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SDTM and define.xml automation made easy

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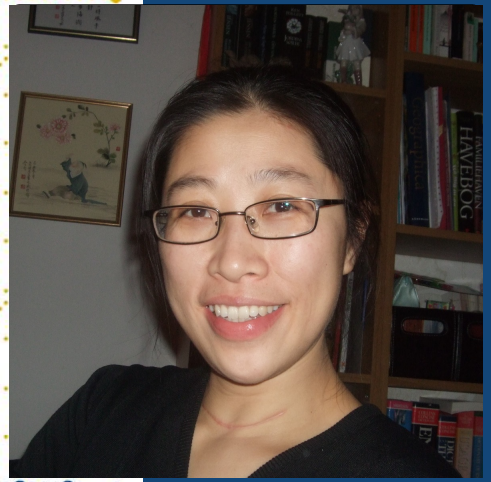
Hanne van Kints, Principal Standards Specialist, Novo Nordisk A/S

Meet the Speakers



Vicky Poulsen

Title: Principal Standards Specialist

Organization: Novo Nordisk A/S

Joined Novo Nordisk A/S in 2015 after being a SAS consultant for a decade in the public health sector specialising in End-to-End BI solutions. She participated in the CDISC Implementation Project shortly after. In her present position, Vicky leads the standard programming strategy and development efforts that drive the SDTM Generation Framework for SDTM and define.xml automation.

Hanne van Kints

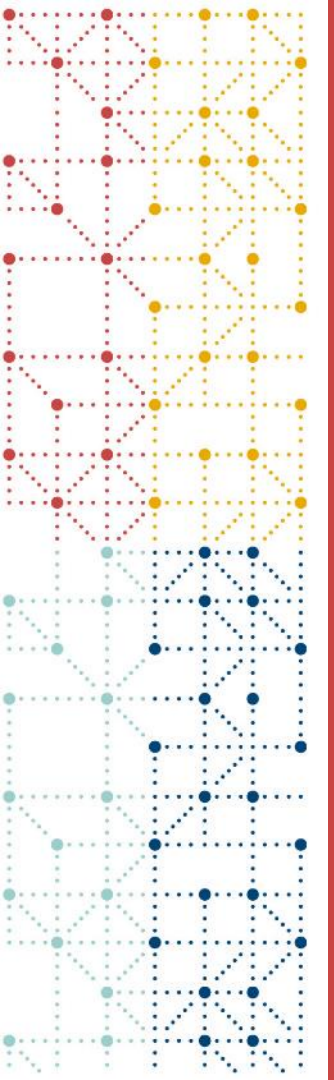
Title: Principal Standards Specialist

Organization: Novo Nordisk A/S

Hanne van Kints has more than 30 years' experience within the pharmaceutical industry and data management. She has worked across all areas within data management and has participated in several IT and business improvement projects. She is supporting end-to-end standardisation, CDISC SDTM implementation, use of DMW and other CDMS systems.

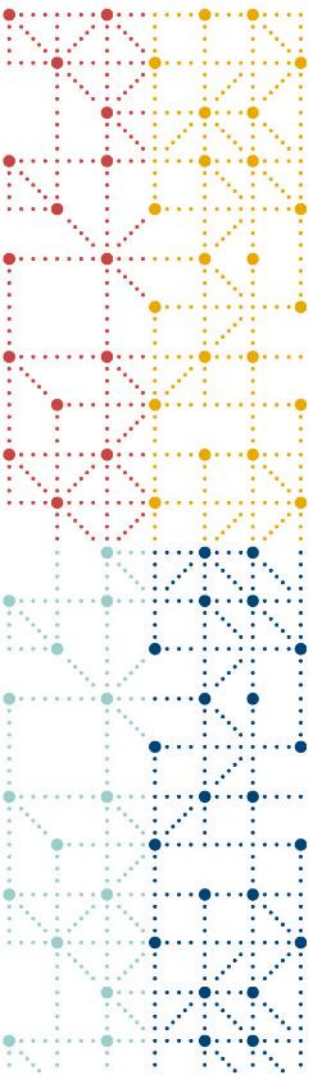
Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the authors' and do not necessarily reflect the official policy or position of CDISC/Novo Nordisk A/S.*



