



Paper SI09

Lab Master List File Makes Easy

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Overview



What is Lab Data



Lab Data End-to-End Process Flow



Major Lab Data Challenges



Lab Master List File & Supported Process



What Is Next On The Horizon



Conclusion

What is Lab Data



Why is Lab Data Important in Clinical Trials?

The primary objectives for collecting lab data in the trial

- To provide the best indicators for systemic toxicities in clinical trials of investigational products
- To evaluate a patient's overall safety experience in a trial

In clinical trials, lab tests are used to:

- Establish inclusion and exclusion criteria
- Determine baseline parameters
- Monitor the safety of the participants
- Demonstrate the efficacy of the investigational product

Lab Data End-to-End Process Flow

STUDY PLANNING

- Protocol / Study Design / CDASH Library / Team Decisions
- Sponsors mandatory Lab Test List per TA Standard per Phase

DATA COLLECTION

- CDASH / EDC, eCRF Spec, CCGs, DMP, DTP
- Central Lab (DTS)

DATA TABULATION

- SDTM / aCRF / aDTS / Mapping Spec / Issues and Challenges
- SEND (Standard Exchange of Non-Clinical Data)*

STATISTICAL ANALYSIS

- ADaM / SAP / TLFs Shell / ADaM Data Spec
- Issues and Challenges

TABLES, LISTINGS, FIGURES

- Tables, Listings, Figures outputs, Lab Data Interpretation
- CSRs, ICH E3 Section 12.4, 14.3.4, 16.2.8

Major Lab Data Challenges

STUDY PLANNING

- What lab tests to be included?
- What laboratory to analyze the lab test?
- Reference CDASH Library
- Sponsors MANDATORY MINIMUM Lab Test List per TA standard per Phase of the clinical trial

DATA COLLECTION

- Different types of EDC systems
- Different types of labs eCRF and/or DTS designs
- Variability in sources of the lab data
- Variability in lab test names
- Hematology differential test

Major Lab Data Challenges (Cont.)

DATA TABULATION

- Standardized lab test name and category
- Standardized units (i.e. Need ONE standard unit per lab parameter)
- Conversion of reported lab values to U.S. Conventional or SI units
- Lab toxicity grading using NCI CTCAE
- FDA requirement for LOINC codes submission for studies that start after March 15, 2020 for NDAs, aNDAs and certain BLAs

ANALYSIS & REPORTING

- Bi-directional lab tests analysis and reporting
- Lab precision

Solution - Lab Master List File Project

- ❖ The project was initiated in 2012 by author, a new process improvement initiative of developing **global EDC, SDTM and ADaM standards across sponsors, TAs and lab vendors.**
 - To resolve identified lab data issues and challenges
 - To facilitate future lab data collection, mapping, analysis and reporting process
- ❖ **Ultimate Objective:** to plan and design a global standard lab tool to:
 - standardize and streamline the overall lab data end-to-end process
 - create high-quality submission-ready SDTM and ADaM lab data packages

Development Process - Initial Stage



What does your lab data process flow look like:

- ❑ “garbage in, garbage out”
- ❑ “garbage in, -with intensive programming cleaning and mapping efforts-, then **quality data out**”
- ❑ “quality data in, quality data out”

Lab Master List File Components

Four major components for the standardization of the SDTM, ADaM and TLFs process including:

- 1) **Lab Test Conversion tab:** all unique source lab test names and their corresponding standardized SDTM lab test names, standardized lab SI units, the specimen type and test method (LBCAT, LBTEST, LBTESTCD, LBSTRESU, LBSPEC and LBMETHOD)
- 2) **Lab Unit Conversion tab(s):** all available source lab test units and their corresponding standardized SDTM lab test units (LBSTRESU), per sponsor defined U.S. Conventional units or SI units conversion factors
- 3) **Lab Test CTCAE Grading tab(s):** all available lab test CTCAE grading, the range criteria for each grade and the direction of the grading (i.e. increase or decrease), one tab per version (i.e. v4.03 and v5.0)
- 4) **Lab Precision tab:** to identify precision to be displayed for specific lab parameters for both U.S. Conventional and SI results

