cdisc

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Metadata Repository (MDR)：E2E Data Transparency and Traceability

Cong, Catherine. Principle Clinical Data Manager
Zhao, Kai. Study Designer,
Global Data Management and Standards,
MSD R&D (China) Co., Ltd

Meet the Speakers

Cong, Catherine

Title: Principle Clinical Data Manager , Associated Director

Organization: Global Data Management and Standards

Working and contributed in multiple TAs including Oncology, Diabetes, Vaccines and ID. With her extraordinary effort, Catherine cumulated solid End-to-End data management experiences from various InForm studies starting from Set-up till DBL.

Certified with CCDM.

Zhao, Kai

Title: Study Designer, Associated Director

Organization: Global Data Management and Standards

Working in Infectious Disease (HIV, COVID-19 etc) and Oncology therapeutic area.

SDTM Tabulate Certification.

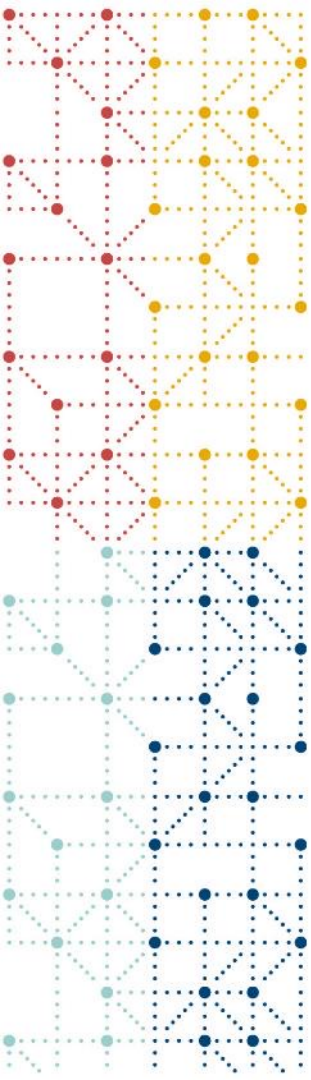
Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or MSD or position of CDISC.*

- *The authors have no real or apparent conflicts of interest to report.*

Agenda

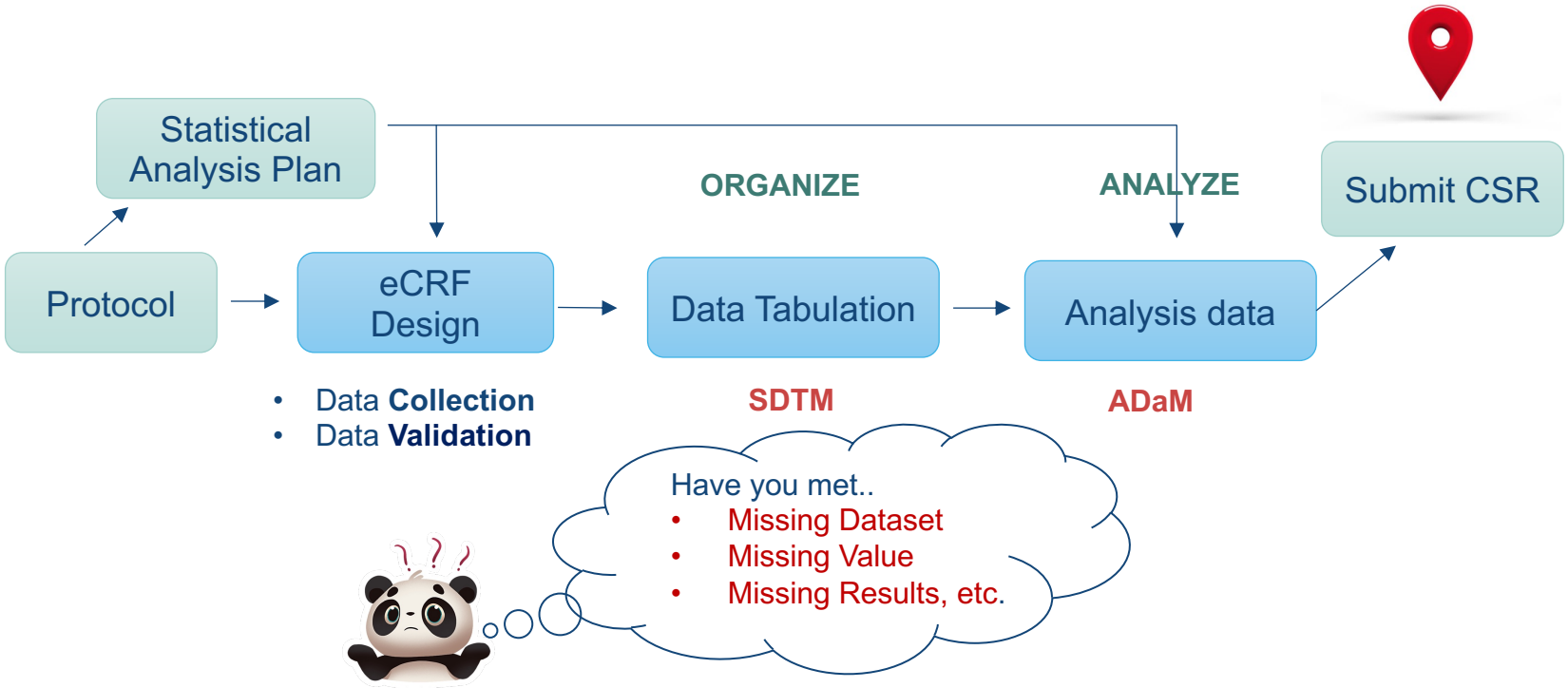
1. Start With the End in Mind
2. MDR：E2E Data Transparency and Traceability
3. Quality by Design by Using MDR
4. Deficiencies and Look Forward