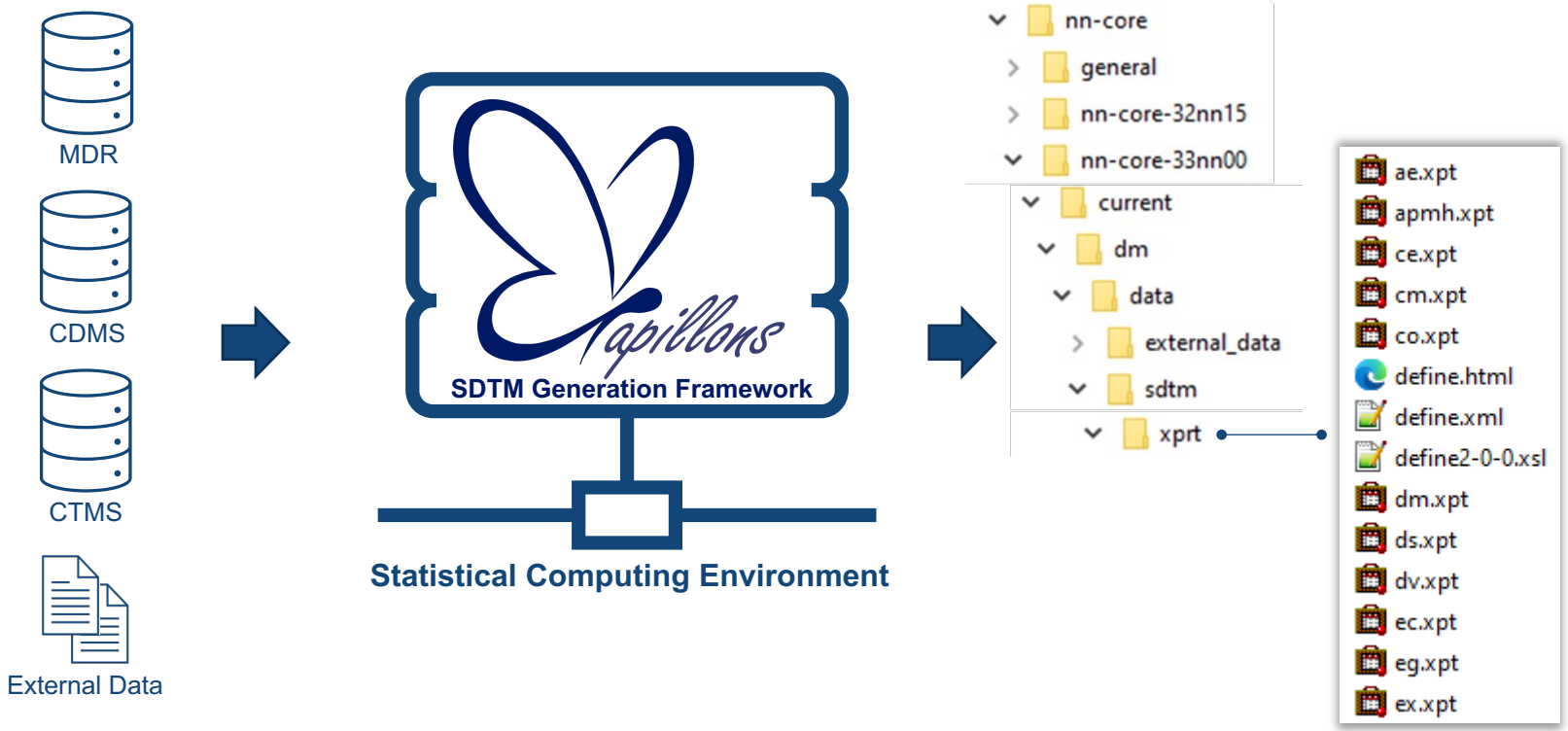
Agenda

1. Introduction
2. Metadata/Data-driven Approach
3. SDTM Generation Framework
4. Standards Governance
5. Conclusion and Outlook

