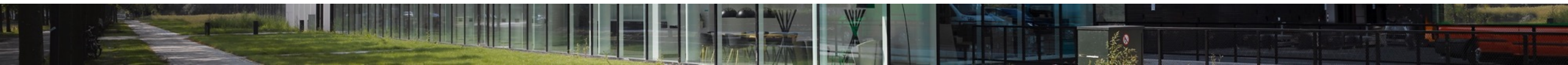




Implementing CDISC standards in an organization that doesn't require CDISC

Presentation by DAAN VAN NIEUWENHUIJZEN AND MARION KASPERS at the PHUSE SDE Utrecht, September 2023



AGENDA

- Background
- SDTM Implementation at DNR
- Collaboration DNR – OCS Life Sciences
- ADaM Implementation at DNR
- Next Steps

BACKGROUND

Danone is a global nutrition company

- Essential dairy and plant-based product
- Waters
- Specialized nutrition (early life nutrition and medical nutrition)

Danone's mission "BRINGING HEALTH THROUGH FOOD TO AS MANY PEOPLE AS POSSIBLE"

Research for Health				
Nutrition for Life	Epilepsy	Physical Frailty	Gut Health	Muscle
Allergy	Growth & Metabolism	Stroke & Dysphagia	Human Milk Research	Neuroscience
Alzheimer's Disease	Oncology	Critical Care	Immunology	

Source <https://www.danonersearch.com/>

STANDARDIZATION

Benefits of using a data standard

- Allows data integration
- Improves clarity
- Enables re-use of programs
- Simplifies data sharing

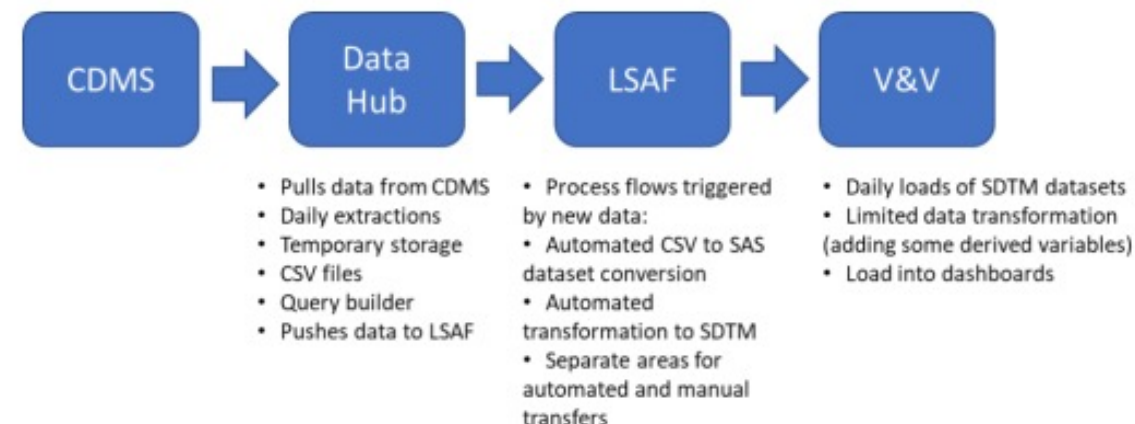
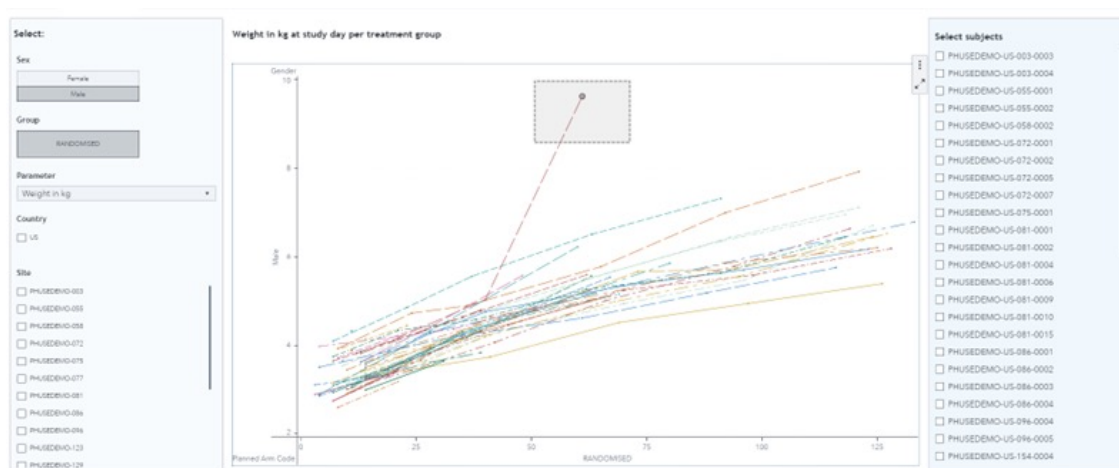
Why then SDTM

- Existing standard, developed and maintained by CDISC
- Simplifies data monitoring and review
- Be prepared for data submissions to regulators like FDA (CDISC not currently required)

DATA USED FOR iCDM

iCDM Interactive Central Data Monitoring - a range of dashboards using SDTM data that allow for near real-time data monitoring during the study conduct.