Module 1

Start With the End in Mind

Simplified Clinical Data Flow



Start With the End in Mind

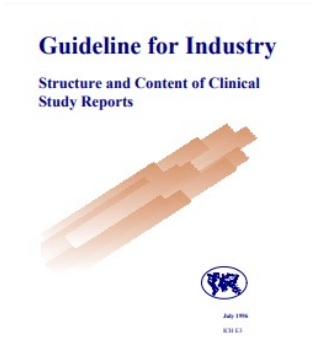
PROTOCOL

SAP

AGENCY REQUIREMENT

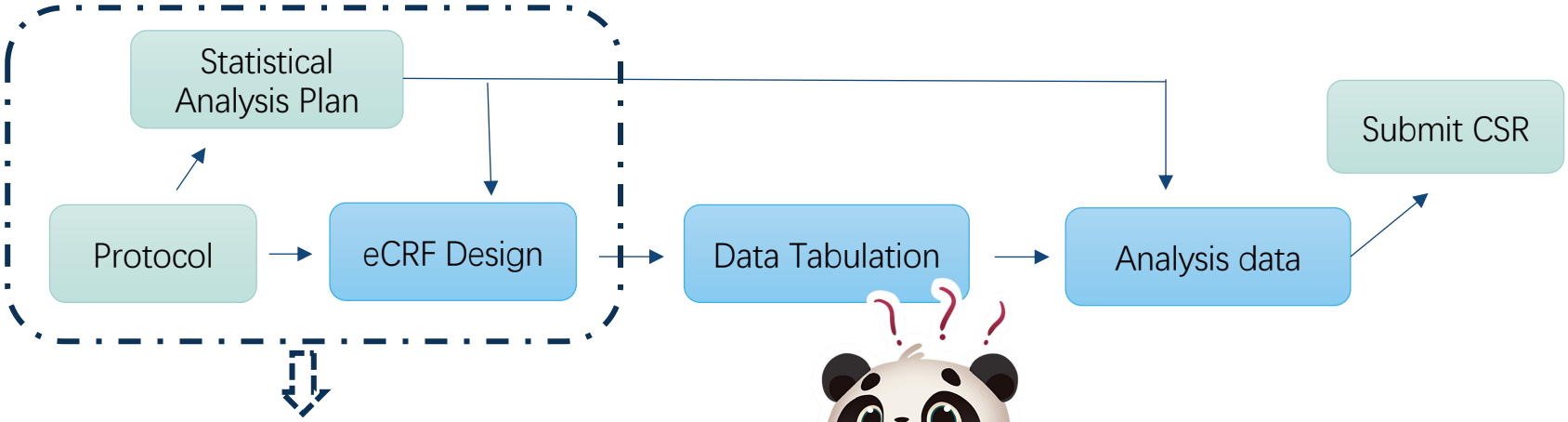
TRIAL DESIGN

- ✓ Critical Data **Collection** & Validation
- ✓ Data Organizing & **Formatting**



Clinical
Study
Report

Start With the End in Mind

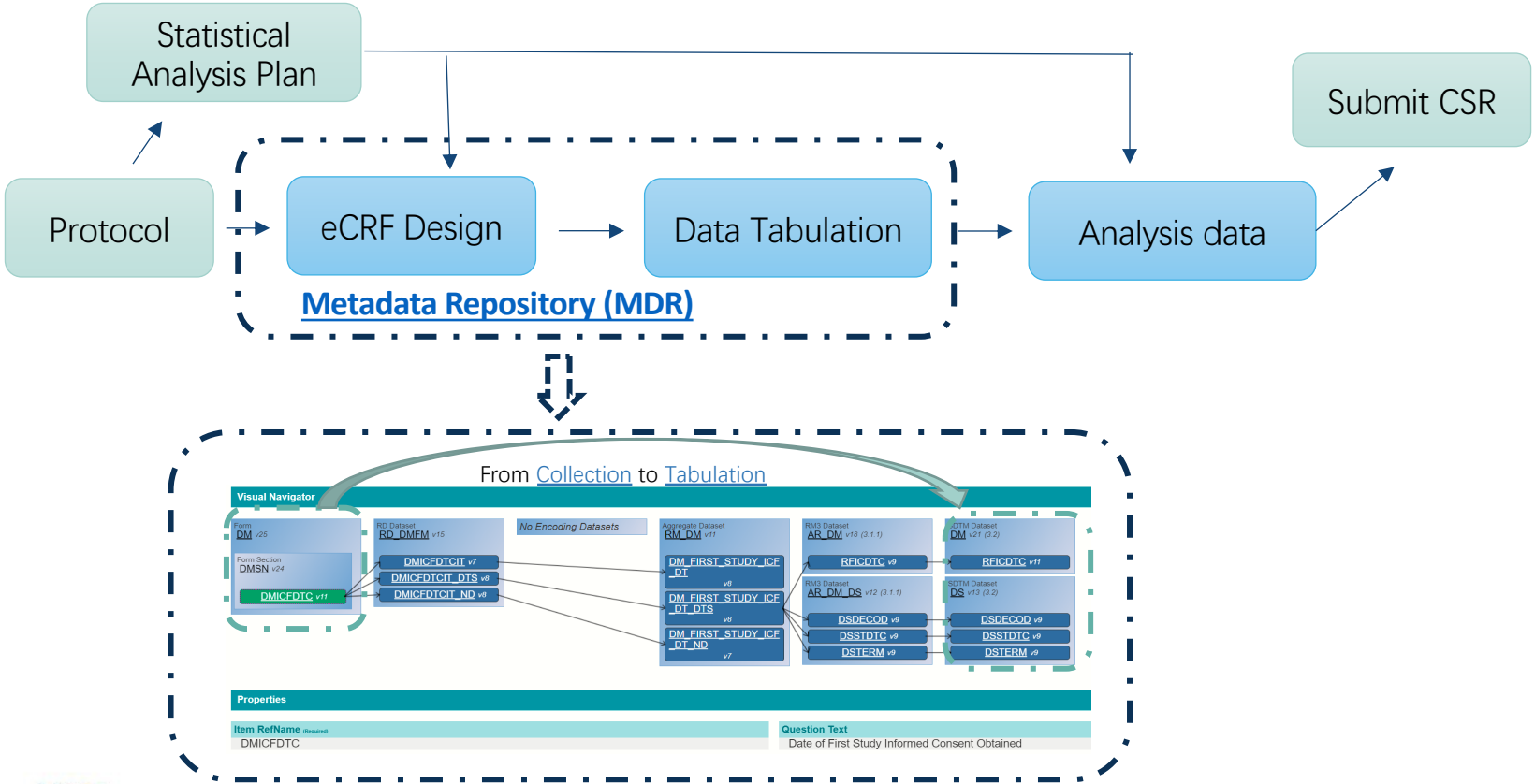


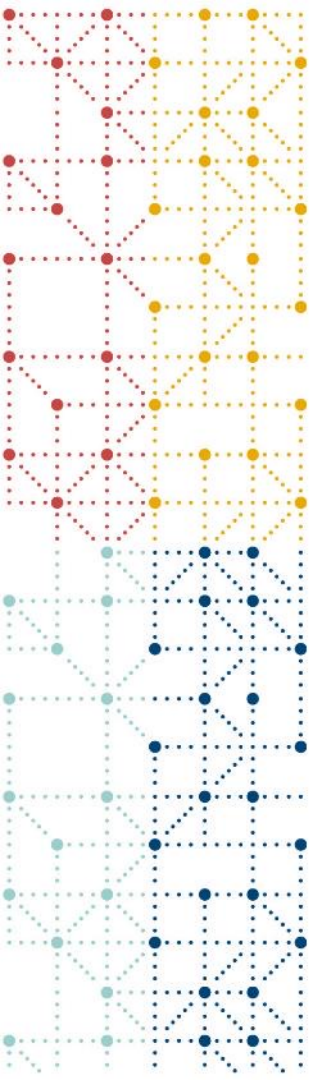
DEMOGRAPHICS (DM) [DMFM]

