



CRT for eCTD submission

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Introduction

Introduction

What is a CRT?

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- CRTs are part of the electronic submission (US only at the moment)
- From the 1st of January 2008, CRT specifications are based on the eCTD (electronic Common Technical Document) rules.
- These new rules implied a lot of changes.
- How Novartis have changed processes to be compliant?
- What have been encountered issues?

What is a CRT?

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- CRT = Case Report Tabulation
- Required by the FDA
- Package created in order to provide to the FDA the raw & derived datasets
- 2 CRTs for one study :
 - One containing only raw datasets (if needed)
 - One containing only derived datasets

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■ Package contains :

- SAS V5 Transport files of either the raw or derived datasets (**<xxx>.xpt**) Format required by FDA.
- The data definition table (**Define.pdf**), regrouping :
 - A table of content of the raw or derived datasets
 - Hyperlinks to the XPT files
 - An alphabetical list of variables and formats
- The CRF / eCRF for raw CRT
- the Data Derivation and handling Document (DDD) for derived CRT

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- The Data Derivation & Handling document is not required by the FDA but Novartis considers the DDD as mandatory.
- The DDD should contain details which are not self-explanatory by the variable label within the data definition table.
- It provides further detailed explanation to the reviewer on special data handling issues and other data imputation rules or convention that were used in the study.

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Data Definition table

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1 Listing Datasets Table of Contents

Dataset	Description of Dataset	Row Count	Location
DATA1	Label for the 1st dataset	4	data1.xpt
DATA2	Label for the 2nd dataset	5	data2.xpt
PFT	Pulmonary Function Test	824	pft.xpt
R_FMTDAT	Raw datasets formats	3	r_fmtdat.xpt

Annotated CRF : Etudeblankcrf.pdf

1.1 DATA1—Label for the 1st dataset

Located on page(s) 1 of the Annotated CRF.

DATA1—Label for the 1st dataset

Variable	Label	Type	Length	Format
VAR1	Label 1	Char	8	
VAR2	Label 2	Num	8	
VAR3	Label 3	Num	8	FMTPERSO
VAR4	Label 4	Num	8	
VAR5	Label 5	Char	8	

	VAR1	VAR2	VAR3	VAR4
1	v1	2	0	5
2	v2	4	1	5
3	v3	78	0	21
4	v4	99	1	1

1.4 Listing Data FORMATS

1.4.1 FMTPERSO

FMTPERSO	
Code	Value
0	Yes
1	No
2	For ever

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[Redacted]	ID	Center No. [] Subject No. []	Screening (Day -35 to -1) EOS/EOT (1,777,778)
	Subject's initials	1. [] 2. [] fam. []	

MRKEVLTC(CRNTC)

Pulmonary function test

Date of test: PFT1D(PFT10 der) [] day [] month [] year

Please mark if evaluation was not done: ☐

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Name of the
dataset

Label of the
dataset

Name of the
variable as it
appears in
the dataset

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ID

Center No. Subject No.

Subject's initials 1. 2. fam.

Screening
(Day -35 to -1)
EOS/EOT
(1,777,778)

MRKEVL1C(CRNTC)

Please mark if evaluation was not done: ☐

Pulmonary function test

PFT1D(PFT1O der)

Date of test: day month year

TOTCPY1N

Total lung capacity: day month year

FVC4N

Forced vital capacity(FVC): day month year

FEVPCT8N

Forced expiratory volume
in one second (FEV1): day month year

FUNCPY1N

Functional residual
capacity: day month year

RSDCPY1N

Residual capacity: day month year

DCODNE1C(YNO1C)

Diffusion capacity for
CO (DLCO) done: ☐ 0 No ☐ 1 Yes

TST1D(TST1O der)

Date of CO (DLCO) test: day month year

DCO1N

Diffusion capacity for
CO (DLCO): day month year

DCOUNT1C(DCOUNT1C)

DLCO unit: ☐ 1 mL/min/torr ☐ 2 mL/min/mmHg ☐ 3 mmol/min/KPa

PLSDNE1C(YNO1C)

Pulse oximetry done: ☐ 0 No ☐ 1 Yes

PLSDNE1D(PLSDNE1O der)