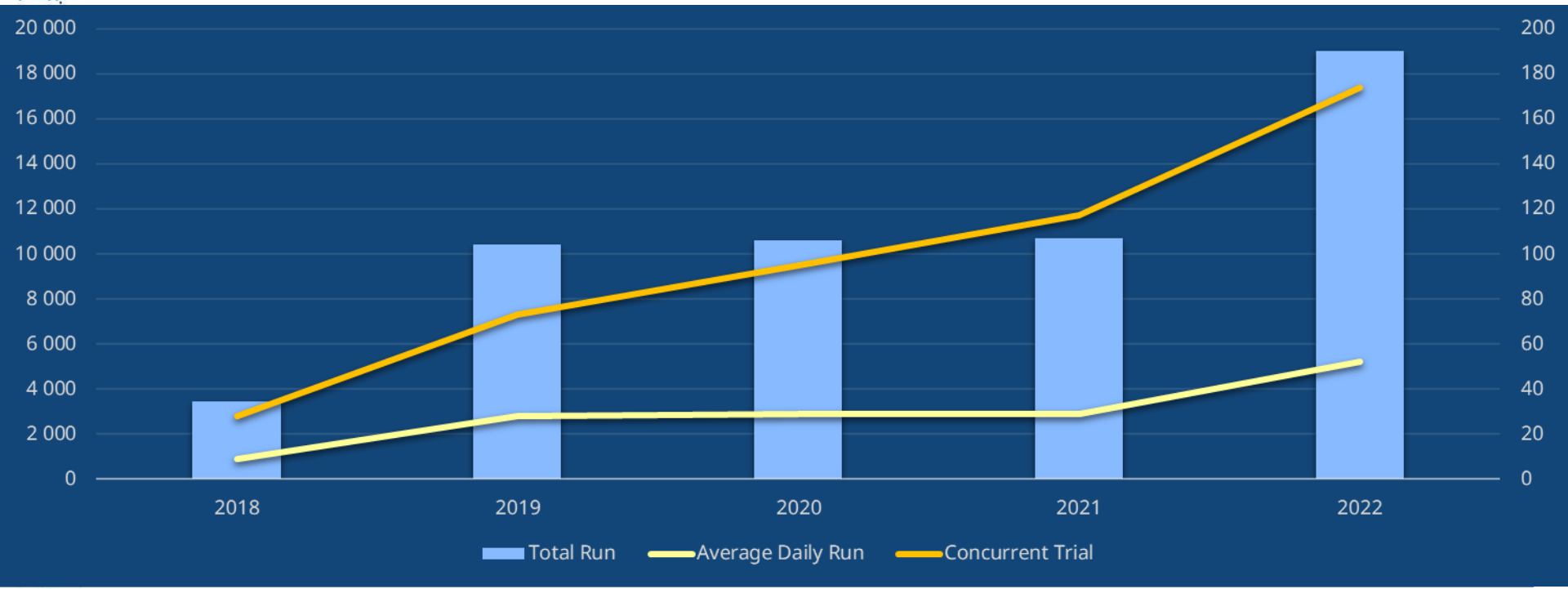


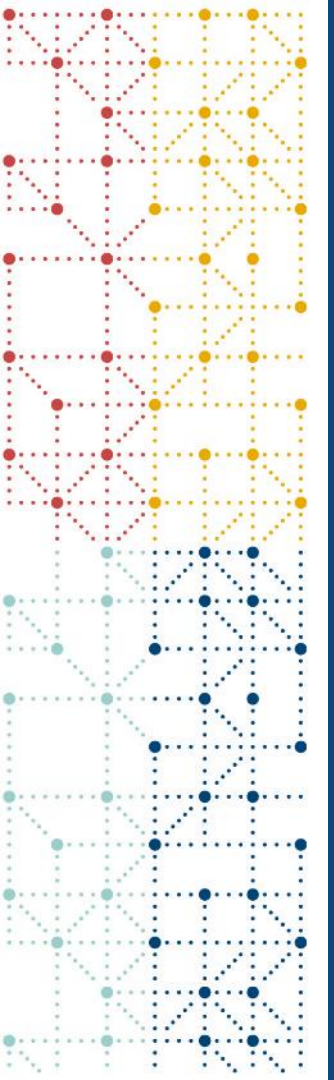
Introduction

Automated SDTM and define.xml Generation



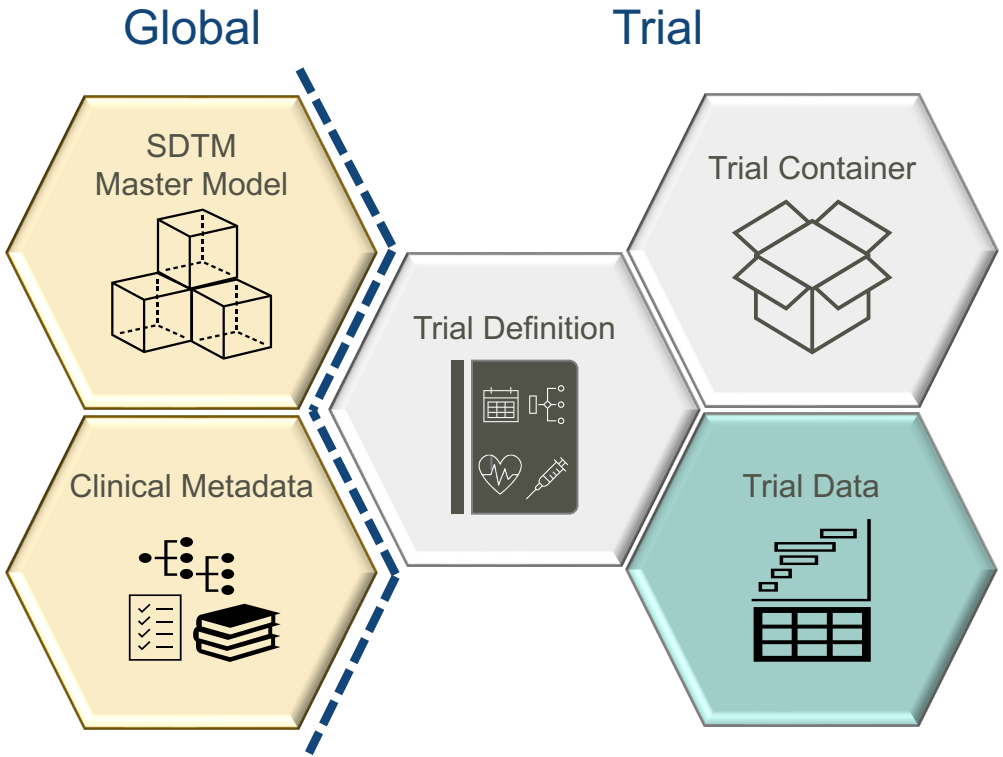
Implementation Timeline





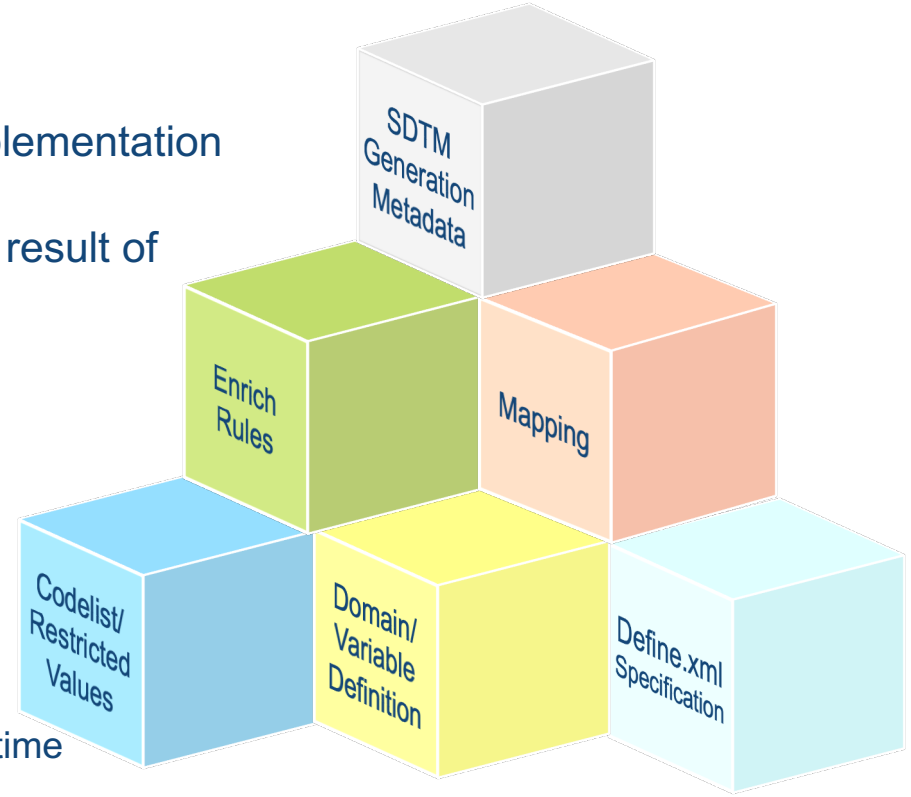
Metadata/Data-driven Approach

Metadata/Data-driven Approach



SDTM Master Model

- NN's approach to standardise SDTM implementation per SDTMIG version
- Contain maximum allowed contents as a result of thorough end-to-end assessment
  - CDISC compliance
  - NN specific implementation
    - Custom domains
    - Non-Standard Variables (NSV)
  - Authorities' requirements
  - Traceability
  - Operationality
- Version-controlled
  - Changes in requirements and usage over time
  - Reproducibility



SDTM Master Model: Domain Definition

Fixed | SDTMIG | Custom

basic_st	Table	Label	Keys	SortKeys	map_domain_fl	suppl_qual_fla	include_in_raw	gen_raw_seqno_fl	extended_doma	enrich_build_orde
Y	DS	Disposition	STUDYID USUBJID DSSTDTC DSDECOD DSTERM	STUDYID USUBJID DSSTDTC DSDTC DSDECOD DSTERM	Y	Y	Y	Y		120
Y	LB	Laboratory Test Results	STUDYID USUBJID LBTESTCD LBSPEC VISITNUM LBTPTNUM LBTPTREF		Y	Y	Y	Y	XL	250
Y	SE	Subject Elements	STUDYID USUBJID SESTDTC SEENDTC ETCD							50
	ZA	Event Adjudication Results	STUDYID USUBJID ZATESTCD ZAOBJ VISITNUM ZATPTNUM ZATPTREF		Y	Y	Y	Y		460

CLASS_COLUMNS | REFERENCE_TABLES | REFERENCE_COLUMNS | REFERENCE_TSPARMS | REFERENCE_ENRICH

- Keys
- SortKeys
- Enable CDMS mapping
- Include in RAW SDTM generation
- Supplemental Qualifiers dataset
- Extended domain
- Build order in Enriched SDTM Generation

SDTM Master Model: Variable Definition

Fixed | SDTMIG | Custom

basic_s	table	columr	order	xmlcodelist	xmlcodelist_multi	origin	term	algorithm	map_var_flag	fixed_mapping	include_in_rav	nn_interna
	APDM	SEX	190	SEX		Assigned	(SEX)		Y		Y	
	APDM	RACE	200	RACE			(RACE)		Y		Y	
	APDM	ETHNIC	210	ETHNIC		CRF	(ETHNIC)		Y		Y	
	APDM	COUNTRY	220	COUNTRY		Assigned	ISO 3166					
	DM	ON_GRP	10							src.src_random_grp	Y	Y
Y	DM	**STUDYID**	20			Assigned			•	src.trl_id	Y	
Y	DM	DOMAIN	30			Assigned	DM		•		Y	

CLASS_COLUMNS | REFERENCE_TABLES | **REFERENCE_COLUMNS** | REFERENCE_TSPARM

basic_s	table	columr	value_lvl_where_col	value_lvl_label_col	value_lvl_collect_ct_val	value_lvl_ct_cdlist_id_col	enrich_build_order	enrich_rule	xmlcodelistvalue
Y	DM	RFXENDTC					10	sdtme_dm_rfdts_v$$	
Y	DM	RFICDTC					10	sdtme_dm_rfdts_v$$	
Y	DM	RFPENDTC					10	sdtme_dm_rfdts_v$$	
Y	DM	DTHDTC					40	sdtme_dm_dth_v$$	
Y	DM	DTHFL					40	sdtme_dm_dth_v$$	Y
Y	DM	SITEID							
Y	DM	INVID							