Lab Master List File Components

SOURCE LBTEST (LBTESTSP/TESTNAME)	SOURCE LBTESTCD (LBTESTSP)	SOTM LB.LBTEST	SOTM LB.LBTESTCD	SOTM LB.LBCAT	SOTM LB.LBSTRESU	SOTM LB.LBSPEC	SOTM LB.LBMETHOD
ALT (Alanine Aminotransferase)		Alanine	ALT	CHEMISTRY	U/L	BLOOD	

Lab Test Conversion tab

Lab Unit Conversion tab(s)

SOURCE LBTEST (LBTESTSP/TESTNAME)	SOURCE LBTESTCD (LBTESTSP)	SOURCE LAB UNIT (LBUNIT/LBORRESU)	LB.LBSTRESU	Conversion factor
BLOOD UREA NITROGEN	BUN	MMOL/L	mmol/L	1
BUN (Blood Urea Nitrogen)		mg/dL	mmol/L	0.357
CALCIUM	CA	MG/DL	mmol/L	0.25
CALCIUM	CA	MMOL/L	mmol/L	1
CALCIUM	CA	MEQ/L	mmol/L	1
Calcium		mg/dL	mmol/L	0.25
CHOLESTEROL: TOTAL	CHOL	MMOL/L	mmol/L	1
CHOLESTEROL: TOTAL	CHOL	MG/DL	mmol/L	0.02586
Cholesterol		mg/dL	mmol/L	0.02586
CHLORIDE	CL	MEQ/L	mmol/L	1
CHLORIDE	CL	MMOL/L	mmol/L	1
Chloride		mmol/L	mmol/L	1
CREATININE	CREAT	MCMOL/L	umol/L	1
CREATININE	CREAT	MG/DL	umol/L	88.4
CREATININE	CREAT	MG/L	umol/L	8.84
CREATININE	CREAT	MMOL/L	umol/L	1000
		UMMOL/L	umol/L	1
		UMOL/L	umol/L	1