Demographics [DMSN]

1.	Date of Birth *[read-only]* [Date of Birth]	[DMBRTHDTCIT] (MM/YYYY) Req/Unk / Req (1900-2015)
2.	Calculated Age *[read-only]* [Calculated Age]	[DMAGEIT] NS
3.	Unit for Calculated Age *[read-only]* [Unit for Calculated Age]	[DMAGEUIT] *[A:HOURS]* Hours *[A:DAYS]* Days *[A:WEEKS]* Weeks *[A:MONTHS]* Months *[A:YEARS]* Years
4.	Collected Age *[read-only]* [Collected Age]	[DMCAGEIT] NS
5.	Unit for Collected Age *[read-only]* [Unit for Collected Age]	[DMCAGEUIT] *[A:HOURS]* Hours *[A:DAYS]* Days *[A:WEEKS]* Weeks *[A:MONTHS]* Months *[A:YEARS]* Years
6.	Sex Reported at Birth *[read-only]* [Sex Reported at Birth]	[DMSEXIT] *[A:F]* Female *[A:M]* Male *[A:UNDIFFERENTIATED]* Undifferentiated *[A:U]* Unknown
7.*	Gender Identity [Gender Identity]	[DMORRESGILISTIT] *[A:LIST]* [DMORRESGIPD] List [DMORRESGI_SV_LIST] *[A:OTHER]* [DMORRESGIOTHTB] Other, Specify: A200*

Start With the End in Mind

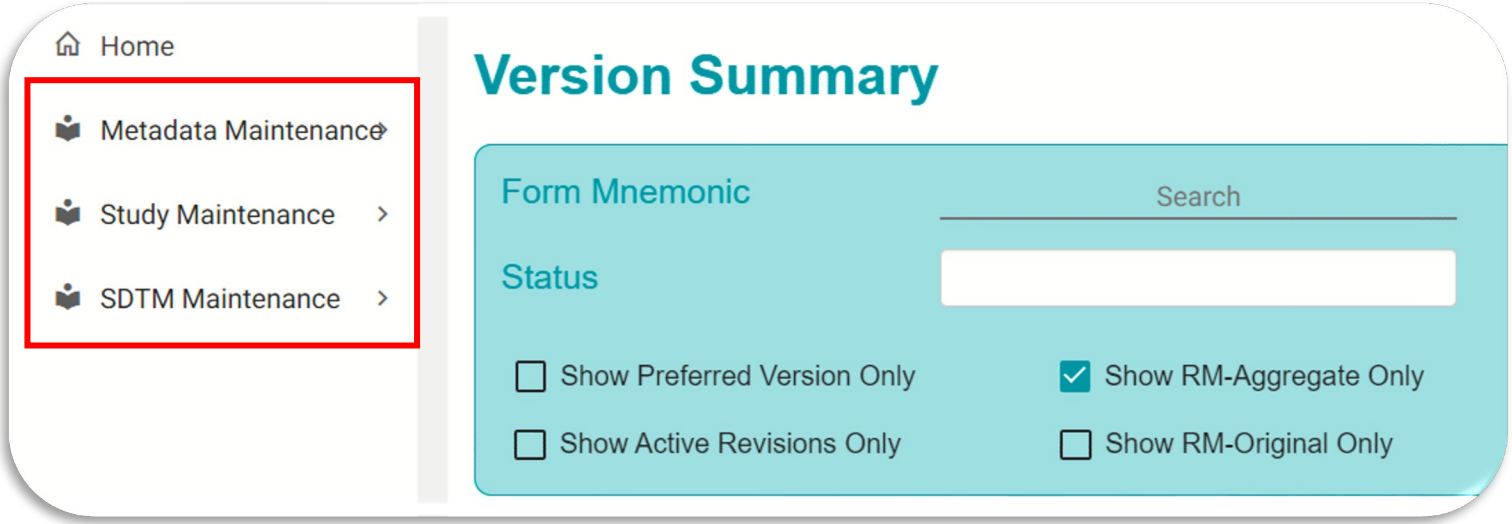




Module 2

MDR：E2E Data Transparency and Traceability

Centralized and Reusable Standards

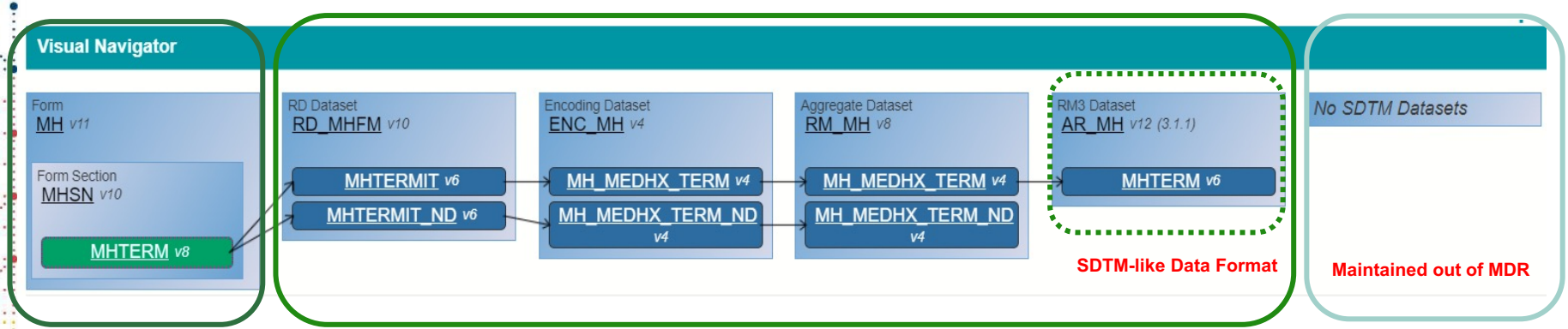


Data Definition Maintenance

Sponsor | SDTM Version

Sponsor	SDTM Version	No.of Domains	Prod Revision	Draft Revision
Merck	3.1.1	114	103	103.1
Merck	3.1.3	105	11	11.1
Merck	3.2	103	161	161.1
Merck	3.3	119	173	173.1

