-2.1-nn07
 - cdisc-adam-2.1-nn08
 - cdisc-adam-2.1-nn09
- ▼ cdisc-sdtm-3.1.3
 - cdisc-sdtm-3.1.3-nn03
 - cdisc-sdtm-3.1.3-nn04
 - cdisc-sdtm-3.1.3-nn05
- ▼ cdisc-sdtm-3.2
 - cdisc-sdtm-3.2-nn01
 - cdisc-sdtm-3.2-nn02
 - cdisc-sdtm-3.2-nn03
 - cdisc-sdtm-3.2-nn04
 - cdisc-sdtm-3.2-nn05
 - cdisc-sdtm-3.2-nn06

NN SDTM Master Model

- An operational model for SDTM automation made possible by the *rigidity* of SDTM data model
- Combining SDTM data model with operational metadata for system integration
 - Well-established clinical metadata repository
 - Frontloaded trial metadata

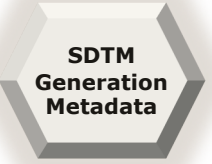


NN SDTM Master Model



SDTM Domain/ Variable Definition

- Definitions of the maximum allowed contents, i.e. domains and variables used in NN



SDTM Generation Metadata

- Parameters that lever the programming framework
 - Stage, standard program version and build order
 - Trial-level adjustment



Mapping

- Specifications of whether data mapping drives the creation of domains and/or variables



Derivation Rules

- Domain- and variable-level data derivation information e.g. age, calibration of normal ranges

NN SDTM Master Model



Codelist / Restricted Values

- Definition of CDISC and sponsor-defined controlled terminologies
- For variables with restriction values, e.g. --BLFL, the allowed values are explicitly specified



Trial Summary Parameters

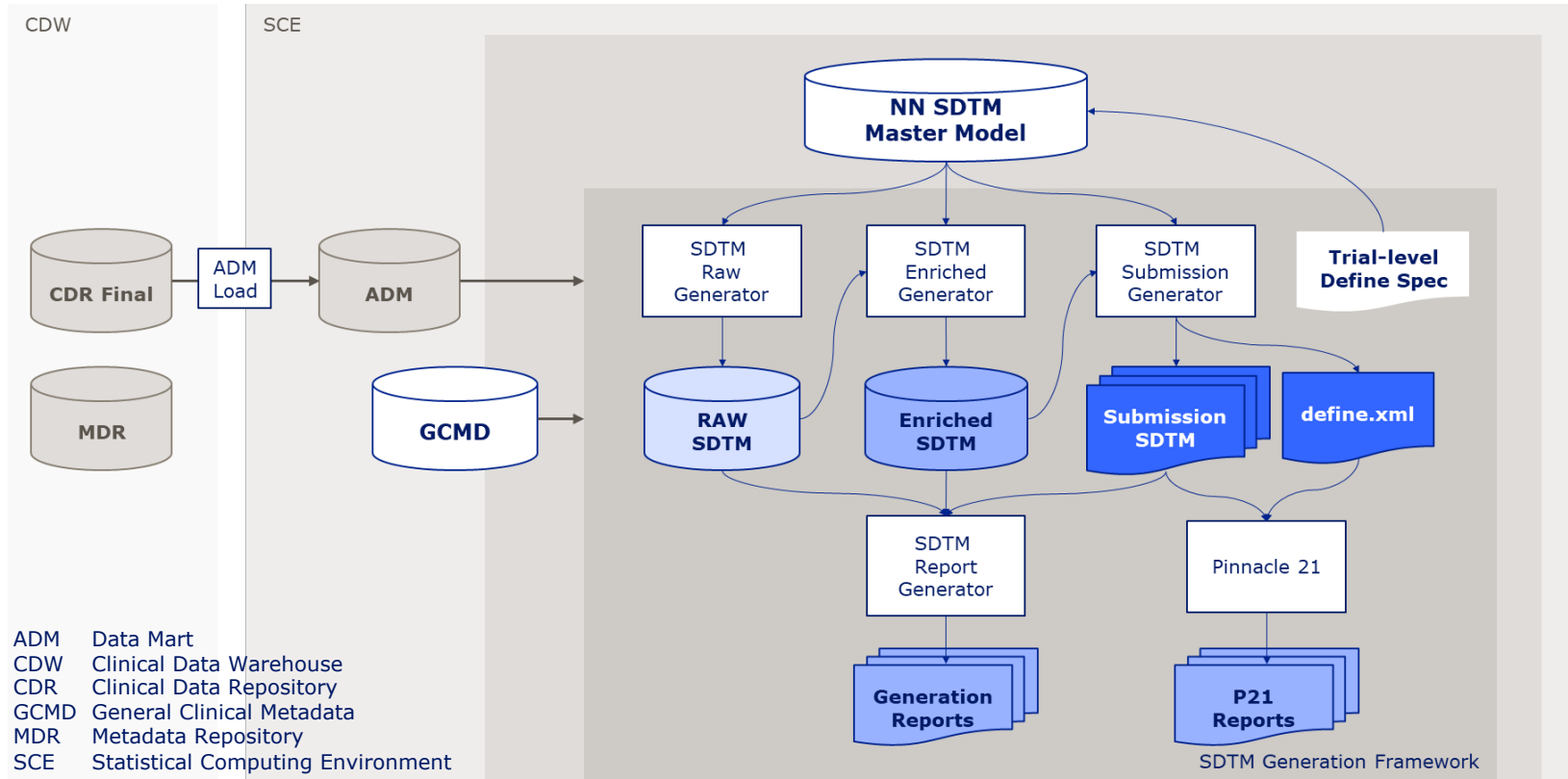
- Definitions of parameters to be created in the Trial Summary domain



