



Reading and Resolving OpenCIDSC Message

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Background

About OpenCDISC

About OpenCDISC

- ▶ An open source community focused on building extensible frameworks and tools for the implementation and advancement of CDISC Standards.
- ▶ OpenCDISC is used by the FDA in the acceptance process of a CDISC submission.
- ▶ Most updated version is v2.0.2
- ▶ Easy to use
- ▶ Free

OpenCDISC: Bitter and Sweet

- ▶ When we open the OpenCDISC report, we expect

Processed Sources							
Domain	Label	Class	Source	Records	Errors	Warnings	Notices
GLOBAL	Global Metadata	--	--	--	0	0	0
AE	Adverse Events	EVENTS	ae.xpt	3746	0	0	0
CM	Concomitant Medications	INTERVENTIONS	cm.xpt	24351	0	0	0
CO	Comments	SPECIAL PURPOSE	co.xpt	4575	0	0	0
DA	Drug Accountability	FINDINGS	da.xpt	31219	0	0	0
DM	Demographics	SPECIAL PURPOSE	dm.xpt	887	0	0	0
DS	Disposition	EVENTS	ds.xpt	4849	0	0	0
DV	Protocol Deviations	EVENTS	dv.xpt	534	0	0	0
EG	ECG Test Results	FINDINGS	eg.xpt	19070	0	0	0
EX	Exposure	INTERVENTIONS	ex.xpt	14138	0	0	0
FA	Findings About Death	FINDINGS ABOUT	fazd.xpt	6	0	0	0
IE	Inclusion/Exclusion Criterion Not Met	FINDINGS	ie.xpt	297	0	0	0
LB	Laboratory Test Results	FINDINGS	lb.xpt	445142	0	0	0
MH	Medical History	EVENTS	mh.xpt	13897	0	0	0
OM	Imaging	FINDINGS	om.xpt	831554	0	0	0
PC	Pharmacokinetic Concentrations	FINDINGS	pc.xpt	2980	0	0	0
SC	Subject Characteristics	FINDINGS	sc.xpt	2733	0	0	0
SE	Subject Elements	SPECIAL PURPOSE	se.xpt	3798	0	0	0
SU	Substance Use	INTERVENTIONS	su.xpt	607	0	0	0

OpenCDISC: Bitter and Sweet

► But the truth is...

Issue Summary					
Source	OpenCDISC ID	Publisher ID	Message	Severity	Found
AE					
	SD0009	FDAC206	No qualifiers set to 'Y', when AE is Serious	Error	163
	SD0058	FDAC027	Variable appears in dataset, but is not in SDTM model	Error	1
	SD0080	FDAC208	AE start date is after the latest Disposition date	Error	2
	CT2002	FDAC341	EPOCH value not found in 'Epoch' extensible codelist	Warning	3696
	SD0021	FDAC117	Missing End Time-Point value	Warning	690
	SD0031	FDAC122	Missing values for AESTDTC, AESTRF and AESTRTPT, when AEENDTC, AEENRF or AEENRTPT is provided	Warning	2
	SD1097	FDAC022	No Treatment Emergent info for Adverse Event	Warning	3746
CM					
	CT2002	FDAC341	CMDOSFRQ value not found in 'Frequency' extensible codelist	Warning	512
	CT2002	FDAC341	CMDOSU value not found in 'Unit' extensible codelist	Warning	1227
	CT2002	FDAC341	CMROUTE value not found in 'Route of Administration' extensible codelist	Warning	182
	CT2002	FDAC341	EPOCH value not found in 'Epoch' extensible codelist	Warning	12053
	SD0021	FDAC117	Missing End Time-Point value	Warning	71
	SD0031	FDAC122	Missing values for CMSTDTC, CMSTRF and CMSTRPT, when CMENDTC, CMENRF or CMENRTPT is provided	Warning	2
CO					
	SD0058	FDAC027	Variable appears in dataset, but is not in SDTM model	Error	1
	SD0072	FDAC065	Invalid RDOMAIN	Error	744
	SD0065	FDAC104	USUBJID/VISIT/VISITNUM values do not match SV domain data	Warning	113
	SD1023	FDAC105	VISIT/VISITNUM values do not match TV domain data	Warning	1249
	SD1076	FDAC031	Model permissible variable added into standard domain	Warning	2
DA					
	CT2002	FDAC341	EPOCH value not found in 'Epoch' extensible codelist	Warning	31197
	SD0065	FDAC104	USUBJID/VISIT/VISITNUM values do not match SV domain data	Warning	31

Type of messages

- ▶ Error
- ▶ Warning
- ▶ Notices
- ▶ Consistency
- ▶ Cross-reference
- ▶ Format
- ▶ Limit
- ▶ Metadata
- ▶ Presence
- ▶ Terminology

Which type need to be fix? Which type need to be explain?