Data Lineage Shown via MDR

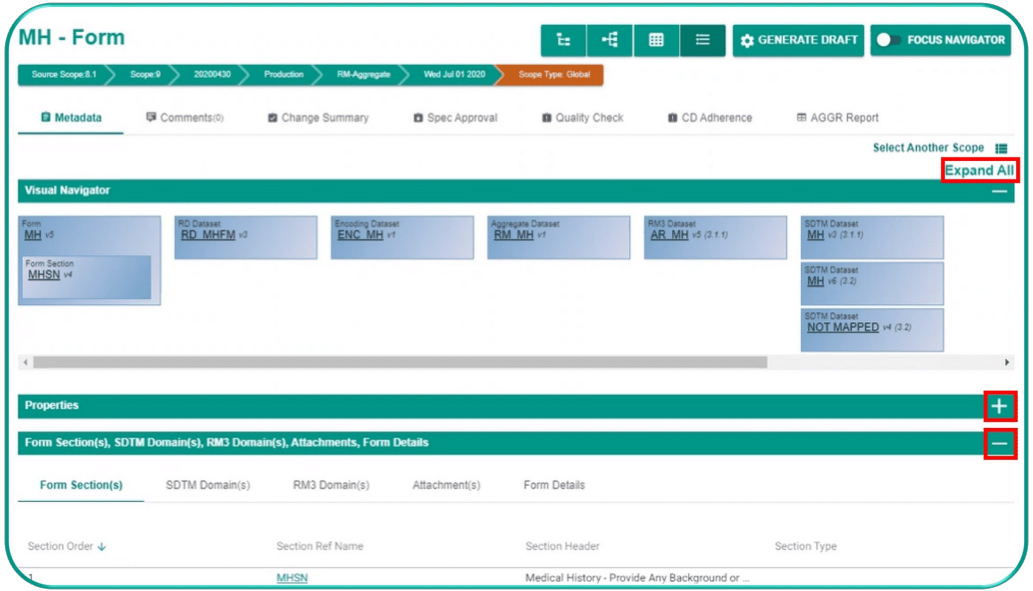


Stage 1:
Data Collection

Stage 2:
Data Integration & Transformation

Stage 3:
SDTM Datasets

From Collection to Tabulation



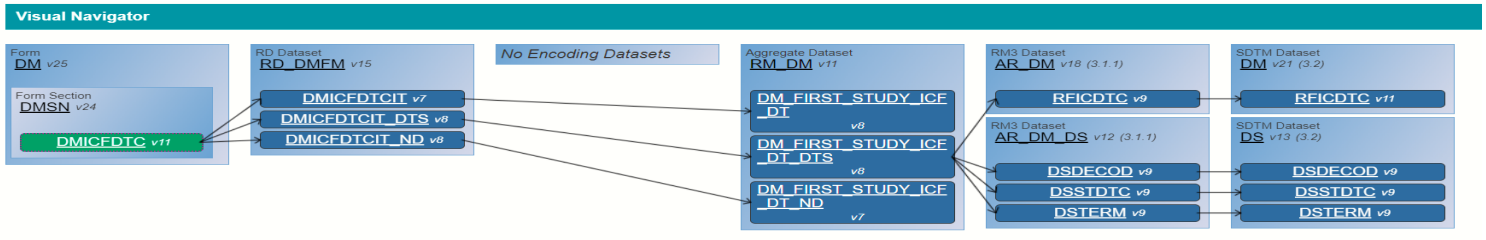
- E2E Data Transparency & Traceability
- Visualization for Stakeholders