Example: Anthropometrics - finding outliers for weight (kg)



PHUSE EU Connect 2022 Belfast Presented by Paul Vervuren (Danone Nutricia Research) and Dennis Menkveld (P&W consulting)

https://phuse.s3.eu-central-1.amazonaws.com/Archive/2022/Connect/EU/Belfast/PAP_AR05.pdf

https://phuse.s3.eu-central-1.amazonaws.com/Archive/2022/Connect/EU/Belfast/PRE_AR05.pdf

SDTM CREATION PROCESS AT DANONE NUTRICIA RESEARCH (DNR)

Building on the experiences gained in creating the data warehouse for infant nutrition (see presentation by Paul Vervuren at PHUSE EU connect 2016 in Barcelona https://phuse.s3.eu-central-1.amazonaws.com/Archive/2016/Connect/EU/Barcelona/PRE_CD09.pdf), nowadays most clinical studies are converted into SDTM standards to be used for the study reporting.

Metadata

 DNR_SDTMIG_32.xlsx

- Based on the CDSIC SDTM IG 3.2
- Added domains from SDTM IG 3.3 (ML, FT, MK) and SDTM IG 3.4 (BE) and XS (custom for SAE)
- Additional columns to describe the implementation of SDTM at DNR
- Added supplemental qualifiers to domains (instead of SUPP dataset)

Controlled Terminology

- SDTM controlled terminology (provided by CDSIC)
- Developing additional DNR controlled Terminology

CDISC members can download CDISC metadata from the CDISC library

SDTM CREATION PROCESS AT DNR – ANNOTATION OF THE CRF

Annotation of CRF

- Add domains and domain variables as comments to the annotated CRF (PDF) from the EDC (Viedoc)
- Export the comments to Forms Data Format file on XML basis (XFDF)
- Use the Annotations in creating the define.xml (origin page number in the CRF, value level metadata)



[CE]

CECAT="GASTROINTESTINAL SYMPTOMS"

CEORIG="ELECTRONIC DIARY"

CEEVAL="SUBJECT"

Gastro Intestinal Symptoms id GIQ

CEDTC
(complete with EVENTDATE)

CEPRES="Y"

CEEVINTX="TODAY"

CEOCCUR
(CEOCCUR="N" in case absent;
CEOCCU="Y" in case mild,
moderate or severe)

CESEV

Did you have any of the following complaints today?

Nausea #1 id NAUSEAQ

CETERM="NAUSEA"

☐ Absent ☐ Mild ☐ Moderate ☐ Severe

Vomiting #2 id VOMITQ_A

CETERM="VOMITING"

☐ Absent ☐ Mild ☐ Moderate ☐ Severe

Burping #3 id BURPINGQ

CETERM="BURPING"

☐ Absent ☐ Mild ☐ Moderate ☐ Severe

Abdominal distension #4 id ABDDISTQ

CETERM="ABDOMINAL DISTENSION"

☐ Absent ☐ Mild ☐ Moderate ☐ Severe

```

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[CE]/p
</body>
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<defaultstyle>
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</freetext>

```

SDTM CREATION PROCESS AT DNR – CREATING THE DOMAINS

Creating the domain datasets (OCS Life Sciences)

```
array vars (9) ABDPAINQ ABDDISTQ BURPINGQ PASSWQ_A REGURGO_A NAUSEAQ VOMITQ_A DIARRHQ CONSTIPQ;
array vals (9) $200 ("ABDOMINAL PAIN", "ABDOMINAL DISTENSION", "BURPING", "FLATULENCE", "REGURGITATION", "NAUSEA", "VOMITING", "DIARRHOEA", "CONSTIPATION");

do i = 1 to dim(vars);
  /* For each subject, a record with CETERM is created */
  ceterm = substr(vals(i),1,1)||lowercase(substr(vals(i),2));

  /* Derive CESTAT and temporary variable _CESEV for later CESEV derivation*/
  if ^missing(vars(i)) then do;
    _cesev = vars(i);
    call missing(cestat);
    output;
  end;
  else if missing(vars(i)) then do;
    call missing(_cesev);
    cestat = "NOT DONE";
    output;
  end;
end;

/* Design is applied and checks are made. */
%sdm_create_domain ( domain      = &sdm_domain
                    , inset      = &sdm_domain
                    , keys       = studyid usubjid ceterm cedtc visitnum
                    , deldupkeys = N);
```

PINNACLE21

DNR IMPLEMENTATION OF SDTM - CONTROLLED TERMINOLOGY

Nutritional studies typically specify the amount of study product administered (often in a single bolus)

Action taken with study product id AEACNP
(in the opinion of the investigator) #8

- ☐ Amount not changed
- ☐ Amount reduced
- ☐ Amount increased AEACN
- ☐ Product interrupted
- ☐ Product withdrawn
- ☐ Not applicable
- ☐ Unknown

ACN (Codelist NOT Extensible)	DNR_ACN
DOSE INCREASED	AMOUNT INCREASED
DOSE NOT CHANGED	AMOUNT NOT CHANGED
DOSE RATE REDUCED	
DOSE REDUCED	AMOUNT REDUCED
DRUG INTERRUPTED	PRODUCT INTERRUPTED
DRUG WITHDRAWN	PRODUCT WITHDRAWN
NOT APPLICABLE	NOT APPLICABLE
UNKNOWN	UNKNOWN

DNR IMPLEMENTATION OF SDTM – SUPPLEMENTAL QUALIFIERS

[AE]

Relationship to study product #6 ☒ AEREL1 ☒ AEREL

☐ Not related
 ☐ Unlikely
 ☐ Possibly
 ☐ Probably
 ☐ Definitely
 ☐ Not applicable