By Severity

By category

Examples

Message and solution

Type I: Issue caused by OCV

OpenCDISC software bugs

▶ Label match? Label mismatch?

CM	CMTRT, Reported Name of Drug, Med, or Therapy	SD0063	SDTM/dataset variable label mismatch	Warning
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CMTRT	Reported Name of Drug, Med, or Therapy	Char		Topic
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▶ Required Variable missing? Non SDTM variable?

When EPOCH is not included in VS

VS	EPOCH, VS	SD1077	FDA Expected variable not found	Warning
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When EPOCH is included in VS

VS	EPOCH	SD1076	Model permissible variable added into standard domain	Information
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Above issues are already fixed in OCV 2.0.1

Type I: Issue from OCV

OpenCDISC too Strict rule

► Insufficient sorting key

OM	VISITNUM, OMEVAL, OMCAT, OMDTC, OMTESTCD, OMLOC, USUBJID, OMMETHOD	2, READER, SESSION 1, 2012-08-30, EROS, DIP2, 1001001, X-RAY	SD1117	Duplicate records
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OMLAT should also be a key variable expected.

► Non-required variable used to check

AE	AESER	Y	SD0009	No qualifiers set to 'Y', when AE is Serious	Error
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Non of the qualifier variable (AESCAN, AESCONG, AESDISAB, AESDTH, AESHOSP, AESLIFE, AESMIE) is collected.

► Unit for category parameter

XE	XESTRESC, XESTRESU, XETEST, XETESTCD	1, null, Swollen Joint Total Score, SWJTSCO	SD0029	Missing value for XESTRESU, when XESTRESC is provided	Warning
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Category parameter, no unit necessary

Type I: Issue from OCV

OpenCDISC too Strict rule

- ▶ Randomized but not dosed

DM	ARMCD, USUBJID	DOSE1, 101001	SD0070	No Exposure record found for subject	Warning
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Randomized subject not necessary to be dosed

- ▶ VISIT/VISITNUM inconsistency for Unplan visit

SV	VISITNUM, VISIT	9.001, UNP_LB	SD0052	Inconsistent value for VISITNUM within VISIT	Warning
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Unplan visit name not exist in TV

- ▶ Comment in label

PC	PCXXXX	XXXX Comment	SD1120	Comments in SUPPFA domain	Warning
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Comment is only a word in the label

Type II: Issue from Data

Data format

- ▶ Label inconsistency

SD0063	SDTM/dataset variable label mismatch	Warning
SD0046	Inconsistent value for QLABEL within QNAM	Warning

- ▶ Sequence of variables

SD1079	Variable is in wrong order within domain	Warning
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Check the SDTM IG or OpenCDISC config.

- ▶ Variable length too long for actual data

SD1082	Variable length is too long for actual data	Error
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Compress the length via actual data

Type II: Issue from Data

Issue caused in submit package

▶ Dataset too large

SD1071 Dataset is greater than 1 GB in size Warning

We need to split the xpt when the size > 1GB

▶ Dataset Empty

SD0001 Domain table should have at least one record Error

No death case then no need to submit ZD

▶ Pure/SUPP inconsistency

IDVAR, IDVARVAL, VSSEQ, 43267,
SUPPVS RDOMAIN, USUBJIDVS, 1001001 SD0077 Invalid referenced record Error

VSSEQ	VSTESTCD	VSTEST	VSPOS	VSORF
43265	SYSBP	Systolic Blood Pressure	SITTING	126.00
43266	WEIGHT	Weight		208.40
43268	WEIGHT	Weight		208.80

IDVAR	IDVARV	QNAM	QLABEL	
VSSEQ	43266	PCSNUM	Precision Number	1
VSSEQ	43267	PCSNUM	Precision Number	1
VSSEQ	43268	PCSNUM	Precision Number	1

Reference record not found in Pure

Type II: Issue from Data

Issue caused in submit package

▶ Invalid RDOMAIN

CO	RDOMAIN	ZE	SD0072	Invalid RDOMAIN	Error
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ZE not submitted, but comment collected.

▶ FA (Finding about) datasets

FA	DOMAIN	ZD	SD0004	Inconsistent value for DOMAIN	Error
SUPPFA	RDOMAIN	ZD	SD0072	Invalid RDOMAIN	Error

- The DOMAIN value would be **FA**
- The dataset names would be the domain name plus up to two additional characters indicating the parent domain
- **FASEQ** must be unique within USUBJID for all records across the split datasets.
- Supplemental Qualifier datasets would need to be managed at the split-file level, and RDOMAIN would be defined as **FA**.