From Spreadsheet to Electronic Platform

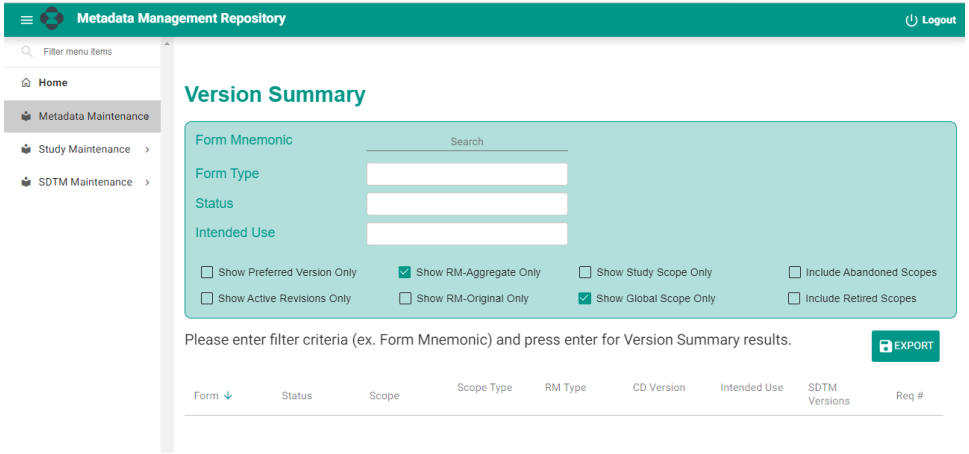
RM3 Target Version: 3.1.1

Item #	Itemref Name	Question	Response(s)	Database Value	Field Type (CONTROLDATA_TYPE)	Field Format	Display Override	Derived in DMW	eCRF Design Guidelines	Mandatory/ Optional	Required/Not Required (Yellow Lights)	SDV'd?
		Demographics			Section Header				This form is mandatory for non-RT studies This is a visit-based form. Form is used once per study This form should be placed in the first visit of the T&E. Form Variations are NOT allowed. -ESD studies: all items must be set as SDV=Critical; not applicable to Late Stage studies	Mandatory		
1	DMBRTHDTC	Date of Birth	REQ/UNK - REQ		Date				This item is mapped in InForm from the Screening (SCR) form. However, the value on the DM eCRF can be updated by the site	Mandatory	Required	TRUE
2	DMAGE	Calculated Age			Text Box	XXXX	Read-Only		This item is used to support Downstream systems (ARIES, PK, IBRMS, etc). This item is not mapped to SDTM. The SDTM AGE is derived in RM3 using the study RFSTDTC; the value in InForm/RM1/RM2 may be different from the value in RM3. Auto-populated in InForm by a derivation rule. Ensure the edit check rule/derivation is adjusted based on the calculated unit to be used in the study. Note: if any portion of the DOB is UNK then the Calculated age may not be precise. The derivation logic is as follows: – If Day is UNK or Blank, then use "15" as the day – If Month is UNK and Day is UNK or Blank, then use "June" as the Month and "30" as the day – The age is derived based on the first visit date This question is used in conjunction with 'Unit for Calculated Age' item.	Mandatory	Not Required	FALSE
3	DMAGEU	Unit for Calculated Age	Hours	HOURS	Radio Button		Read-Only		This question is used in conjunction with the 'Calculated Age' item. This item uses the 'units (CDISC UNIT) dictionary in eVOC. -Study team to determine which unit to be populated for all subjects and ensure the edit check rule/derivation is adjusted accordingly. Remove any units that are not applicable for the study. -This item is not mapped to SDTM. The SDTM AGE Unit is derived by a DMW derivation using the study RFSTDTC. Auto-populated in InForm by a derivation rule (see edit check spec to update the unit value which should be used in the study). – The standard calculation for age is in years; however, the edit check derivation can be modified to be calculated in a different unit	Mandatory	Not Required	FALSE
			Days	DAYS	Radio Button							
			Weeks	WEEKS	Radio Button							
			Months	MONTHS	Radio Button							
			Years	YEARS	Radio Button							
4	DMCAGE	Collected Age			Text Box	XXXX			Collected age is optional. This is intended for site to manually enter the age into InForm at the time of first DOV. -Note: this value could be different from the calculated age -Study team to determine if this item should be included. Some examples of when this might be needed: – When partial DOB is collected, either by design or based on country specific regulations that prevent a full DOB from being collected, and a precise age at time of enrollment is needed. – If age is being used for stratification and precision is required. Example: patient is 5 yrs and was born 23June and entered the study 01June. The collected age is 5 yrs but the calculated age would be 6 yrs.	Optional	Required	TRUE

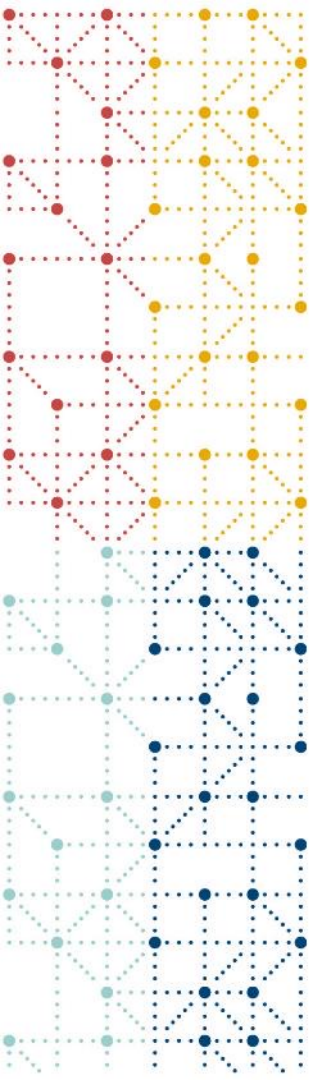
- Silos to Network
- Human-readable to Machine-readable



MDR Application in Clinical Data Management



- ✓ E2E Data Flow Transparency and Traceability
- ✓ Efficiency in Data Collection, Use and Sharing
- ✓ Data Management Capabilities

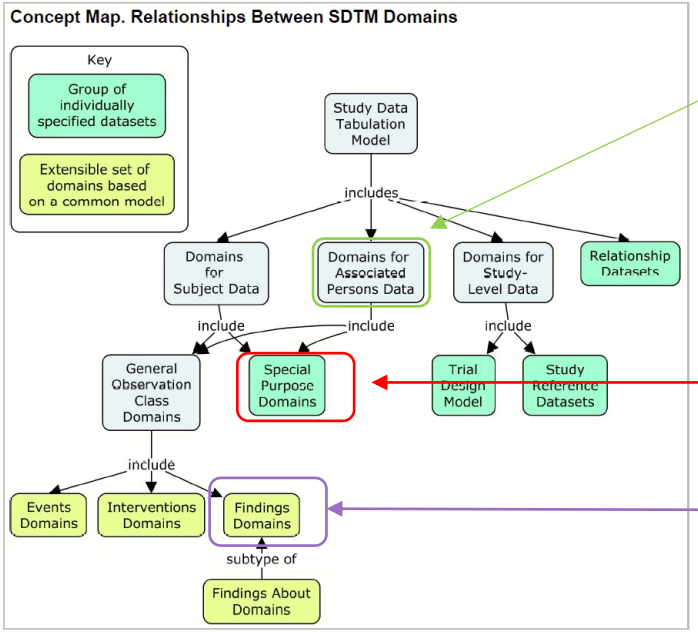


Module 3

Quality by Design by using MDR

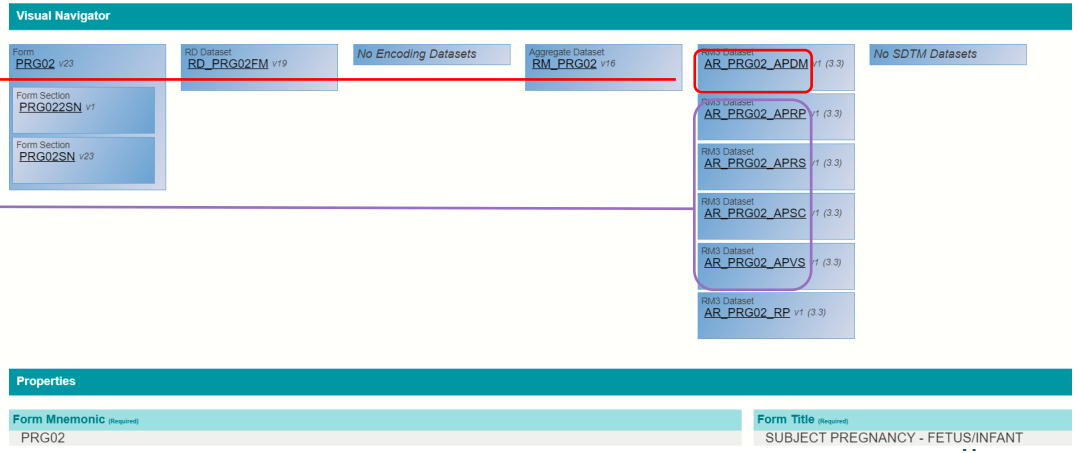
What data will be collected and where will they go?