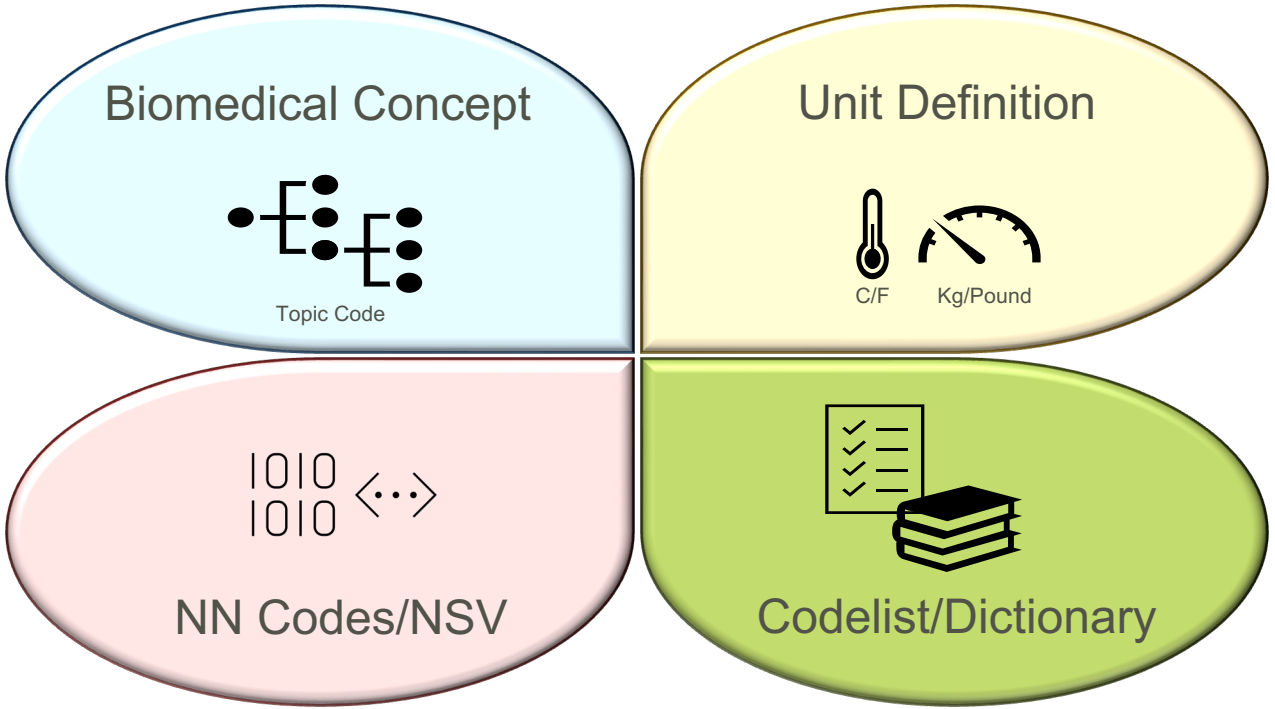
SDTM Standard Program

CLASS_COLUMNS | REFERENCE_TABLES | **REFERENCE_COLUMNS** | REFERENCE_TSPARMS

- Order
- Codelist/restricted values
- Origin
- Algorithm
- Comment

- Enable CDMS mapping
- Include in RAW SDTM generation
- Value-level Metadata
- Enrich Rule

Global Clinical Metadata

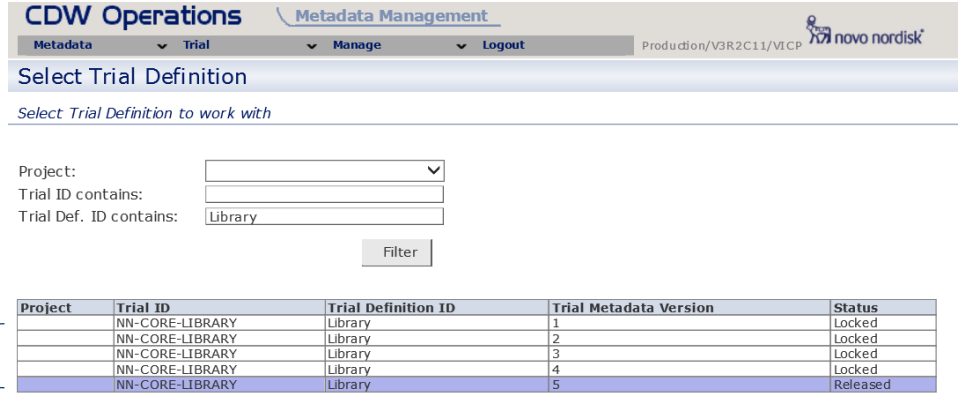


Trial Definition

A Collection of Trial Metadata

- Flowchart
- Trial Attributes
- Trial Population
- Trial Design
  - Arm
  - Element
  - Epoch
- Trial Summary Parameters
- Intervention: Compound
- Visit structure

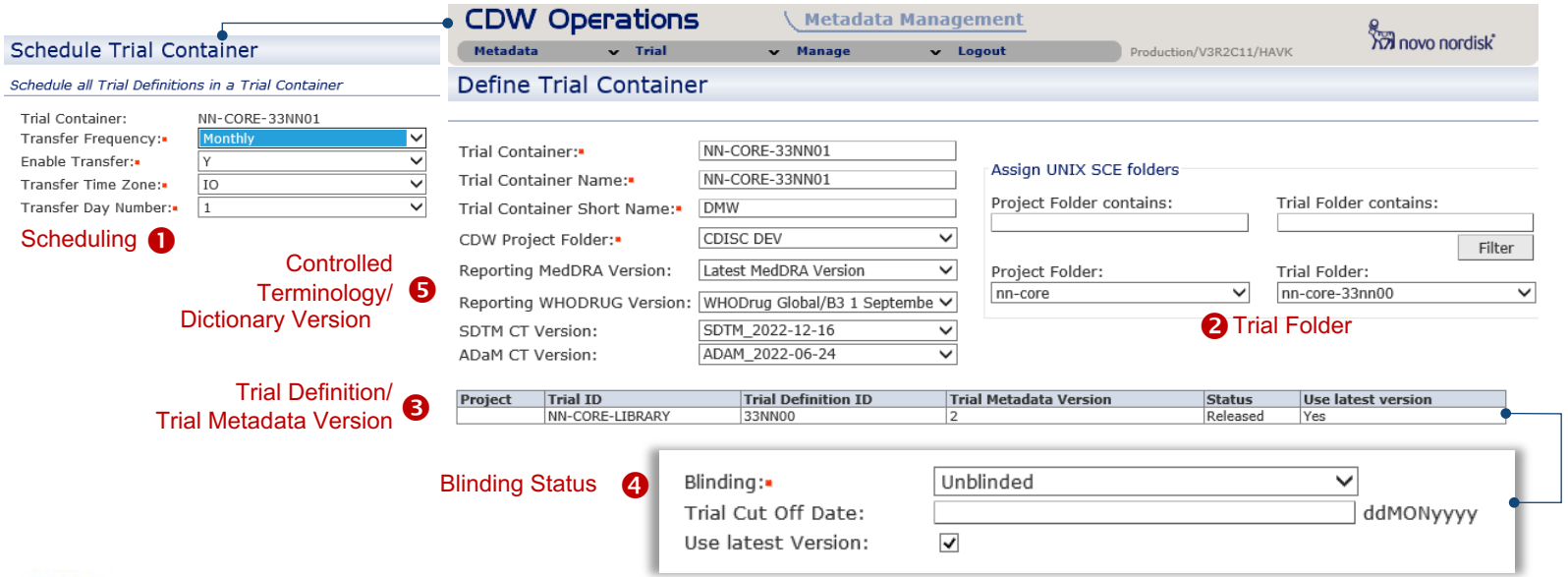
- Version control: Trial Metadata Version



