创建LB/ADLB过程中遇到的问题和经验总结-案例分享

Presented by
李舒新, 统计编程经理, 凯莱英临床(凯诺)

Meet the Speaker

李舒新

Title: 统计编程经理

Organization: 凯莱英临床(凯诺)

从事统计编程工作6年多，曾任职于杰纳医药、君实生物，在肿瘤、血液病、新型冠状病毒等治疗领域有丰富的编程及项目管理经验。

2024年4月加入凯莱英临床（凯诺）统计编程部门，目前主要负责项目管理与执行、部门建设等工作。

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

- *The author(s) have no real or apparent conflicts of interest to report.*

Agenda

1. Lab data概述
2. 关于LB/ADLB最新的行业指南规定
3. 关于LB/ADLB的一些热门问题讨论/分享

Lab data概述

- Lab Data简介
- Lab Data处理时的疑难点

Lab Data简介

What is lab data exactly?

Any test normally performed by a clinical laboratory is considered a lab test.

Lab data is often referred to as the clinical laboratory data or the laboratory test results.

CDISC SDTM LB is defined as the SDTM domain captures laboratory data collected on the CRF or received from a central provider or a third party vendor.

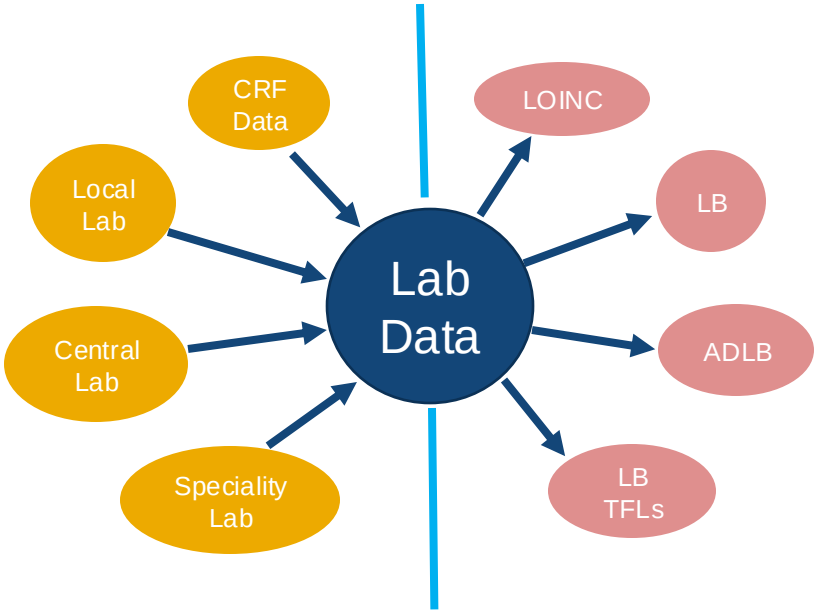
Lab Data简介

Importance

- 决定受试者是否入组、评估药物的安全性甚至疗效

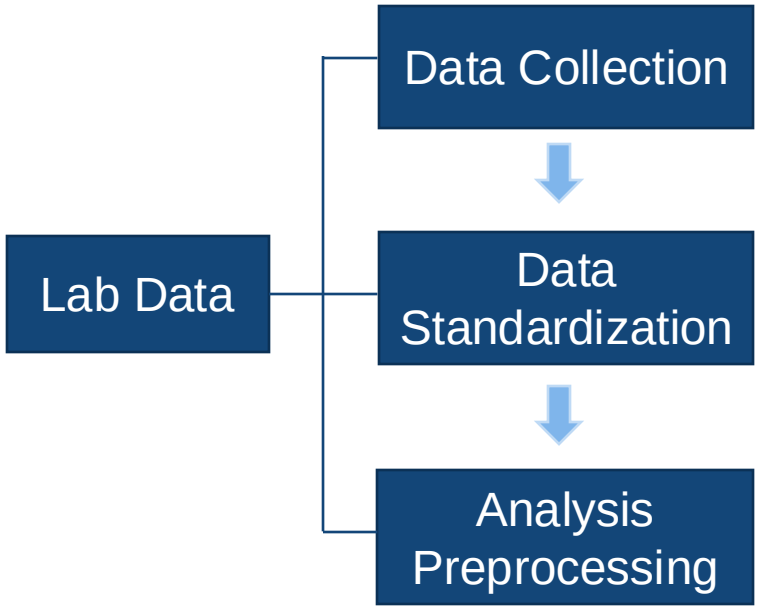
Challenges

- 实验室数据来源广泛、数据量大，如何将其转换为可递交的LB/ADLB数据集？



During the PharmaSUG 2019 Open Session, the PharmaSUG Family Feud Survey voted ADLB the least favorite ADaM data set to program.