Fig.1 Concept map from SDTM 2.0



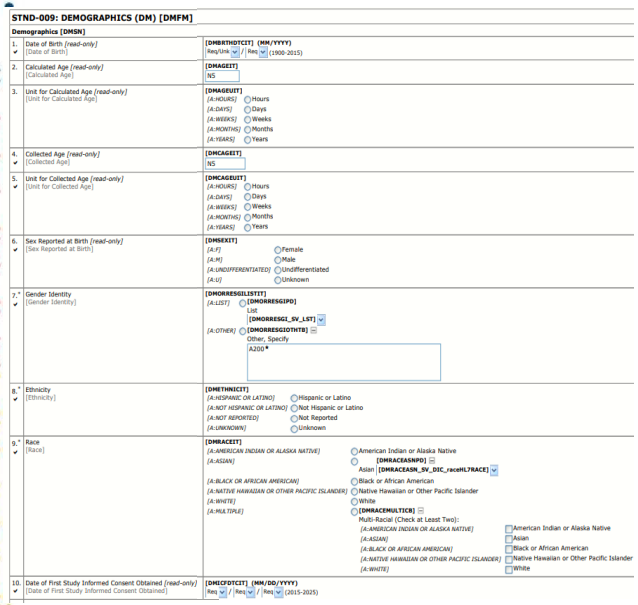
When a subject is pregnant or becomes pregnant, it is important and may be necessary to collect both prenatal and postnatal data on the infant.

Fig.2 Subject pregnancy-fetus/infant in MDR



E2E Data Visualization for an eCRF

Fig.1 DM eCRF



STND-009: DEMOGRAPHICS (DM) [DMFM]

Demographics [DMSN]

1. ✔	Date of Birth *[read-only]* (Date of Birth)	[DMBRTHDTCIT] (MM/YYYY) Req/Unk / Req (1900-2015)
2. ✔	Calculated Age *[read-only]* (Calculated Age)	[DMAGEIT] NS
3. ✔	Unit for Calculated Age *[read-only]* (Unit for Calculated Age)	[DMAGEUIT] (A:HOURS) Hours (A:DAYS) Days (A:WEEKS) Weeks (A:MONTHS) Months (A:YEARS) Years
4. ✔	Collected Age *[read-only]* (Collected Age)	[DMCAGEIT] NS
5. ✔	Unit for Collected Age *[read-only]* (Unit for Collected Age)	[DMCAGEUIT] (A:HOURS) Hours (A:DAYS) Days (A:WEEKS) Weeks (A:MONTHS) Months (A:YEARS) Years
6. ✔	Sex Reported at Birth *[read-only]* (Sex Reported at Birth)	[DMSEXIT] (A:F) Female (A:M) Male (A:UNDIFFERENTIATED) Undifferentiated (A:U) Unknown
7.* ✔	Gender Identity (Gender Identity)	[DMORRESGILISTIT] (A:LIST) [DMORRESGIPD] List [DMORRESGI_SV_LST] (A:OTHER) [DMORRESGIOTHTX] Other, Specify A200*
8.* ✔	Ethnicity (Ethnicity)	[DMETHNICIT] (A:HISPANIC OR LATINO) Hispanic or Latino (A:NOT HISPANIC OR LATINO) Not Hispanic or Latino (A:NOT REPORTED) Not Reported (A:UNKNOWN) Unknown
9.* ✔	Race (Race)	[DMRACEIT] (A:AMERICAN INDIAN OR ALASKA NATIVE) American Indian or Alaska Native (A:ASIAN) [DMRACEASNPO] Asian [DMRACEASN_SV_DIC_raceHL7RACE] (A:BLACK OR AFRICAN AMERICAN) Black or African American (A:NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER) Native Hawaiian or Other Pacific Islander (A:WHITE) White (A:MULTIPLE) [DMRACEMULTICR] Multi-Racial (Check at Least Two): (A:AMERICAN INDIAN OR ALASKA NATIVE) American Indian or Alaska Native (A:ASIAN) Asian (A:BLACK OR AFRICAN AMERICAN) Black or African American (A:NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER) Native Hawaiian or Other Pacific Islander (A:WHITE) White
10. ✔	Date of First Study Informed Consent Obtained *[read-only]* (Date of First Study Informed Consent Obtained)	[DMICFDTCIT] (MM/DD/YYYY) Req / Req / Req (2015-2025)

Fig.2 eCRF E2E Data Visualization in MDR

Fig. 3 SDTMIG version for domains

Form Section(s), SDTM Domain(s), RM3 Domain(s), Attachments, Form Details

Form Section(s) | SDTM Domain(s) | **RM3 Domain(s)** | Attachment(s) | Form Details

SDTM Version(for RM3 Datasets) ↓	SDTM Domain(for RM3 Datasets)
3.1.1	DM
3.1.1	DS
3.1.1	SC

E2E Data Visualization for an eCRF

Fig.1 eCRF E2E Data Visualization for an item in MDR

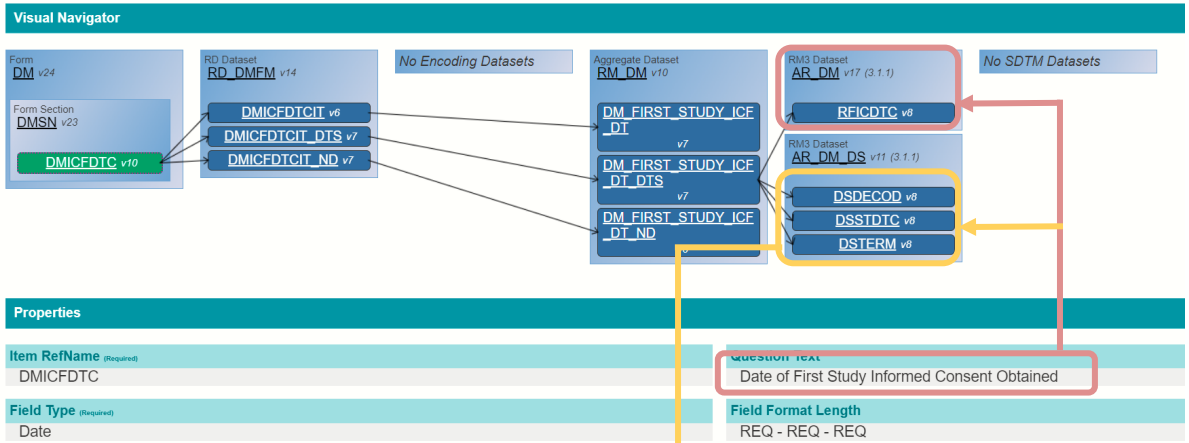
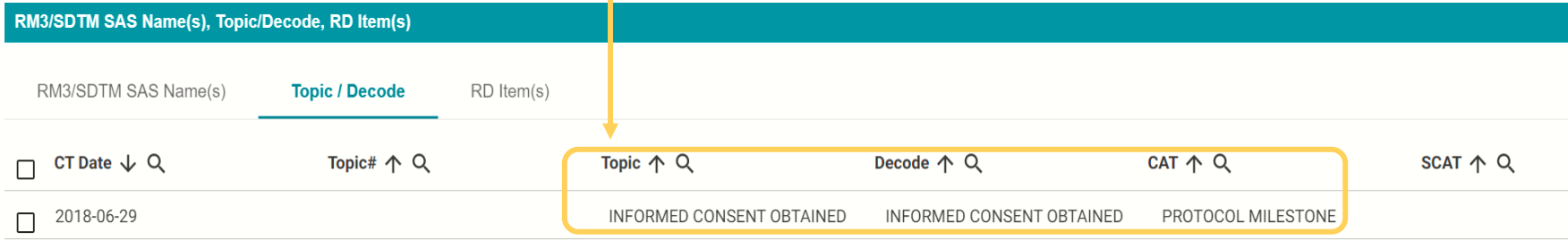