Type II: Issue from Data

Data Issues can be fixed

▶ Invalid subject

EG	USUBJID	1001001	SD0064	Subject is not present in DM domain	Error
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Data issue, report to DM and resolved.

▶ Required variable missing

CM	CMTRT	null	SD0002	Required	Error
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CM not coded, report to DM and resolved.

AE: AEDECOD, CM: CMTRT, MH: MHTERM, EX: EXTRT

VS	VSSTRESC VSORRES	Null, 5.71	SD0026	Missing value for VSORRESU, when VSORRES is provided	Error
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Programming issue when convert unit, fixed

Type II: Issue from Data

Data Issues can be fixed

▶ Redundancy in paired variables values

AE	AECAT, AESCAT	GENERAL, GENERAL	SD1041	Values for AECAT and AESCAT are identical	Warning
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Remove SCAT or remap the SCAT value

▶ Standard unit consistency

LB	LBMETHOD, LBTESTCD, LBSCAT, LBSTRESU, LBCAT, LBSPEC	null, CA, null, mg/dL	SD0007	Inconsistent value for Standard Units	Error
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Remove SCAT or remap the SCAT value

▶ SV inconsistency with other domains

SD0065	USUBJID/VISIT/VISITNUM values do not match SV domain data			Warning
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Reconcile SV

Type II: Issue from Data

Data Issues related with CT

Rule ID	Message	Category	Severity
CT00XX	Value for --XXX not found in (XXX) CT codelist	Terminology	Warning

▶ Non-extensible CT

- Must be remapped or check.
Example: SEX, AGEU

▶ Extensible CT

- Can be remapped.
Example: Q2W to EVERY 2 WEEKS in UNIT
DEATH to FATAL in AEOUT
XRAY to X-RAY in METHOD
- Can be listed in the SDRG.
Example: ECG tests,
Study specific EPOCH

Type II: Issue from Data

Data Issues have to be explained

- ▶ Data issue because of PD

SE	SESTDTC, SEENDTC	2012-07-26, 2012-07-12	SD0080	SESTDTC is after SEENDTC	ERROR
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Special case, re-randomized subject sign IFC after dose, PD entered.

- ▶ Multi assessment on one day

VS	VISITNUM, VSDTC, USUBJID, VSTESTCD	1, 2012-03-01, 1001001, PULSE	SD1117	Duplicate records	Warning
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This subject assess twice on the same day.

Type III: Issue from Study

Study specific design

▶ Obs after last disposition

AE	USUBJID, AESTDTC	1001003, 2014-06-18	SD0080	AE start date is after the latest Disposition date
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Study specific cut off rule use first dose of extension.

▶ Variable not necessary

ZN	VARIABLE	ZNBLFL	SD1044	No ZNBLFL variable in custom Findings domain	Warning
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ZN only collected on randomization, no BLFL needed

▶ No baseline record

DM	ARMCD, USUBJID	DOSE1, 101001	SD0006	No baseline result in EG for subject	Warning
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Time used to define baseline EG/LB. Randomize visit maybe regarded as post-baseline.

Issue caused by multi reasons

Real case

QS	SD0065	USUBJID/VISIT/VISITNUM values do not match SV domain data	Warning	12241
QS	SD1023	VISIT/VISITNUM values do not match TV domain data	Warning	18877

▶ Type I issue:

Visit name of unplanned visits are not included in TV, already Explained in SDRG.

▶ Type II issue:

Visitnum not given for some planned visit, data issue, need to report to DM to fix the visitnum and rebuild SV.

A message may caused by different reasons, we must check the detail to prevent hidden type II issue.

Summary

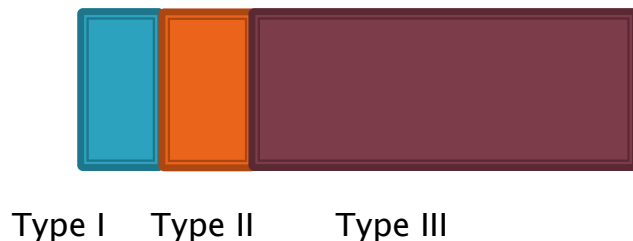
Summary

► OpenCDISC message component:

Before:



After:



Most of the type II issues can be identified before DBL and need to be fixed in the submission package.

Summary

- ▶ We are not able to expect 100% clean OpenCDISC report, but we need to let it as clean as possible.
- ▶ Generally, We need to recognize type I issue, fix type II issue, explain type III issue.
- ▶ Perform the OpenCDISC check the sooner, the better, try to have all type II issue fixed before lock.

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