Lab Data处理时的疑难点



- 来源广泛（local & central）
- 不同类型（血常规/尿常规/便常规）

导致数据量大、格式不统一等问题

- 数据储存（ SDTM IG）
- 单位(LBSTRESU, LCSTRESU)
- 检查项目(LBCAT, LBTEST)

- CTCAE毒性等级(LBTOXGR, ATOXGR)
- 行业指南规定（ADaM IG, TCG, Pilot OCE/OOD Standard Safety Data Requests, etc）

关于LB/ADLB最新的行业指南规定

- SDTM IG 对于Lab Data的规定
- sdTCG 对于Lab unit存放的最新规定
- FDA pilot OCE/OOD关于ADLB数据集的要求

FDA Data Standards Catalog v10.3

FDA Data Standards Catalog v10.3

Full description of column headings in Instr.& Column Descriptions tab. Rows with data models are in bold with blue fill. Dependant properties (i.e., IG, technical do

Use	Standard	Exchange Format	SDO	Property	Related Properties	FDA Center(s)	Date Support Begins	Date Support Ends	Date Requirement Begins [10] [11]	Date Requirement Ends	St G Sc
Clinical study datasets	**ADaM**	**XPT**	**CDISC**	**ADaMv2.1**		**CDER, CBER**	**Ongoing**		**12/17/2016 [1] 12/17/2017 [2]**		**St**
Clinical study datasets	ADaM	XPT	CDISC	ADaMIGv1.0		CDER, CBER	Ongoing	03/15/2019 [1] [12] 03/15/2020 [2] [12]	12/17/2016 [1] 12/17/2017 [2]	03/15/2019 [1] [12] 03/15/2020 [2] [12]	St
Clinical study datasets	ADaM	XPT	CDISC	ADaMIGv1.1		CDER, CBER	2017/10/2		03/15/2019 [1] 03/15/2020 [2]		St
Clinical study datasets	ADaM	XPT	CDISC	ADaMIGv1.2 ADaMIGv1.3		CDER, CBER	07/18/2022		03/15/2024		St
Clinical study datasets	**SDTM**	**XPT**	**CDISC**	**SDTMv1.1**		**CDER, CBER**	**Ongoing**	**01/28/2015 [12]**			**St**
Clinical study datasets	SDTM	XPT	CDISC	SDTMIGv3.1.1		CDER, CBER	Ongoing	01/28/2015 [12]			St
Clinical study datasets	SDTM	XPT	CDISC	SDTMIGv3.1.2		CDER, CBER	2009/10/30	03/15/2019 [1] [12] 03/15/2020 [2] [12]	12/17/2016 [1] 12/17/2017 [2]	03/15/2019 [1] [12] 03/15/2020 [2] [12]	St
Clinical study datasets	SDTM	XPT	CDISC	SDTMIG Version 3.1.2 Amendment 1		CDER, CBER	08/07/2013	03/15/2019 [1] [12] 03/15/2020 [2] [12]	12/17/2016 [1] 12/17/2017 [2]	03/15/2019 [1] [12] 03/15/2020 [2] [12]	St
Clinical study datasets	**SDTM**	**XPT**	**CDISC**	**SDTMv1.3**		**CDER, CBER**	**12/01/2012**	**03/15/2021 [12]**	**12/17/2016 [1] 12/17/2017 [2]**	**03/15/2021 [12]**	**St**
Clinical study datasets	SDTM	XPT	CDISC	SDTMIGv3.1.3		CDER, CBER	12/01/2012	033/15/2021 [12]	12/17/2016 [1] 12/17/2017 [2]	03/15/2021 [12]	St
Clinical study datasets	**SDTM**	**XPT**	**CDISC**	**SDTMv1.4**		**CDER, CBER**	**08/17/2015**		**03/15/2018 [1] 03/15/2019 [2]**		**St**
Clinical study datasets	SDTM	XPT	CDISC	SDTMIGv3.2		CDER, CBER	08/17/2015	12/13/2023 [12]	03/15/2018 [1] 03/15/2019 [2]	12/13/2023 [12]	St
Clinical study datasets	**SDTM**	**XPT**	**CDISC**	**SDTMv1.7**		**CDER, CBER**	**07/07/2020**		**03/15/2023**		**St**
Clinical study datasets	SDTM	XPT	CDISC	SDTMIGv3.3		CDER, CBER	07/07/2020		03/15/2023		St
Clinical study datasets	**SDTM**	**XPT**	**CDISC**	**SDTMv2.0**		**CDER, CBER**	**12/13/2023 [12]**		**03/15/2025 [12]**		**St**
Clinical study datasets	SDTM	XPT	CDISC	SDTMIGv3.4		CDER, CBER	12/13/2023 [12]		03/15/2025 [12]		St