In case possibly, probably, definitely related, please provide physician's rationale ☒ AEREL1CO

AERELCO

Relationship to study procedure #7 ☒ AEREL2 ☒ AERELP

☐ Not related
 ☐ Unlikely
 ☐ Possibly
 ☐ Probably
 ☐ Definitely
 ☐ Not applicable

In case possibly, probably, definitely related, please provide physician's rationale ☒ AEREL2CO

AERELPCO

Variable Name	Variable Label
AERELCO	Physician's rationale for relationship to study product
AERELP	Causality to Study Procedure
AERELPCO	Physician's rationale for relationship to study procedure
AEDICT	Dictionary and Version
AESOCLST	Primary and Secondary SOC Abbreviations
CodedOnDate	Coded on date (UTC)
InitiatedDate	Initiated date (UTC)
LastEditedDate	Last edited date (UTC)
SUBJID	Subject Identifier for the Study

DNR IMPLEMENTATION OF SDTM – SUPPLEMENTAL QUALIFIERS

[CM] CMCAT="CONCOMITANT MEDICATION;
NUTRITIONAL SUPPLEMENTS" [RELREC]

Concomitant Medications and Nutritional Supplements id CM

No. id CMSPID Medication or Nutritional Supplement id CMTRT ?

[CMSPID] [CMTRT]

[RELREC.IDVARVAL]

Dose id CMDOSTXT Unit #1 id CMDOSU Frequency #2 id CMFRQ

[CMDOSE] [CMDOSTXT] [CMDOSU] [CMDOSFRQ]

Specify "Other Frequency" id CMFRQSP

[CMDOSFRQ]

Variable Name	Variable Label
CMATC1	ATC level 1
CMATC2	ATC level 2
CMATC3	ATC level 3
CMATC4	ATC level 4
CMDICT	Dictionary and Version
CodedOnDate	Coded on date (UTC)
InitiatedDate	Initiated date (UTC)
LastEditedDate	Last edited date (UTC)
SUBJID	Subject Identifier for the Study

DNR IMPLEMENTATION OF SDTM – INFANT FORMULA

[EC] [ML] [FA]

Study Diary ☐ SD

ECORIG="PAPER DIARY" MLORIG="PAPER DIARY"

ECCAT="STUDY PRODUCT" ECTRT="STUDY FORMULA"

MLCAT="NON-STUDY INFANT FORMULA" MLTRT="NON-STUDY INFANT FORMULA"

Date ☐ SDDAT

ECBTC FADTC

ECEVINTX="TODAY" ECEVAL="PARENT/LEGAL GUARDIAN"

MLEVINTX="TODAY" MLEVAL="PARENT/LEGAL GUARDIAN"

ECDOSFRM="SUSPENSION"

MLDOSFRM="SUSPENSION"

[FA]

FAEVINTX="TODAY" FAORIG="PAPER DIARY"

FACAT="STUDY PRODUCT" (in case 'Not SP' is not ticked)

FACAT="NON-STUDY INFANT FORMULA" (in case 'Not SP' is ticked)

FAOBJ="STUDY FORMULA" (in case 'Not SP' is not ticked)

FAOBJ="NON-STUDY INFANT FORMULA" (in case 'Not SP' is ticked)

Feeding

Number of scoops powder

Amount of water

How much left in the bottle after feeding?

Not Study Product (SP)

1st

FASPID

FATESTCD="COUNT"

FATEST="Count"

FAORRES

FAORRESU="scoops"

FATESTCD="VOLPRP"

FATEST="Volume Prepared"

FAORRES

FAORRESU="fl Oz"

FATESTCD="VOLLFT"

FATEST="Volume Leftover"

FAORRES

FAORRESU="fl Oz"

FASTRESU="mL"

2nd

SF_PSN02

SF_FW2

SF_LO2

SF_F2_U1

CF_NH1

CF_NH2

(Conversion fl Oz to mL:
mL = fl Oz x 29.57353)

[ML] [FA] [CE]

FAORIG="PAPER DIARY"

MLORIG="PAPER DIARY" MLEVINTX="TODAY"

MLEVAL="PARENT/LEGAL GUARDIAN"

Did your infant used a formula that is NOT the Study product?

#21 ☐ SD_CFYN

☐ No

☐ Yes

MLCAT="NON-STUDY INFANT FORMULA" MLTRT="NON-STUDY INFANT FORMULA"

Brand name and type of formula details

MLTRTSP

Did your infant receive any other feedings today?

#22 ☐ SD_OFYN

☐ No ☐ Yes

MLCAT="OTHER FEEDING, COMPLEMENTARY / WEANING PRODUCTS"

(Should only be mapped in case SD_OFYN is Yes)

If yes, please describe type of feeding below

SD_OFSP

Amount

SD_OFAM

MLTRT

MLDOSTXT

DNR IMPLEMENTATION OF SDTM – PROCEDURES (PR)

[PR] [CM] [FA]

Anti-cancer treatment id CANCTREAT

PRCAT="ANTI-CANCER TREATMENT DETAILS"

CMCAT="ANTI-CANCER TREATMENT DETAILS"

Treatment Cycle

id TRTSEQ

Type of cancer #1 id SUBJSP1

☐ CRC

☐ NSCLC

CMINDC

PRINDC

Type of treatment #2 id TREATSP2

☐ Chemotherapy

☐ Concurrent chemoradiotherapy

☐ Immunotherapy

☐ Targeted therapy

☐ Combination of chemotherapy and immunotherapy

{(Not mapped)}

{(For visibility purposes only)}

#3 id TRTNS

☒ Treatment cycle not started

PRCYCND where PRMOOD="PERFORMED" (NOT DONE if ticked)