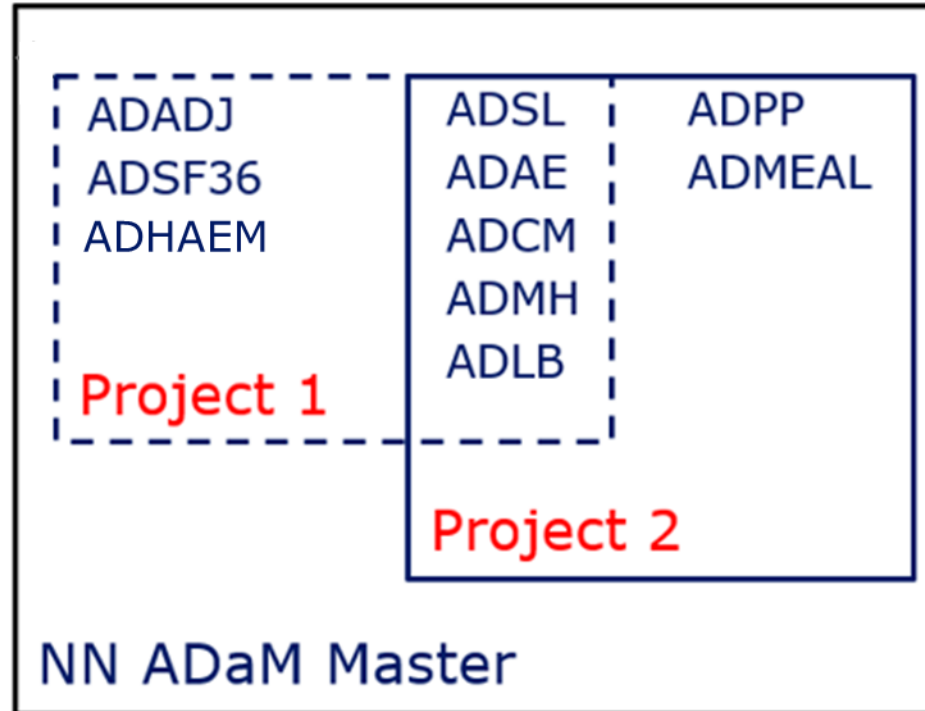
Define.xml Specification

- **Guidance** specifications for define.xml generation
 - KEYS and COMMENT at domain level
 - ORIGIN, ALGORITHM and COMMENT at variable level
 - value-level metadata definition