Data Standards Catalog v10.3：
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-standards-catalog

LB Domain Changes Across SDTMIG v3.2 through SDTMIG v3.4

SDTMIG Version	Version Date	non-host microorganism tests (非宿主微生物检测)	other subject immune response assessments* （其他的受试者免疫反应评估）	Variables Update
v3.2	2013-11-29	√	√	-
v3.3	2018-02-20	χ	√	Add LBSTREFC, LBLOBXFL, LBENDY
v3.4	2021-11-29	χ	χ	Add LBTSTCND, LBBDAGNT, LBTSTOPO, LBRESSCL, LBRESTYP, LBCOLSRT, LBLLOD, LBSPCUFL, LBANMETH, LBORREF, LBSTREFN, LBTMTHSN, LBCLSIG, LBPTFL, LBPDUR

*other subject immune response assessments: except study therapy-induced subject immune response (研究疗法诱导的受试者免疫反应以外的免疫反应)

SDTM IG v3.4对于Lab Data的规定

BE (Biospecimen Events)

RELSPEC (Related Specimens)

BS (Related Specimens)

CP (Cell Phenotype Findings)

GF (Genomics Findings)

IS (Immunogenicity Specimen Assessments)

LB (Laboratory Test Results)

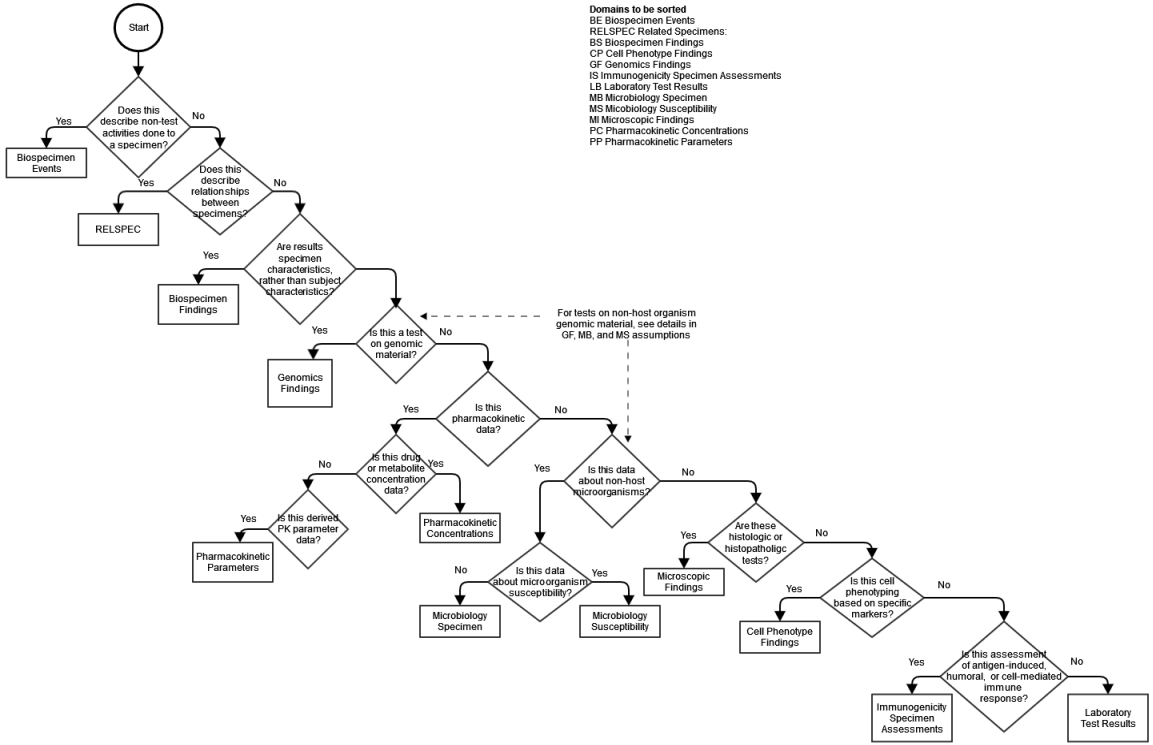
MB (Microbiology Specimen)