Was the start of the treatment cycle delayed? #4

☐ Yes ☐ No

{(Not mapped)}

{(Leading question for visibility purposes only)}

PRMOOD = "PLANNED", "PERFORMED"

Actual Start Date of this cycle

id ACTCYCLSTDAT

PRSTDTC where
PRMOOD="PERFORMED"

Planned Start Date of this cycle

id PLCYCLSTDAT

PRSTDTC where
PRMOOD="PLANNED"

Number of days delayed

id DELDAYS

PRDDEL where
PRMOOD="PERFORMED"

Reason for delay #5

id TREATDELREAS

PRREAS where
PRMOOD="PERFORMED"

Other please specify id DELOTHREAS

PRREASSP where
PRMOOD="PERFORMED"

id TRTSEQ	id SUBJSP1	id TREATSP2	id ACTCYCLSTDAT	id PLCYCLSTDAT	id DELDAYS	id SAMETREAT
1	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-01-23	2022-01-16	7	
2	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-02-20	2022-02-06	14	N
3	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-03-07			Y

id DRUGTYPECCOT

OTHER

id DRUGCHOTH

Lonsurf

id IMMUNOCC

Bevacizumab

Bevacizumab

id DOSRDOC1

N

id DOSRDIIM

N

id TRTSTPROC1

N

id TRTSTPRIMM

N

id TRTINTOC1

N

id TRTINTIMM

N

N

id PRSPID	id PRLNKID	id PRTRT	id PRINDC	id PRSTDTC	id PRMOOD	id PRDEL
1		COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-01-23	PERFORMED	7
1	CMR3	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-01-16	PLANNED	
2		COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-02-20	PERFORMED	14
2	CMR4	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-02-06	PLANNED	
3		COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-03-07	PERFORMED	
3	CMR5	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-03-07	PLANNED	

DNR IMPLEMENTATION OF SDTM – CONCOMITANT MEDICATION (CM)

[CM]

Chemotherapy details

CMSCAT = "CHEMOTHERAPY" (in case Type of treatment = "Chemotherapy" or "Concurrent chemoradiotherapy" or "Combination of chemotherapy and immunotherapy"), "TARGETED THERAPY" (in case Type of treatment = "Targeted therapy")

id DRUGTYPECC

CMMOOD="PLANNED"

Type of chemotherapy drug(s) colorectal cancer #7

☒ Capecitabine ☒ 5-Fluorouracil ☐ Leucovorin ☒ Oxaliplatin ☒ Irinotecan
☒ Other

CMTRT

CMOCCUR="Y"

CMPRESP="Y"
(except for Other)

id DRUGTYPELC

Type of chemotherapy drug(s) lung cancer #8

☒ Cisplatin ☒ Carboplatin ☒ Gemcitabine ☒ Pemetrexed ☒ Etoposide
☒ Paclitaxel ☒ Docetaxel ☒ Vinorelbine ☒ Other

CMTRT

CMOCCUR="Y"

CMPRESP="Y"
(except for Other)

id DRUGCHOTH

Other type chemotherapy drug(s)

CMTRT

[CM]

Immunotherapy details

CMSCAT = "IMMUNOTHERAPY" (in case TREATSP2 Immunotherapy or Combination of Chemotherapy and Immunotherapy)

CMMOOD="PLANNED"

Type of immunotherapy lung cancer #54 id IMMUNOLC

☒ Pembrolizumab ☒ Nivolumab ☐ Ipilimumab ☒ Atezolizumab ☒ Other

Specify Other id IMMULCOTH

CMTRT

CMOCCUR="Y"

CMPRESP="Y"
(except for Other)

Type of immunotherapy colorectal cancer id IMMUNOCC

CMTRT

Planned dosage immunotherapy per day

Unit id PLDOSIT_U

id PLDOSIT

CMDOSTXT

CMDOSE

CMDOSU

CMDOSEFRQ = "QD"

⊕ TRTSEQ	△ SUBJSP1	△ TREATSP2	△ ACTCYCLSTDAT	△ PLCYCLSTDAT	⊕ DELDAYS	△ SAMETREAT
1	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-01-23	2022-01-16	7	
2	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-02-20	2022-02-06	14	N
3	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-03-07			Y

△ DRUGTYPECCOT

△ DRUGCHOTH

△ IMMUNOCC

OTHER

Lonsurf

Bevacizumab

Bevacizumab

△ DOSRDOC1

△ DOSRDIMM

△ TRTSTPROC1

△ TRTSTPRIMM

△ TRTINTOC1

△ TRTINTIMM

N

N

N

N

N

N

N

N

N

CMSPID	△ CMTRT	△ CMSCAT	△ CMSTDTC	△ CMMOOD	△ CMLNKID	△ CMLNKGRP
	Bevacizumab	... IMMUNOTHERAPY	2022-01-16	PLANNED	CMFA4	CMPR3
	Lonsurf	CHEMOTHERAPY	2022-01-16	PLANNED	CMFA5	CMPR3
	Bevacizumab	... IMMUNOTHERAPY	2022-02-06	PLANNED	CMFA6	CMPR4
	Bevacizumab	... IMMUNOTHERAPY	2022-03-07	PLANNED	CMFA7	CMPR5