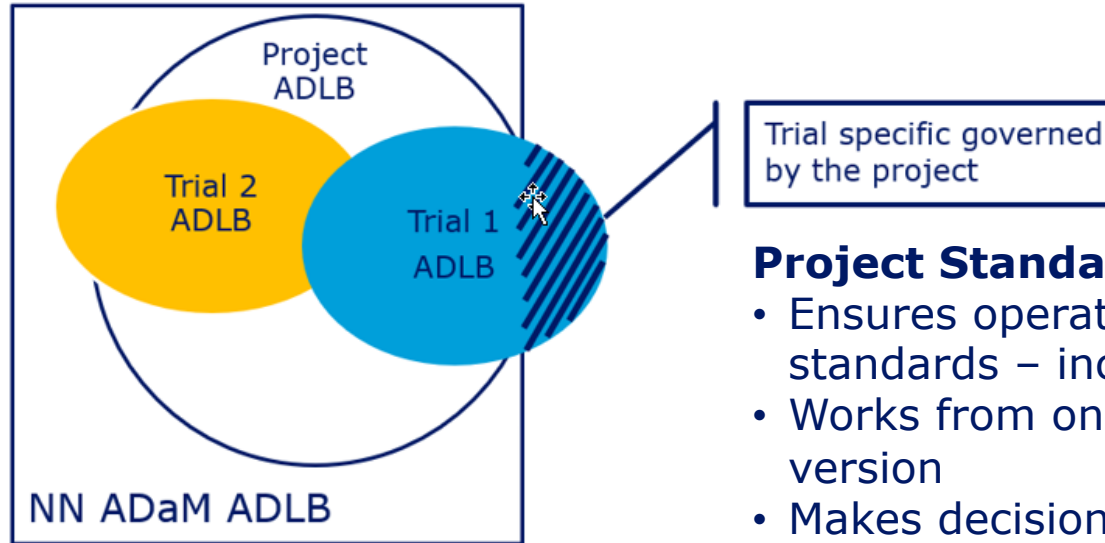
NN SDTM Master Model



SDTM versus ADaM at the project level



ADaM trial definitions



ADaM Global Standard Team

- Ensures long-term control of the NN standard
- Updates the Master bi-annually

Project Standard Team

- Ensures operational control of project standards – including project ADaM definition
- Works from one selected NN ADaM Master version
- Makes decision about trial specific ADaM variables not relevant for the NN ADaM Master

ADaM Master Model

ADaM
Dataset/
Variable
Definition

- Definitions of the maximum cross-project relevant contents, i.e. datasets and variables used in NN

Codelist /
Restricted
Values

- Definition of CDISC and sponsor-defined controlled terminologies

Define.xml
Specification

- **Guidance** specifications for define.xml generation
 - KEYS and COMMENT at dataset level
 - at variable level for
 - ORIGIN, some for ALGORITHM and COMMENT

~~Generation
Metadata~~

~~Mapping~~

~~Trial
Summary
Parameters~~

~~Derivation
Rules~~

Supporting material

CDISC I.G. Supplements

NN SDTM

Implementation

Guide

NN ADaM

Implementation

Guide

- 1 Introduction
- ✓ 2 Fundamentals of the ADaM Model
 - 2.1 Fundamental Principles
 - 2.2 Traceability
 - ✓ 2.3 The ADaM Data Structures
 - 2.3.1 The ADaM Subject-Level Analysis Dataset (ADSL)
 - 2.3.2 The ADaM Basic Data Structure (BDS)
- ✓ 3 Standard ADaM Variables
 - NN Core Variable
 - ✓ 3.1 ADaM Variable Conventions
 - 3.1.1 Generable Variable Conventions
 - 3.1.2 Timing Variable Conventions
 - 3.1.3 Date and Time Imputation Flag Variables

