

Using OpenCDISC to Prepare for FDA Submissions

Regulatory requirements and common data issues

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Disclaimer

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Topics

- › Regulatory requirements
- › General recommendations
- › Common data issues

Be aware of regulatory expectations

- › ICH
- › FDA Guidances
- › New FDA requirements
 - › CDER Common Data Standards Issues
 - › Study Data Technical Conformance Guide
 - › Upcoming data validation rules
- › CDISC Standards

- › Sponsor should comply with Regulatory Guidance and Standards
- › Sponsors can outsource work, but not their responsibility for data quality
 - › “trust but verify”
- › High data quality can be achieved only by well-designed process
- › OpenCDISC Validator is a tool to help, but process is also important

Regulatory landscape is changing

- › CDISC Standards are becoming required
- › FDA reviewers want CDISC
- › FDA is starting an enforcement of Standards and Data Quality
- › Science, technology and industry are ready
- › There are no more excuses to avoid CDISC

Recommendations

- › Design your process
- › Start CDISC implementation early
 - › IND, not NDA
 - › CRF design
 - › Map to SDTM before data collection
 - › Prescriptive metadata
 - › Run validation during data collection to fix issue

- › Build up internal expertise
- › Validate deliveries from vendors
- › Use the most advanced science and utilize features of new versions of
 - › Standards
 - › Validation Rules

- › Fix all identified data issues if possible
- › Provide explanations for false-positive validation messages
- › Provide explanations with sensitivity analysis on non-fixable issues
- › Communicate with FDA on their expectations

Most common data issues

#1 Metadata

- › Most commonly overseen area
- › Data without definition is useless
- › Poor quality of metadata reduce quality of data

Define.xml Origin

- › Missing Origin
- › Inconsistency. E.g.,
 - › Origin="CRF Page x" and populated Method
- › Origin="CRF" without reference to particular page

CRF

- › Annotations as a highlighted text
- › Annotations to original EDC variables

Reviewers Guide

- › Usage of outdated OpenCDISC versions.
E.g., v1.3
 - › It's not an excuse for low quality data
- › Meaningless explanations for issues.
E.g.,
 - › “Expected result”
 - › “As received from our vendor”

Additional documents are welcome

- › Supplemental data definition
- › Complicated algorithms
- › Mapping specifications
- › Conversion and look-up tables

#2 Control Terminology (CT)

- › Ignoring extensible CT. E.g.,
 - › “Sponsor defined CT”
 - › “We can add whatever we want”
- › You can only add terms that are not already represented in standard CT
- › If it’s not CT compliant, it’s not CDISC data

- › Collecting data as a free text
 - › Mapping problems
 - › No control
- › Converting standard terms into Upper Case

Recommendations

- › Start using CT during CRF design. E.g.,
 - › Pre-specified options instead of free text
 - › AEACN=“DOSE CHANGED”. Is it increased or decreased?
 - › Any mapping introduces a risk of loosing or changing data

#3 Additional FDA Requirements

- › EPOCH
- › Study Days
- › Baseline Flag
- › AETRTEM flag
- › Trial Summary and Trial Design domains
- › Re-sizing variable length to actual max value

#4 Usage of outdated standards

- › Example:
 - › Oncology domains were introduced in SDTM IG v3.1.3
 - › Sponsors try to implement them within SDTM IG v3.1.1
 - › New variables are kept in SUPPQUAL
 - › RELREC links SUPPQUAL records
 - › Data is not reviewable and not CDISC compliant

- › FDA wants new variables. E.g., DTHFL, full MedDRA coding
- › Problems with CT. E.g.,
 - › VSLOC="LEFT ARM" instead of
 - › VSLOC="ARM", VSLAT="LEFT"
- › Usage of old standard is not an excuse for low quality data!

#5 Programming/Mapping

- › Inconsistent Standard Units
- › Leading space characters. E.g.,
 - › “ Glucose”
- › <Line break> symbol
- › Usage of Actual time instead of Planned for –TPT
- › Usage of –STRF, --ENRF for Screen Failures

- › Inconsistency in paired variables
 - › --TESTCD/--TEST
 - › QNAM/QLABEL
 - › -TPT/--TPTNUM
 - › VISIT/VISITNUM
- › Inconsistency in paired CT. E.g.,
 - › EGTESTCD="QTC" and EGTEST="QT
Uncorrected"

- › Comments in SUPPQUAL domains
- › Missing TS and Trial Design domains
- › Incorrect order of variables and non-standard labels
- › Data management info in submission data. E.g.,
 - › Samples or scans tracking
- › Imputation of study days for partially missing dates

#6 Data Collection

- › Duplicate records. E.g.,
 - › LB results on the same test and time point as “Normal” and “Abnormal”
- › AE Seriousness Criteria were not collected
- › Missing Original Units for Lab Test Results

Recommendations

- › “Risk Based” monitoring
 - › Safety data
 - › Baseline/End Point records
 - › Death info
- › “Quality by design”
- › Catch errors as soon as possible
- › Start data validation early

New check examples

- › Sponsor is responsible for data quality
- › OpenCDISC can help
- › SDRG expect Sponsors to execute their additional validation checks
- › Data quality is defined not by low number of identified issues, but by actual data content
- › New checks are helpful, not a threat

- › “If any of AE Seriousness Criteria variables has value ‘Y’, then AESER must be ‘Y’ “ – Error
- › “CMDECOD value is expected to be populated” – Warning
 - › CMDECOD is Permissible variable
 - › When its value is missing it’s usually due to wrong type of info. E.g.,
 - › ‘Lung Biopsy’
 - › ‘Colonoscopy’

Questions

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