DNR IMPLEMENTATION OF SDTM – FINDINGS ABOUT (FA)

[FA]

FACAT
(Same value as PRCAT or CMCAT)

FASCAT
(Same value as PRSCAT or CMCSAT)

FASPID
(Same value as PRSPID or CMSPID)

Was there a dose reduction >10% for other type chemotherapy drugs 1? #69

☐ Yes ☐ No

FATESTCD="REDUCT"

FAORRES="Y", "N"

FATEST="Dose reduction"

FAOBJ=CMTRT, PRTRT
(For Chemotherapy or Immunotherapy same value as CMTRT as ticked in the beginning of the form; For radiotherapy same value as PRTRT)

Was there a dose reduction >10% for other type chemotherapy drugs 2? #70

☐ Yes ☐ No

FATESTCD="REDUCT"

FAORRES="Y", "N"

FATEST="Dose reduction"

FAOBJ=CMTRT, PRTRT
(For Chemotherapy or Immunotherapy same value as CMTRT as ticked in the beginning of the form; For radiotherapy same value as PRTRT)

Was there a dose reduction >10% for radiotherapy? #97

☐ Yes ☐ No

FATESTCD="REDUCT"

FAORRES="Y", "N"

FATEST="Dose reduction"

FAOBJ=CMTRT, PRTRT
(For Chemotherapy or Immunotherapy same value as CMTRT as ticked in the beginning of the form; For radiotherapy same value as PRTRT)

Was there a dose reduction >10% for immunotherapy? #98

☐ Yes ☐ No

FATESTCD="REDUCT"

FAORRES="Y", "N"

FATEST="Dose reduction"

FAOBJ=CMTRT, PRTRT
(For Chemotherapy or Immunotherapy same value as CMTRT as ticked in the beginning of the form; For radiotherapy same value as PRTRT)

Did administration of other type chemotherapy drugs 1 stop prematurely? #113

☐ Yes ☐ No

Did administration of immunotherapy stop prematurely? #142

☐ Yes ☐ No

Was administration of other type chemotherapy drugs 1 interrupted and re-started later? #157

☐ Yes ☐ No

Was administration of immunotherapy interrupted and re-started later? #185

☐ Yes ☐ No

TRTSEQ

SUBJSP1

TREATSP2

ACTCYCLSDAT

PLCYCLSDAT

DELDAYS

SAMETREAT

1	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-01-23	2022-01-16	7	
2	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-02-20	2022-02-06	14	N
3	CRC	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	2022-03-07			Y

DRUGTYPECCOT

DRUGCHOTH

IMMUNOCC

OTHER	Lonsurf	Bevacizumab
		Bevacizumab

DOSRDOC1

DOSRDIMM

TRTSTPROC1

TRTSTPRIMM

TRTINTOC1

TRTINTIMM

N	N	N	N	N	N
	N		N		N

FASPID

FATESTCD

FATEST

FAOBJ

FASCAT

FAORRES

FASTRESC

FALNKGRP

SAMETRT

1	INTERRUP	Interruptions and re-starts	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA4	
1	REDUCT	Dose reduction	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA4	
1	STOPPED	Prematurely stopped	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA4	
1	INTERRUP	Interruptions and re-starts	Lonsurf	CHEMOTHERAPY	N	N	CMFA5	
1	REDUCT	Dose reduction	Lonsurf	CHEMOTHERAPY	N	N	CMFA5	
1	STOPPED	Prematurely stopped	Lonsurf	CHEMOTHERAPY	N	N	CMFA5	
2	INTERRUP	Interruptions and re-starts	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA6	N
2	REDUCT	Dose reduction	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA6	N
2	STOPPED	Prematurely stopped	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA6	N
3	INTERRUP	Interruptions and re-starts	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA7	Y
3	REDUCT	Dose reduction	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA7	Y
3	STOPPED	Prematurely stopped	Bevacizumab	IMMUNOTHERAPY	N	N	CMFA7	Y

DNR IMPLEMENTATION OF SDTM – RELATIONS (RELREC)

△ RDOMAIN	△ IDVAR	△ IDVARVAL	△ RELTYPE	△ RELID					
CM	CMLNKID		ONE	CMFA	←				
FA	FALNKGRP		MANY	CMFA	←				
PR	PRLNKID		ONE	CMPR	←				
CM	CMLNKGRP		MANY	CMPR	←				
△ CMSPID	△ CMTRT	△ CMSCAT	△ CMSTDTC	△ CMMOOD	△ CMLNKID	△ CMLNKGRP			
1	Bevacizumab	... IMMUNOTHERAPY	2022-01-16	PLANNED	CMFA4	CMPR3	←		
1	Lonsurf	CHEMOTHERAPY	2022-01-16	PLANNED	CMFA5	CMPR3	←		
2	Bevacizumab	... IMMUNOTHERAPY	2022-02-06	PLANNED	CMFA6	CMPR4	←		
3	Bevacizumab	... IMMUNOTHERAPY	2022-03-07	PLANNED	CMFA7	CMPR5	←		
△ PRSPID	△ PRLNKID	△ PRTRT	△ PRINDC	△ PRSTDTC	△ PRMOOD	⊕ PRDEL			
1		COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-01-23	PERFORMED	7			
1	CMPR3	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-01-16	PLANNED		←		
2		COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-02-20	PERFORMED	14			
2	CMPR4	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-02-06	PLANNED				
3		COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-03-07	PERFORMED				
3	CMPR5	COMBINATION OF CHEMOTHERAPY AND IMMUNOTHERAPY	CRC	2022-03-07	PLANNED				
△ FASPID	△ FATESTCD	△ FATEST	△ FAOBJ	△ FASCAT	△ FAORRES	△ FASTRESC	△ FALNKGRP	△ SAMETRT	
1	INTERRUP	Interruptions and re-starts	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA4		←
1	REDUCT	Dose reduction	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA4		←
1	STOPPED	Prematurely stopped	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA4		←
1	INTERRUP	Interruptions and re-starts	Lonsurf	... CHEMOTHERAPY	... N	N	CMFA5		←
1	REDUCT	Dose reduction	Lonsurf	... CHEMOTHERAPY	... N	N	CMFA5		←
1	STOPPED	Prematurely stopped	Lonsurf	... CHEMOTHERAPY	... N	N	CMFA5		←
2	INTERRUP	Interruptions and re-starts	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA6	N	
2	REDUCT	Dose reduction	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA6	N	
2	STOPPED	Prematurely stopped	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA6	N	
3	INTERRUP	Interruptions and re-starts	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA7	Y	
3	REDUCT	Dose reduction	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA7	Y	
3	STOPPED	Prematurely stopped	Bevacizumab	... IMMUNOTHERAPY	... N	N	CMFA7	Y	