- Lock Trial Metadata Version at key milestones for traceability e.g. Protocol Approval, DBL

Trial Container

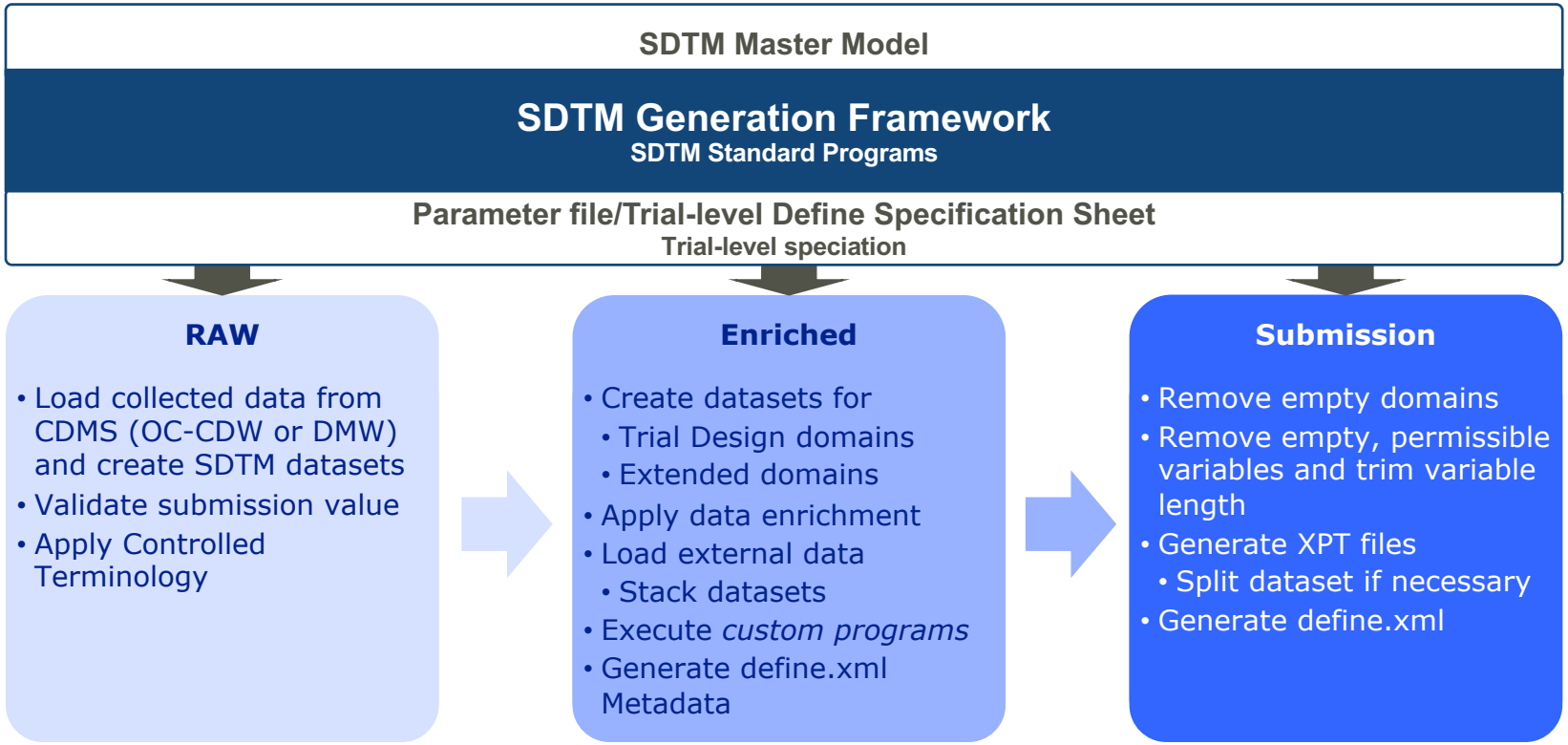
- Trial Container holds **trial-level operational metadata** required for **transfer of clinical data/trial metadata from CDMS/MDR to SCE** for automated SDTM and define.xml generation