One Model to Rule Them All

- SDTM and ADaM reach the objective by two different methods
 - Rigid SDTM
 - 'One Model' is a definite term that applies strictly across projects and trials
 - Elusive ADaM
 - 'One Model' applies to the project level with 'optional' features
 - The protocol drives the ADaM definition at the trial level

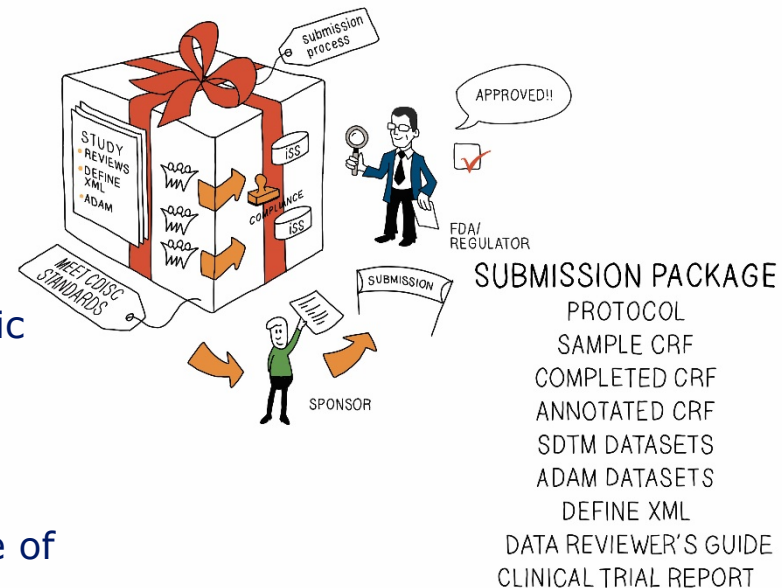
...and in the Trial Bind Them

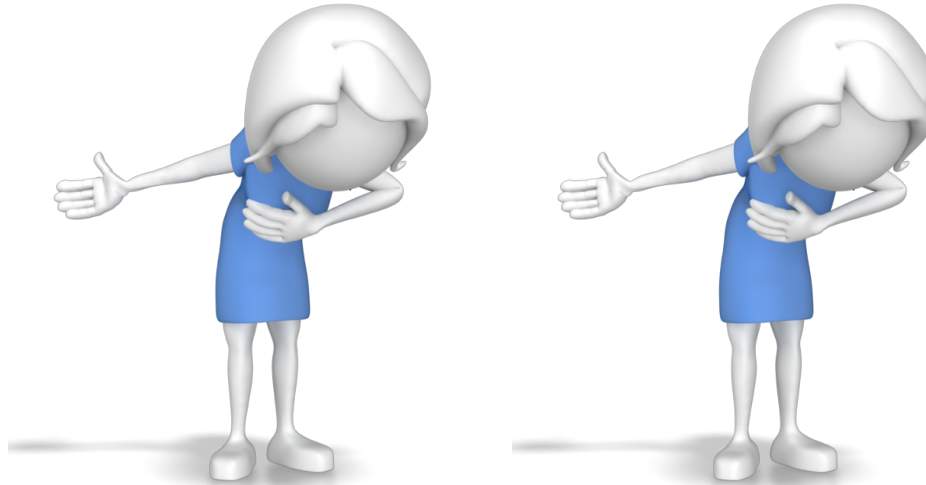
Learnings and reflections

- Governance standard implementation reflects organisational structure, size and diversity of therapeutic areas
- Resource-intensive task
 - Coordination between standard teams
 - Harmonisation in use of SDTM and ADaM
 - SDTM: dependency and traceability amongst systems and standards
 - ADaM: balance between general guidance and project-specific use

Learnings and reflections

- Benefits
 - Consistent end-to-end implementation throughout organisation
- SDTM:
 - Established an explicit guideline for use
 - Automation frees up resources for trial-specific details
- ADaM:
 - Supports alignment in dataset design and use of ADaM concepts.
 - Encourages project planning for data pooling and integration





Thank you for your attention !