COLLABORATION DNR AND OCS

>10 years – data management, SAS programming, statistics

Data warehouse for infant nutrition studies

- Completed studies added to data warehouse
- OCS and DNR providing SDTM knowledge and experience
- OCS developing tooling (mapping, programs, macros)

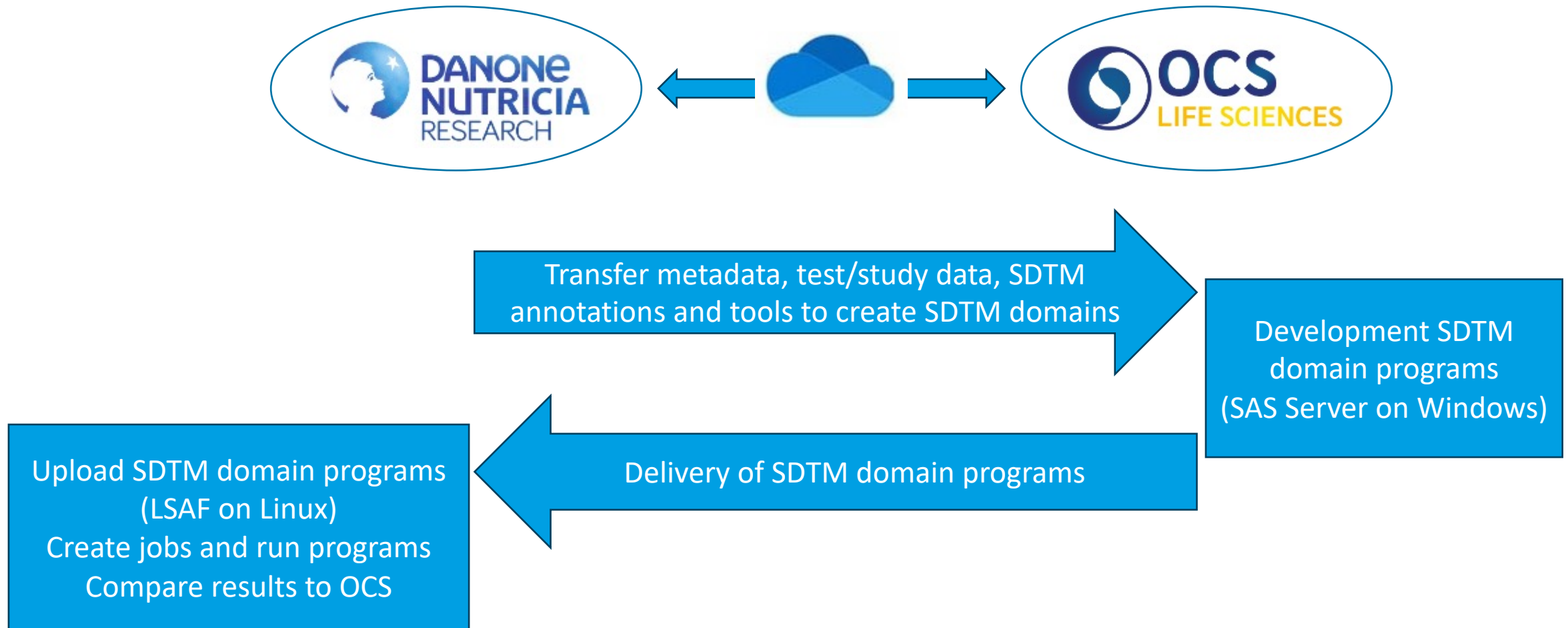
Delivery-and-collaboration model – OCS is part of SDTM team

- More SDTM domains for legacy studies
- Apply SDTM on ongoing studies
- Apply SDTM on new studies:
 - More pressure on timelines
 - Kick off meeting to explain CRF
 - SDTM annotated CRF → used for define.xml
 - Regular meetings to discuss implementation issues
 - Good quality test data