SDTM Generation Framework

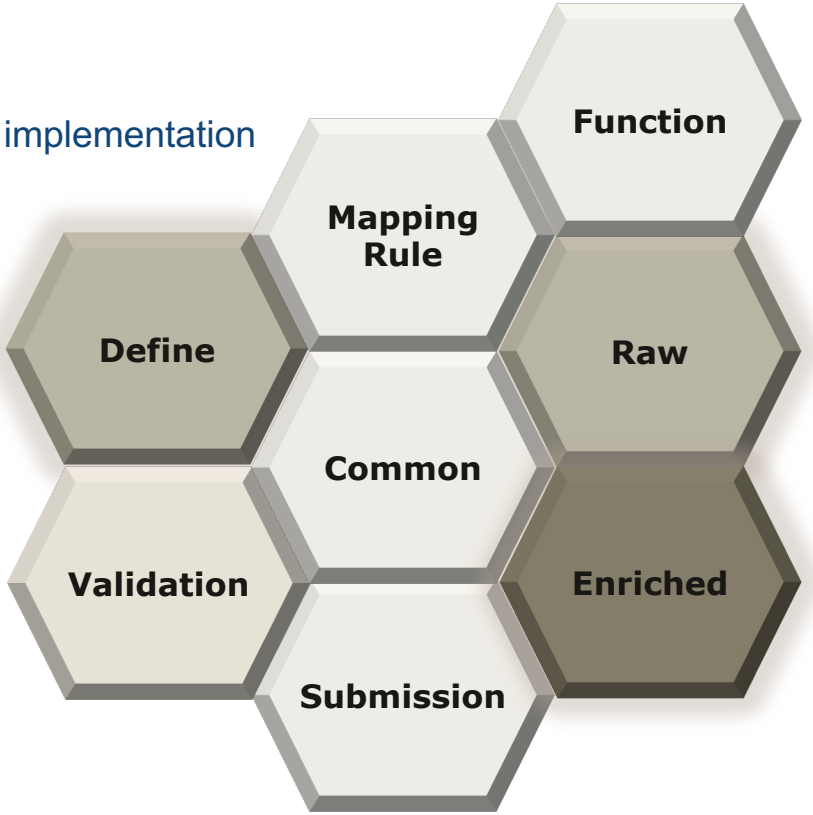
Statistical Computing Environment

SDTM Generation Stages

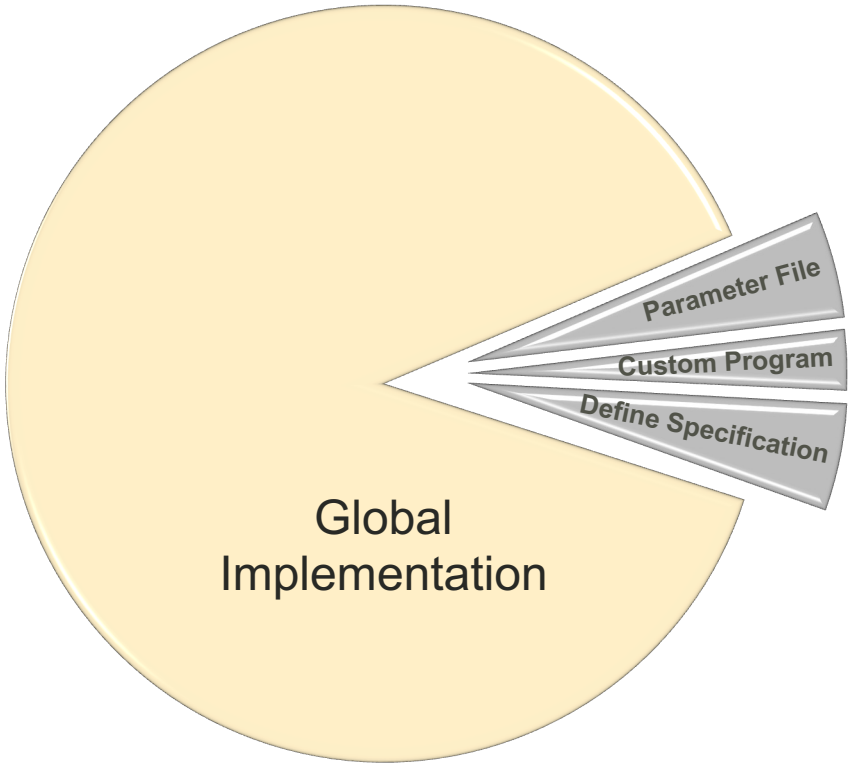


SDTM Standard Programs

- Component-based Design
  - Governed and maintained centrally for global implementation
- Metadata/Data-driven code automation
  - **SDTM Master Model**
  - Global Clinical Metadata
  - Parameter file
  - Trial-level Define Specification
- Plus:
  - Robust
  - Maximise reusability and flexibility
  - Minimise maintenance
  - Versioning
- Minus:
  - Dependency between components
  - Increased complexity



Trial-level Leverage



Parameter File

Controls SDTM Generation

```
# Stages
raw             = Y             |stage
enrich          = Y             |stage
submit          = N             |stage
ocv             = N             |stage
#
# General parameters, for gcmd_version and sdtmuos_date (DBL date) the value must be in yyyymmdd format
gcmd_version    =               |param
sdtmuos_date    =               |param
optional_report = N             |param
#
# Specify columns to be excluded from DMW data extract (remove # when specifying value), use ! as separator
#dmw_excludecol  =               |param
#
# Trial Parameters
# - topicode_qnam: default to topicod, do not change/delete
# - lparm_topic1-: one per LPARM to Topic Code mapping, ! as separator
# - aetrtem_end_vis: treatment emergent end visits, (space) as separator
# - minrang: dummy lower reference range
# - maxrang: dummy upper reference range
# - elem_dostxt1-: one per EXLBMID to EXDOSTXT mapping, ! as separator
#
topicode_qnam   = topicod       |param
lparm_topic1    =               |param
aetrtem_end_vis =               |param
minrang         =               |param
maxrang         =               |param
elem_dostxt1    =               |param
#
# OCV Parameters
#
#Reference to OCV program version
cl_ocvprogversion  = p21e       |param
#
# End of parameter file.
```

Generation Stage

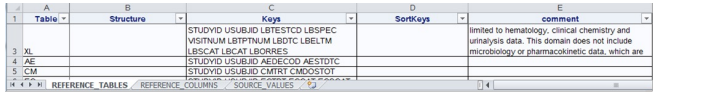
Parameter input to Standard Programs

Custom Program

Covers trial-specific requirements, such as special trial design

Define Specification

Table-/column-/value-level adjustments as supplement to SDTM Master Model



	A	B	C	D	E
1	Table	Structure	Keys	SortKeys	comment
3	XL		STUDYID USUBJID LBTESTCD LBSPEC VISITNUM LBTPTNUM LBDTC LBELTM LBSCAT LBCAT LBORRES		limited to hematology, clinical chemistry and urinalysis data. This domain does not include microbiology or pharmacokinetic data, which are
4	AE		STUDYID USUBJID AEDECOD AESTDTC		
5	CM		STUDYID USUBJID CMTRT CMDOSTOT		

REFERENCE_TABLES | REFERENCE_COLUMNS | SOURCE_VALUES

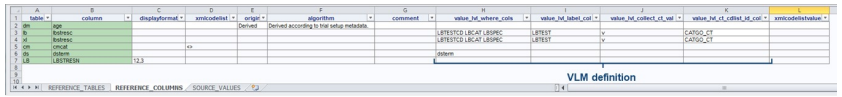
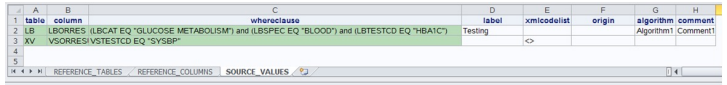


	table	column	displayformat	xmlcodelist	origin	algorithm	comment	value_lvl_where_cols	value_lvl_label_col	value_lvl_collect_ct_val	value_lvl_ct_cdlist_id_col	xmlcodelistvalue
2	dm	age			Derived	Derived according to trial setup metadata.						
3	lb	lbstresc						LBTESTCD LBCAT LBSPEC	LBTEST	v	CATGO_CT	
4	vi	lbstresc						LBTESTCD LBCAT LBSPEC	LBTEST	v	CATGO_CT	
5	cm	cmcat		<>								
6	ds	dsterm						dsterm				
7	LB	LBSTRESN	12.3									

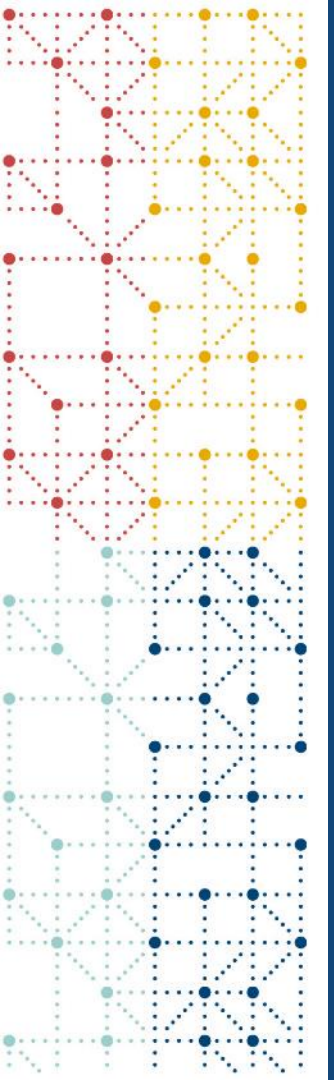
REFERENCE_TABLES | REFERENCE_COLUMNS | SOURCE_VALUES