Fig.2 DSTERM, DSDECOD, DSCAT



E2E Data Visualization for an eCRF

Fig.1 DM eCRF

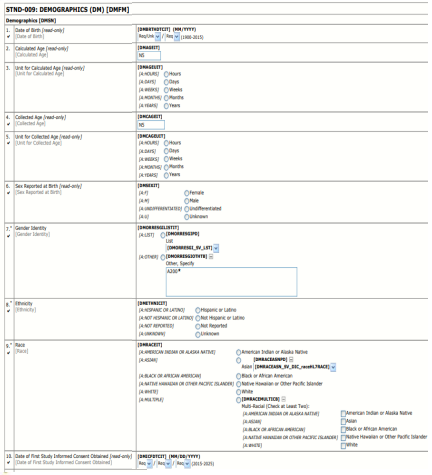


Fig.2 eCRF E2E Data Visualization for an item in MDR

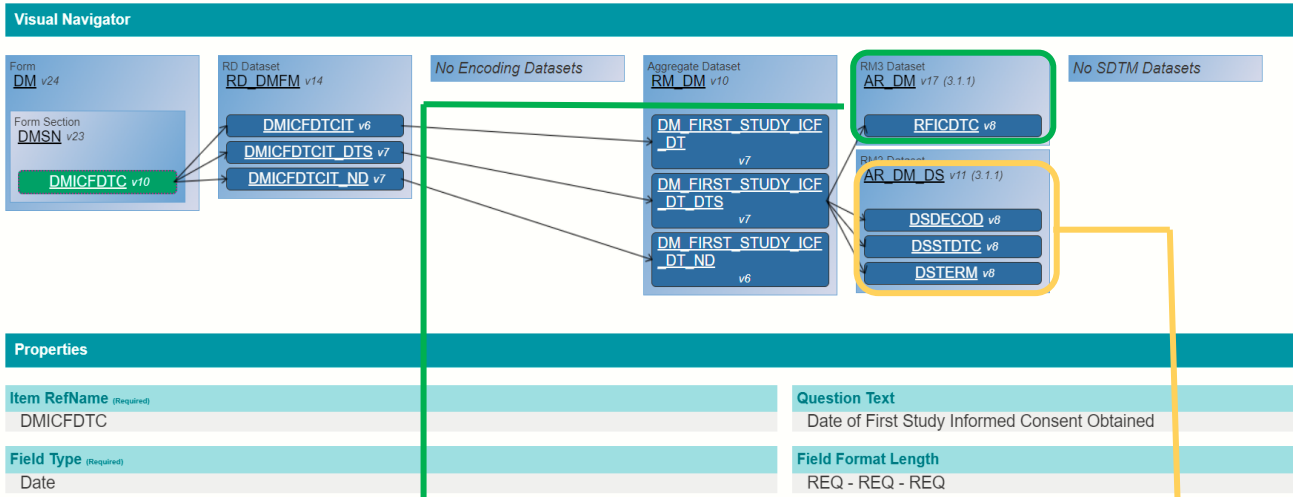


Fig.3 SDTM datasets

dm.xpt

Row	STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM	BRTHDTC	AGE	AGEU
1	ABC123	DM	123101	01001	2006-01-12	2006-03-10	2006-01-12	2006-03-10	2006-01-03	2006-04-01	01	JOHNSON, M	1948-12-13	57	YEARS

ds.xpt

Row	STUDYID	DOMAIN	USUBJID	DSSEQ	DSTERM	DSDECOD	DSCAT	DSSCAT	EPOCH	DSDTC	DSSTDTC
1	ABC123	DS	123101	1	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE		SCREENING	2006-01-03	2006-01-03

Data Conformance

FDA-STUDY DATA TECHNICAL CONFORMANCE GUIDE

8.2.2 Support on Data Validation Rules

Sponsors should evaluate their study data before submission against the conformance rules published by an SDO, the eCTD Technical Rejection Criteria for Study Data (See Appendix F), and the FDA Business Rules. Sponsors may also wish to use the FDA Validator Rules to understand what is available to the FDA reviewer. Sponsors should either correct any discrepancies between study data and the standard or the business rules or explain meaningful discrepancies in the relevant Reviewer Guide (RG). Additional information about conformance to the standard, FDA Business Rules, or FDA Validator Rules that could facilitate review of the submitted data, or establish consistency and traceability between the study data and the Study Report, should also be provided in the relevant RG.

Study Data Technical Conformance Guide – Technical Specifications Document | FDA

PMDA-Technical Conformance Guide on Electronic Study Data Submissions

3.6.1 Validation of data conforming to the CDISC standards

The PMDA will perform validation of data that conform to the CDISC standards using Pinnacle 21 Enterprise.

The rules used for validation have been classified by the level of importance taking into consideration the characteristics of each rule and based on conformity to the standards, ease of use of the data in review, quality of the clinical study data which the PMDA should know beforehand, and future uses of the clinical study data by the PMDA. The levels of importance are shown below.

(a) Rules which, if violated, will cause the review to be suspended until corrections have been made

Very basic rules such as the presence/absence of necessary datasets for each clinical study

(b) Rules which, if violated, will require an explanation

In many cases, these rules are clearly stated in each standard and implementation guide, and if violated, the applicant should explain in the reviewer's guide about the reason for the violation and the reason why it is not possible to correct it.