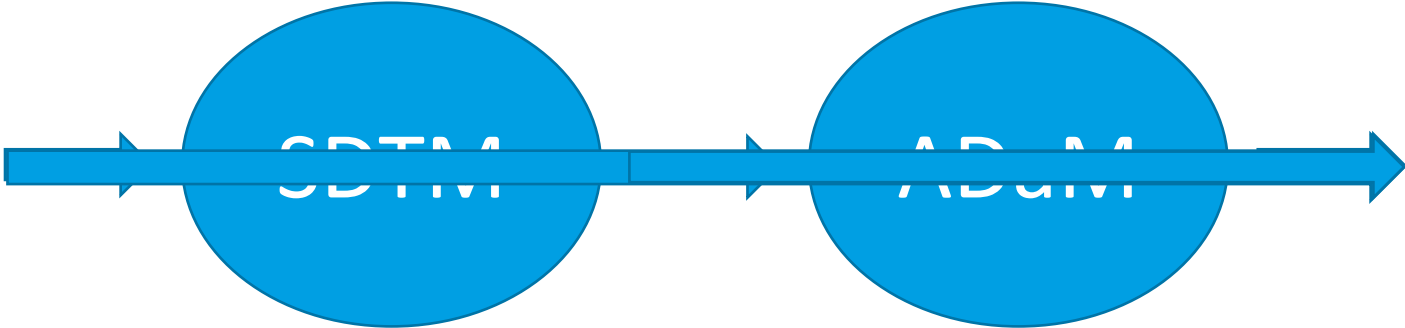
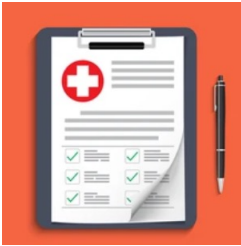


COLLABORATION DNR – OCS

18



STANDARDIZATION PROCESS



Standardized
case report
forms

Table 02.1: Medical history, number of medical history events and number and percentage of subjects with at least one medical history event, by System Organ Class, Preferred Term and study group - Population

Preferred term (MedDRA xx.x)	<group 1>			<group 2>			<etc.>		
	N=xx	k	%	N=xx	k	%	N=xx	k	%
Any Event	xx	xx	x.x%	xx	xx	x.x%	xx	xx	x.x%
Any System organ class									
SOC1									
Any Event	xx	xx	x.x%	xx	xx	x.x%	xx	xx	x.x%
PT1	xx	xx	x.x%	xx	xx	x.x%	xx	xx	x.x%
PT2									
SOC2									
Any Event	xx	xx	x.x%	xx	xx	x.x%	xx	xx	x.x%
PT3	xx	xx	x.x%	xx	xx	x.x%	xx	xx	x.x%

N = Number of subjects of the analysis population; k = number of medical history events; n = number of subjects with one or more medical history event; % relates n to N

Listing 03.3: Comparison of Concomitant medication (CM) and Adverse Event (AE) information, sorted by Subject ID, and AE number

Subject ID	Study group	AE #	Verbatim	Action taken	AE start date	Medication, verbatim	CM start date	Old/new/amended
xxx-xx-	<group			Medication				
xxx	1><group							
	2><etc.>							

Standardized
reports

IMPLEMENTATION OF ADAM - PREPARATIONS

ADaM training provided by OCS

- Introduction to ADaM
- Overview of variables
 - ADSL
 - Basic Data Structure (BDS)
 - Occurrence Dataset (OCCDS)
- DNR specific part



ADaM implementation workgroup

- Templates for ADaM datasets for safety (AE, MH, CM)
- Working towards standardized reports
- By-weekly meetings
- Stand-by for questions

IMPLEMENTATION OF ADAM - DOCUMENTATION

Milestones: Safety Review, Data Review Meeting, Interim Analysis, Key Results, Study Report, Post-hoc Analysis,...

OLD WAY	NEW WAY
Analysis Conventions Document	define-xml Analysis Data Reviewer's Guide (ADRG)
Advantages: - One document	Advantages: - Macro to create define-xml - Template for standard variables
Disadvantages: - A lot of work - Specified topics, but no template	Disadvantages: - Two documents - ADRG complex