VLM definition



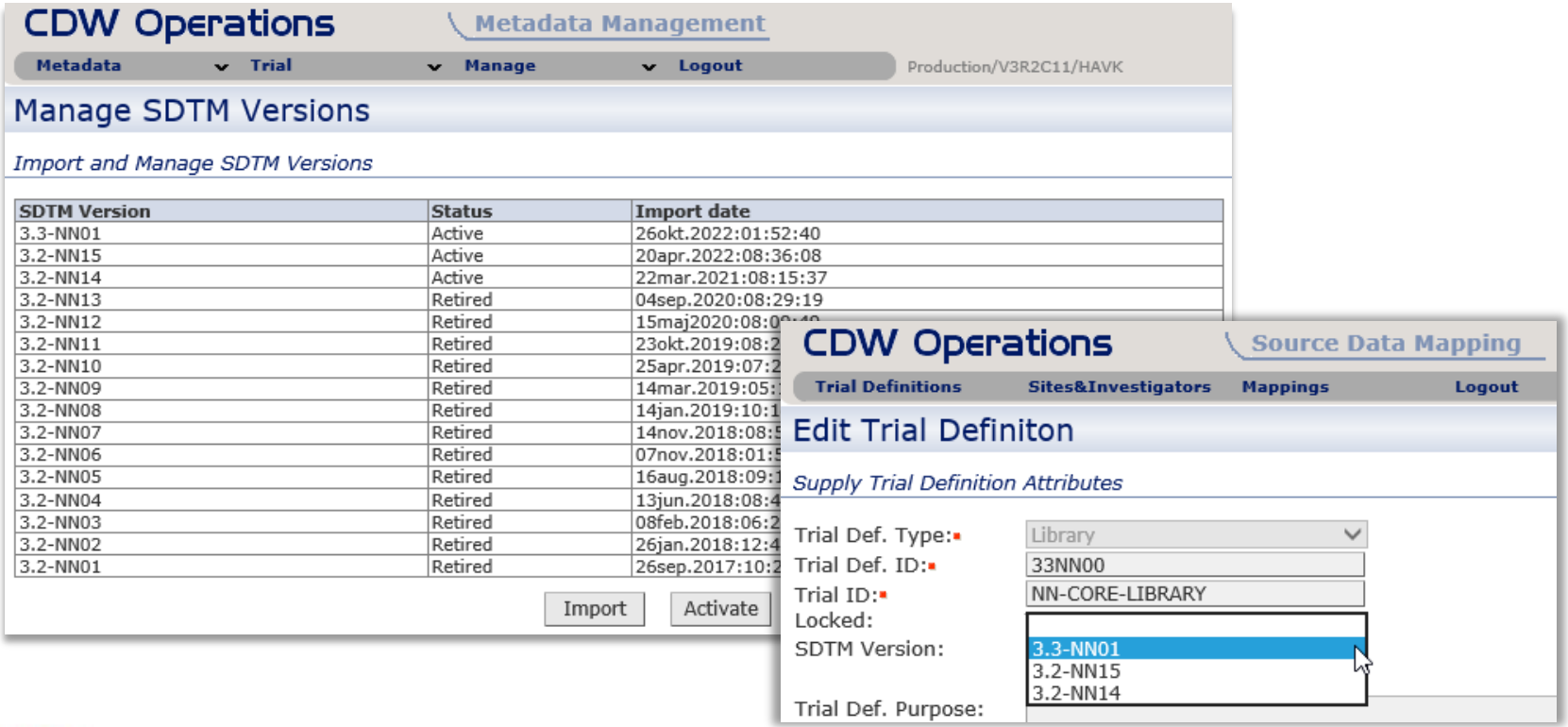
	A	B	C	D	E	F	G	H
1	table	column	whereclause	label	xmlcodelist	origin	algorithm	comment
2	LB	LBORRES	(LBCAT EQ "GLUCOSE METABOLISM") and (LBSPEC EQ "BLOOD") and (LBTESTCD EQ "HBA1C")	Testing			Algorithm1	Comment1
3	XV	VSORRES\ VSTESTCD EQ "SYSBP"			<>			
4								
5								