(c) Rules which, even when violated, will not necessarily require any explanation

The reason for the violation possibly is requested separately for the above (c) from the perspective of the quality of the clinical study data.

https://www.pmda.go.jp/english/review-services/reviews/0002.html

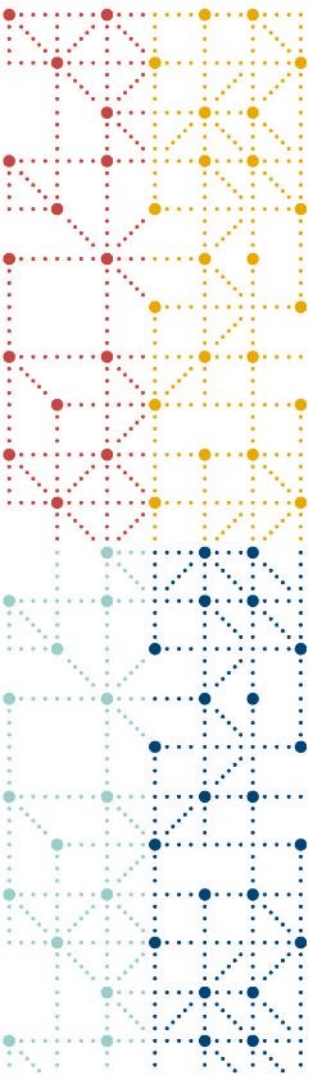
Data Conformance

Rule ID	Publisher ID	Message	Description	Domains	FDA	PMDA 2010.2	PMDA 2211.0	NMPA	FDA Severity	PMDA Severity	3.1.2	3.1.3	3.2	3.3	Notes
SD1035	FDAB014	Missing value for DSCAT	Category for Disposition Event (DSCAT) should be populated.	DS	X	X	X			Warning	X	X	X	X	
SD1315	CG0066	DSDECOD is not the same as DSTERM, when DSCAT='PROTOCOL MILESTONE'	Reported Term for the Disposition Event (DSTERM) and Standardized Disposition Term (DSDECOD) should contain the same value, when Category for Disposition Event (DSCAT) is 'PROTOCOL MILESTONE'.	DS	X	X	X	X		Warning	X	X	X		

RM3/SDTM SAS Name(s), Topic/Decode, RD Item(s)

RM3/SDTM SAS Name(s) | **Topic / Decode** | RD Item(s)

CT Date	Topic#	Topic	Decode	CAT	SCAT
2018-06-29		INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	

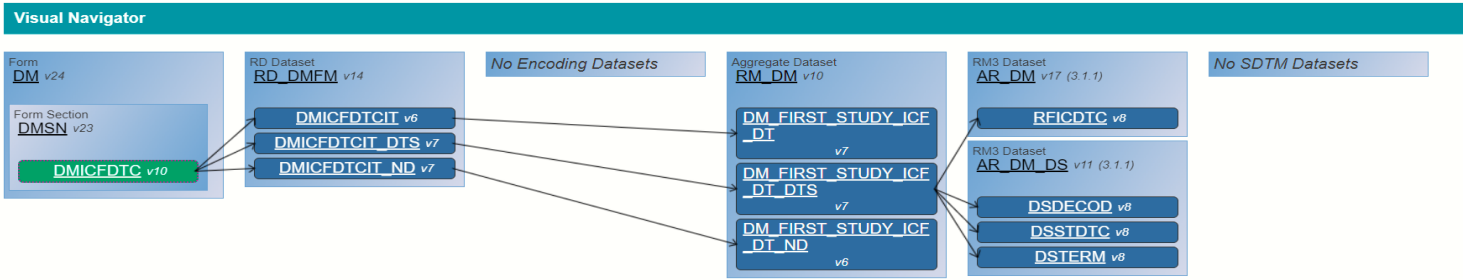


Module 4

Deficiencies and Look Forward

Deficiencies

- SDTM dataset is maintained out of MDR
- Controlled Terminology is maintained out of MDR



Properties

Item RefName (Required)
DMICFDTC

Question Text
Date of First Study Informed Consent Obtained

Field Type (Required)
Date

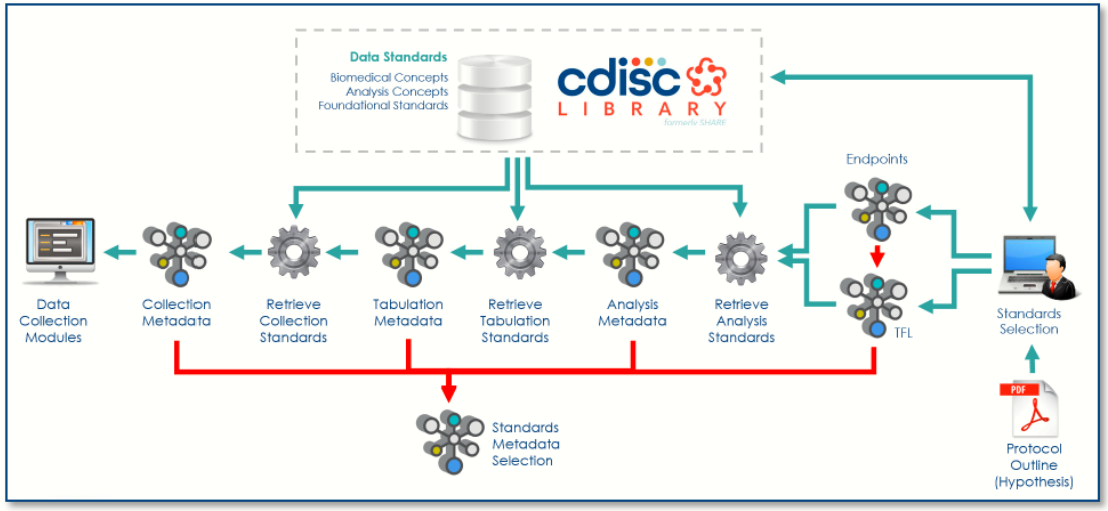
Field Format Length
REQ - REQ - REQ

RM3/SDTM SAS Name(s) | **Topic / Decode** | RD Item(s)

CT Date	Topic#	Topic	Decode	CAT	SCAT
2018-06-29		INFORMED CONSENT OBTAI...	INFORMED CONSENT OBTAI...	PROTOCOL MILESTONE	

Look Forward

CDISC 360 Piloted development of linked biomedical concept metadata to enable end to end automation



cdisc https://www.cdisc.org/cdisc-360

Thank You!