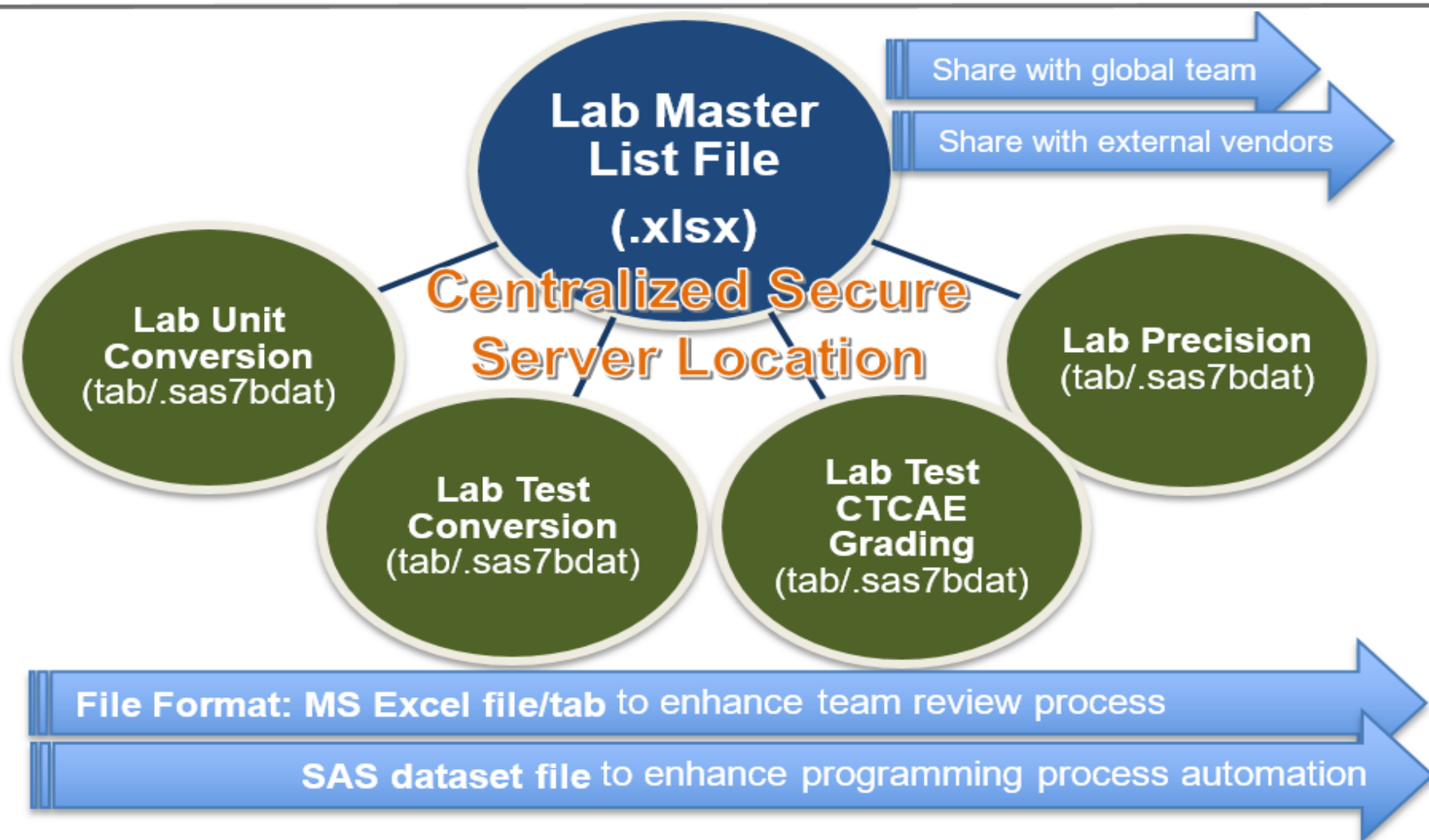
GRADE	RANGE1	LBTEST	LBTESTCD	RANGE2	LBSTRESU	DIR	TERM
1	1	Aspartate Aminotransferase	AST	3	*ULN	i	Aspartate aminotransferase increased
2	3	Aspartate Aminotransferase	AST	5	*ULN	i	Aspartate aminotransferase increased
3	5	Aspartate Aminotransferase	AST	20	*ULN	i	Aspartate aminotransferase increased
4	20	Aspartate Aminotransferase	AST	1.00E+11	*ULN	i	Aspartate aminotransferase increased
1	1	Bilirubin	BILI	1.5	*ULN	i	Blood bilirubin increased
2	1.5	Bilirubin	BILI	3	*ULN	i	Blood bilirubin increased
3	3	Bilirubin	BILI	10	*ULN	i	Blood bilirubin increased
4	10	Bilirubin	BILI	1.00E+11	*ULN	i	Blood bilirubin increased
1	1	Calcium	CA	2	mmol/L	d	Hypocalcemia
2	2	Calcium	CA	1.75	mmol/L	d	Hypocalcemia
3	1.75	Calcium	CA	1.5	mmol/L	d	Hypocalcemia
4	1.5	Calcium	CA	0	mmol/L	d	Hypocalcemia
1	1	Calcium	CA	2.9	mmol/L	i	Hypercalcemia
2	2.9	Calcium	CA	3.1	mmol/L	i	Hypercalcemia
3	3.1	Calcium	CA	3.4	mmol/L	i	Hypercalcemia
4	3.4	Calcium	CA	1.00E+11	mmol/L	i	Hypercalcemia
1	1	Glucose	GLUC	3	mmol/L	d	Hypoglycemia
2	3	Glucose	GLUC	2.2	mmol/L	d	Hypoglycemia
3	2.2	Glucose	GLUC	1.7	mmol/L	d	Hypoglycemia
4	1.7	Glucose	GLUC	0	mmol/L	d	Hypoglycemia
1	1	Glucose	GLUC	8.9	mmol/L	i	Hyperglycemia
2	8.9	Glucose	GLUC	13.9	mmol/L	i	Hyperglycemia
3	13.9	Glucose	GLUC	27.8	mmol/L	i	Hyperglycemia
4	27.9	Glucose	GLUC	1.00E+11	mmol/L	i	Hyperglycemia