REFERENCE_TABLES | REFERENCE_COLUMNS | SOURCE_VALUES

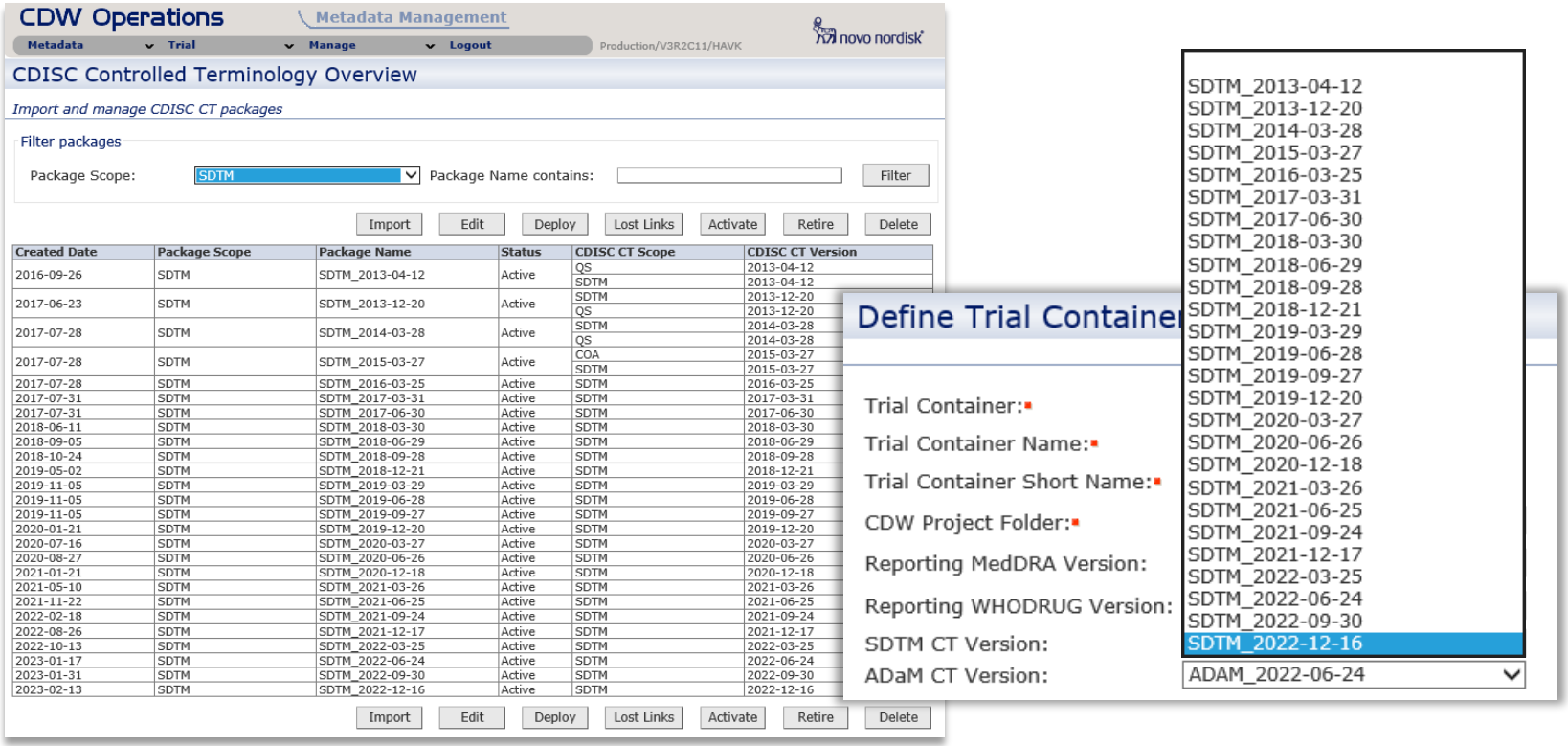


Standards Governance

SDTM Master Model Version

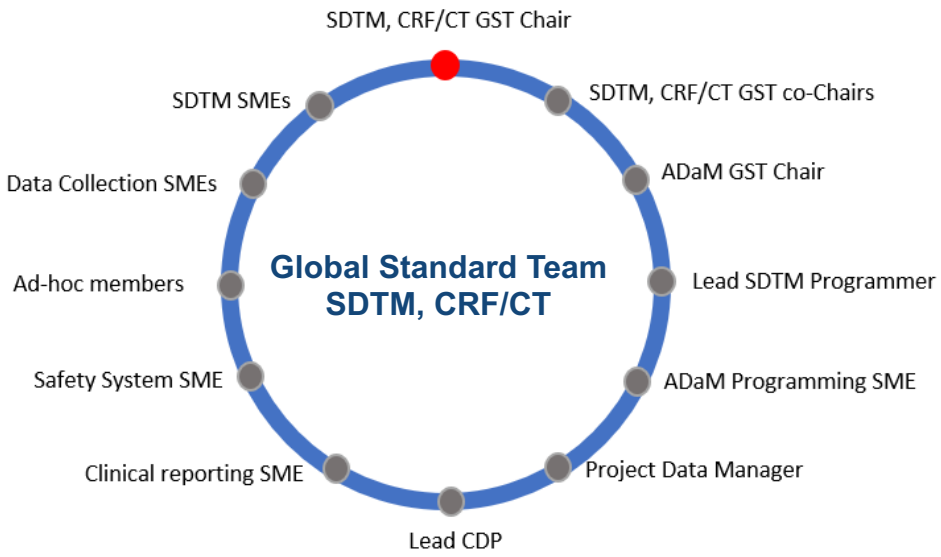


CDISC Controlled Terminology Version

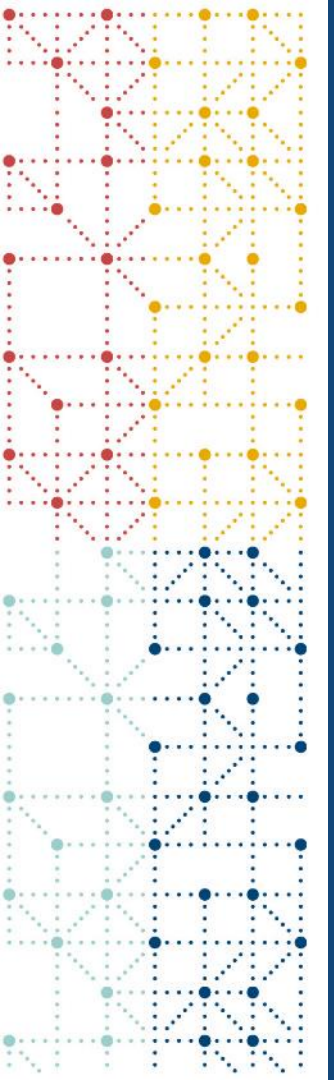


Centralised Governance

- QRS
- Global Template
- Data Collection Standards
- Controlled Terminology



- QNAM/CAT
- Master Model
- Device/New Data Sources and Types
- Validation
- Programming



Conclusion and Outlook

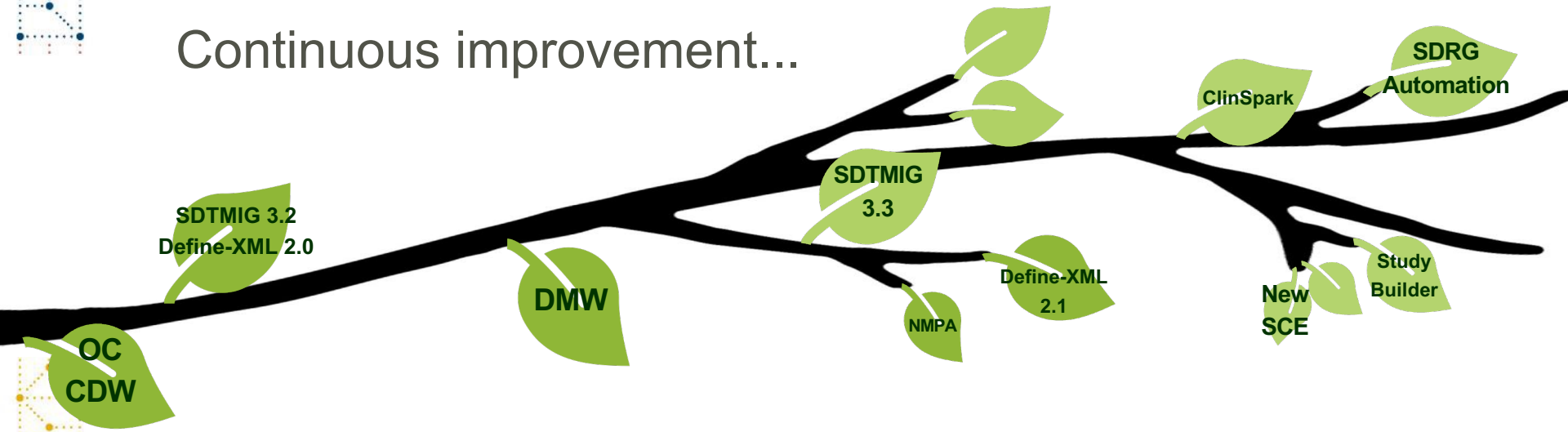
SDTM and define.xml automation made easy

- Mature Metadata Repository
- Centralised governance
- High level of standardisation
  - Data collection
  - EDC-CDMS Mapping
  - Trial Metadata Setup
  - SDTM Generation Framework
- End-to-end mindset
- Focus on global implementation while allowing for trial-specific adjustments in a controlled manner
- Strive for continuous improvement

Outlook

...embrace changes

Continuous improvement...



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Thank You!

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