Document in between
Analysis Conventions
Document and ADRG

SAS MACROS %SDTM_CREATE_DOMAIN AND %ADAM_CREATE_AD

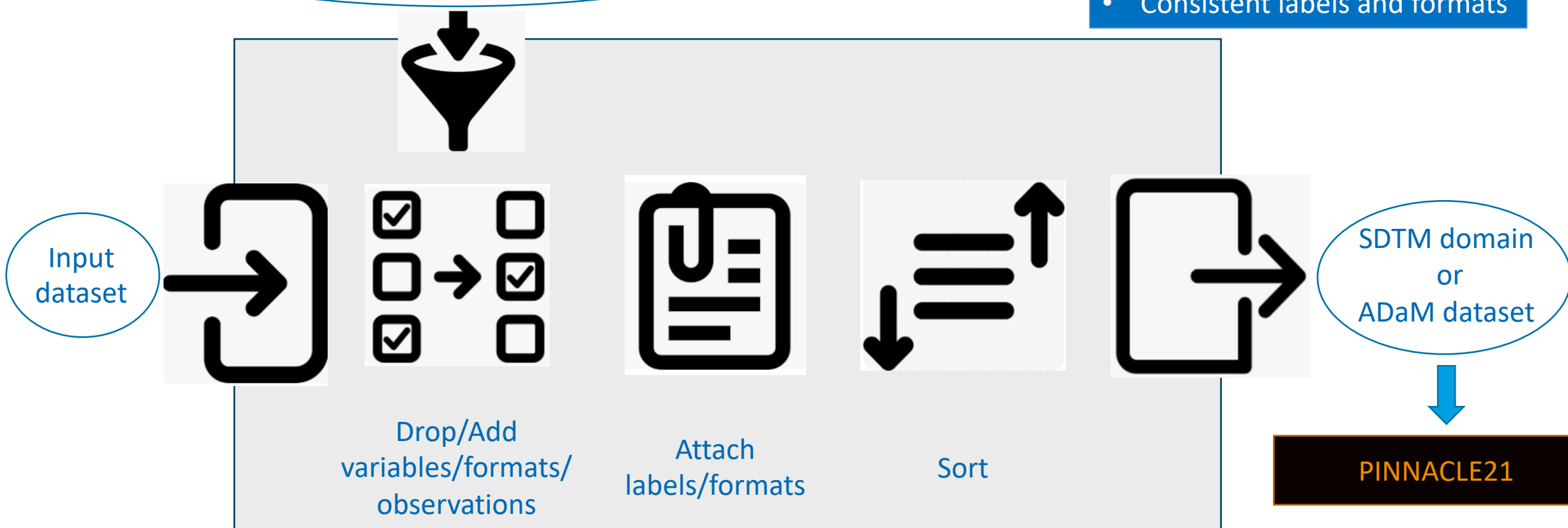
Metadata: DNR-IG

ADaM-IG for ADSL and BDS, OCCDS

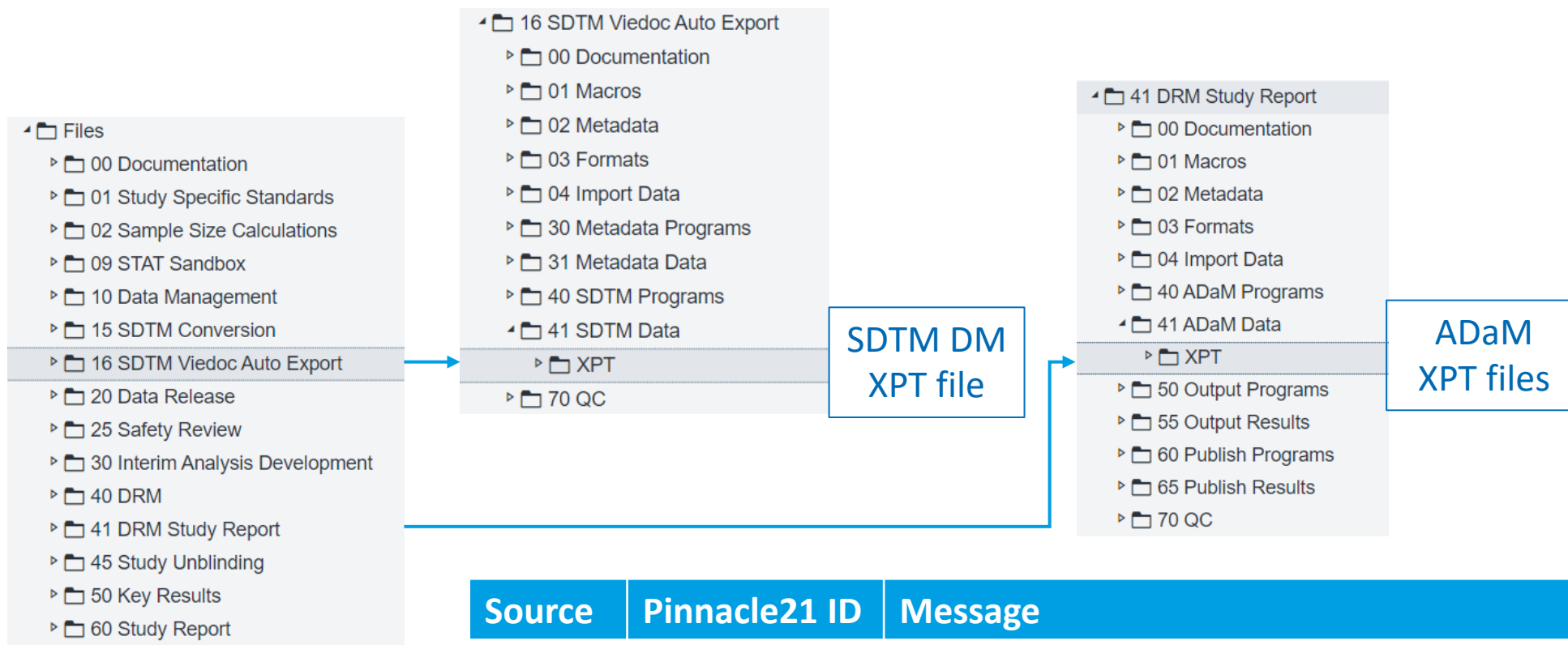
Controlled Terminology

Benefits:

- Order of variables
- Sorting order
- Consistent labels and formats



IMPLEMENTATION OF ADAM - PINNACLE21 VALIDATOR ISSUES



Source	Pinnacle21 ID	Message
GLOBAL	DD0101	Missing define.xml file
GLOBAL	AD0126	Traceability rules not executed due to missing EX dataset
ADSL	CT2002	RACE value not found in 'Race' extensible codelist
ADxx	AD0034	xxxFL value is not Y or null

NEXT STEPS

SDTM:

- Training of data managers outside SDTM implementation workgroup
- define.xml

ADaM:

- ADaM-IG for DNR
- Standardization of reports other than safety (growth, gastro-intestinal symptoms)
- Template for documentation
- define.xml



QUESTIONS?