PARAMCD	PARAMN	CONV PREC	SI PREC
WBC	1	1	1
HGB	2	1	1
HCT	3	0	2
NEUTLE	5	0	2
LYMLE	6	0	2
MONOLE	7	0	2
EOSLE	8	0	2
BASOLE	9	2	4
NEUT	10	0	0
LYM	11	0	0
MONO	12	0	0
EOS	13	0	0
BASO	14	0	0

Lab Precision tab

Lab Test CTCAE Grading tab(s)

Lab Master List File Formats



Biometrics Group R&Rs

☐ Lab Master List File Owner:

- ☐ to initiate the creation and update of the file, set up standard SDTM LB mapping rules, prepare supported guideline and programming implementation document
- ☐ to serve as the owner and primary contact for updating this document

☐ Study CDM:

- ☐ to help query missing or questionable lab tests and units for data cleaning
- ☐ to help safeguard the source data quality
- ☐ to communicate with EDC, central and local lab vendors to ensure lab data test names and units design and entries following this standards document

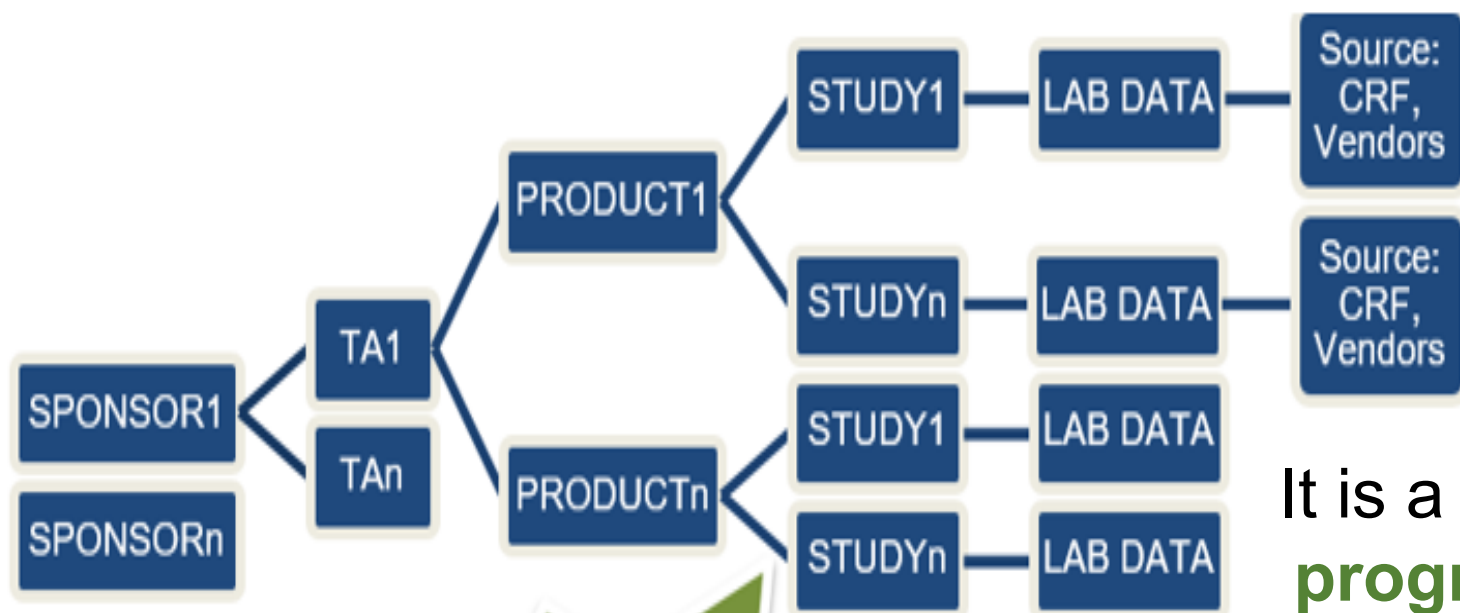
☐ Study Statistician:

- ☐ general review of the file
- ☐ to follow this lab master list file for Protocol, SAP and TLFs shells design

☐ Study Programmer:

- ☐ to implement this file during SDTM, ADaM and TLFs programming process
- ☐ to provide new identified lab tests and units against the existing list
- ☐ to review and cross-check per most current CT and codelists

Development Process - Ongoing Strategies



It is a **continued programming**

effort to maximum the collection of **unique** source **lab test names, units** and **conversion factors**

****New****
Version of CDISC CT
Sponsor defined codelist

Implementation Process

PLANNING

- Protocol / Study Design process: use the standardized lab test names and associated lab test units as possible
- TA/project/study KO Meeting: to set the ground rule to implement the set standards for lab data design, collection, SDTM, ADaM, TLFs process

DATA COLLECTION

- EDC, CDASH, CRF, DTS source lab data standardization process: CDM to reference and use the standard lab test names and units
- CDM effort to promote active communications with vendors, sites for data design, entry and queries

DATA TABULATION

- SDTM LB standardization process: Programming to use during the mapping and conversion
- To assign the standard LBCAT, LBTEST, LBTESTCD, LBSTRESU, LBSPEC, LBMETHOD
- To apply conversion factors to LBSTRESC, LBSTRESN, LBSTNRLO, LBSTNRHI
- To create LBTOXGR, LBTOXGRN
- To inform CDM and note the omission of LBLOINC if not provided by vendors

STATISTICAL ANALYSIS

- ADaM / SAP / TLFs Shell standardization process: Statistician to use the standardized lab test names and units for SAP and shells design to be consistent with SDTM settings
- Programming to create bi-directional lab analysis parameters

TABLES, LISTINGS, FIGURES

- Tables, Listings, Figures outputs: use the standardized lab test names and units as possible
- Apply lab data precision for summary table reporting purpose

General Considerations

❑ Programming:

- To be more actively involved in the Protocol, CRF planning, EDC UAT, SAP and TLFs shell process.
- What is the appropriate lab Standard Unit (LBSTRESU) to use?
 - ❖ Misconception between the “Standardized Unit” and “SI Unit”.
- Set up automate process to incorporate these tools to streamline the lab tests, lab units standardization and conversion, CTCAE grading and lab precision process.

❑ Keep External Vendors In The Loop

Benefits Of Using Lab Master List File

- ❑ It is important and beneficial to have a **centralized one-stop-shop lab tool** for all lab data process needs to enhance the process automation
- ❑ The project team, especially the Biometrics group have significantly **improved their overall efficiency and consistency**, as we all follow the same set of lab data standards throughout the study life cycle
- ❑ Promote proactive and effective communications with internal study team and external vendors, to create **standardized, harmonized, accurate and high-quality lab data package**
- ❑ This tool **has been Implemented by multiple sponsors and their CRO partners**, supported multiple successful FDA NDA/BLA SDTM and ADaM submission packages

What Is Next On The Horizon

- ❑ Sponsors are required to submit LOINC using SDTM LBLOINC for studies that start after **March 15, 2020** for NDAs, aNDAs and certain BLAs.
- ❑ Recommendations in term of the lab data process flow
 - **Data Collection:** CDM need to add this field to the EDC eCRF and DTS to ensure LOINC is available at the source data
 - **Data Tabulation:** If such LOINC codes are not available from the laboratory, then
 - Sponsors DO NOT attempt to derive a mapping to LOINC when create the SDTM files that can lead to serious data quality issues
 - For any lab test where a LOINC code is not submitted, the reason of this omission should be noted in the cSDRG

Conclusion

- ❑ The Lab Master List File is a **living document** with **continued effort** to collect and standardize new **unique** lab test names, units and unit conversion factors.
- ❑ This is a **jointed Biometrics team effort** to standardize, harmonize and streamline the overall study lab data end-to-end process.
- ❑ This is a **one-stop-shop shared tool** to make study team and programming job easier and more efficient when come to lab data process.



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Thank You !

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