Date of pulse oximetry: day month year

INPOXY1N

% Inspired oxygen: day month year

OXYSAT1N

% oxygen saturation: day month year

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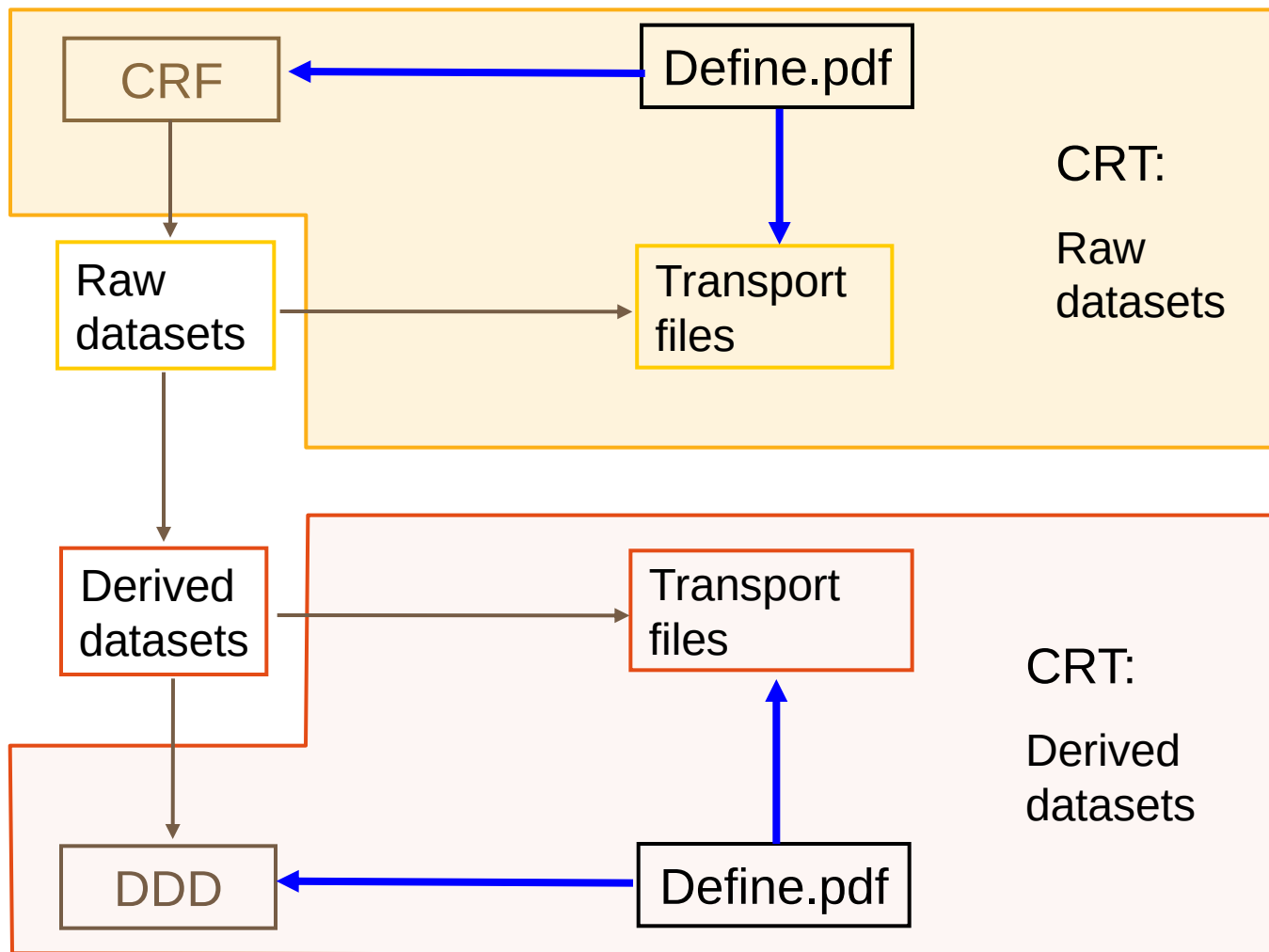
Data definition table

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New eCTD rules

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- The new electronic format of CRT required additional rules to be followed:
 - Naming conventions (no underscores)
 - Specific folder structure (listings, analysis)
- No underscores:
 - Previous naming convention for a derived dataset was a_dataset.
 - For old studies, underscores are removed at the moment of the translating in SAS version 5 transport files.
- The specific folder structure implied to create two CRTs instead of one.

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Before :

Raw and
derived datasets
in the same
define

Dataset	Description of Dataset	Row Count	Location
AEV	Adverse events	224	..\2303\RAW\aev.xpt
CMD	Concomitant medication	723	..\2303\RAW\cmd.xpt
CMP	Study completion	382	..\2303\RAW\cmp.xpt
CND	Medical history/Current cond.	563	..\2303\RAW\cnd.xpt
COM	Comments	395	..\2303\RAW\com.xpt
DMG	Demography	194	..\2303\RAW\dmg.xpt

Now :

Raw datasets



Listings CRT

Derived datasets



Analysis CRT

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- A standard macro create the data definition table automatically.
- The macro works with a call of parameters, the update to be compliant with the new eCTD rules have added a new parameter.
- The different parameters are:
 - DVD or NODVD: to include the Data Derivation and Handling document or not.
 - RAW or NORAW: to include Listings datasets or not.
 - eCTD: to apply the new rules during the creation of the CRT.

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- The programmer have to deliver the CRT to DRA (Drug Regulatory Affair) in Novartis.
- DRA is the primary contact with FDA. They have to transfer CRTs.
- As the CRT is the last part of the programming work, these have to be fully reviewed by both programmer and statistician.
- A final review is done by the project programmer and the global manager

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- FDA have recently asked us to provide more information in the data definition table.

==> Here is what the **Novartis CRT tool** produce

1.34 A_PTR—Prior Therapy:Radiotherapy

A_PTR—Prior Therapy:Radiotherapy				
Variable	Label	Type	Length	Format
AGE_1N	Age at Baseline	Num	8	
BESRES1C	Best response	Num	8	BESR11_
COU1A	Country code	Char	3	

==> Here is the **formatting expected by the FDA:**

Variable Name	Label	Type	Formats(Codes)	ORIGIN	ROLL	Comments
ACYCLE	Analysis Cycle	char		Derived		See acyclec.pdf
ACYCLEC	Analysis Cycle Code	num		Derived		See acyclec.pdf
AGE	Age (years)	num		Derived		(date of randomization – date of birth + 1)/365.25
AGEGRP	Age Group	char		Derived		Group by age
AGEGRP2	Age Group2	char		Derived		Group by age

- Actually, because of the automation the only document we can modify is the DDD.
- The standard macro will be updated.

Conclusion

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- CRT: final step of Statistical Reporting work
- CRT is one of the most important SR document but the working time to create a CRT is often underestimated...
- Next step: CRT in XML format

Questions ?