MS (Microbiology Susceptibility)

MI (Microscopic Findings)

PC (Pharmacokinetics Concentrations)

PP (Pharmacokinetics Parameters)



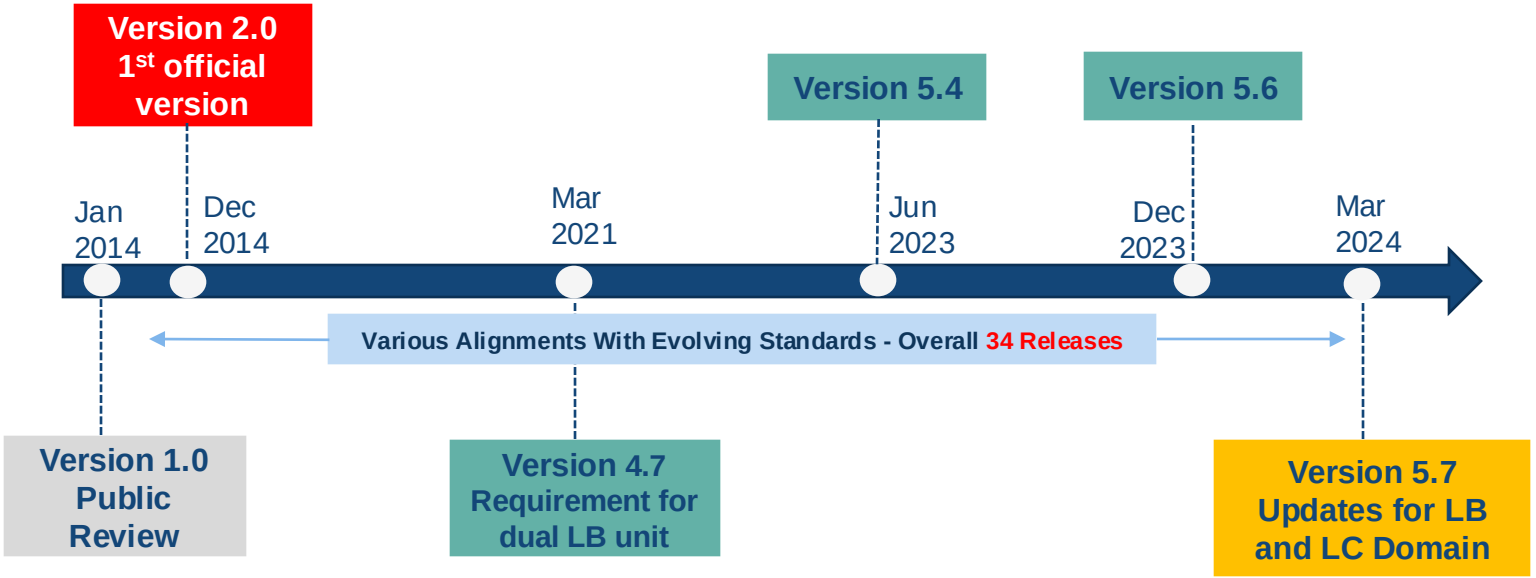
Where Does My Lab Data Go in SDTMIG v3.4? https://www.cdisc.org/kb/articles/where-does-my-lab-data-go-sdtmig-v3-4

Study Data Technical Conformance Guide(sdTCG)

- **发布机构：** FDA
- **发布原因：**This Guide provides technical recommendations to sponsors for the submission of animal and human study data and related information in a standardized electronic format in INDs, NDAs, ANDAs, and BLAs.
- **发布计划：**The plan is to publish updated versions in March and October of each calendar year. However, the Guide will be posted sooner if important issues arise.
- **最新版本：**v5.7(2024-03)

sdTCG(v5.7) link：https://www.fda.gov/media/153632/download

Study Data Technical Conformance Guide (sdTCG)



sdTCG(v5.7)对于Lab unit存放的规定

Section 4.1.1.3 SDTM Domain Specifications - LB and LC Domain (Laboratory)

For clinical studies, please submit two separate domains for lab results. The LB domain should contain SI units in LBSTRESU for the SI results in the LBSTRESC and LBSTRESN fields. An additional custom domain called LC structured identically to LB should contain conventional units in --STRESU for the results in conventional units in the --STRESC and --STRESN variables. It is ideal if both conventional and SI units come directly from the lab vendor. Submit the results of all tests obtained on subjects, including the results from unscheduled tests or visits, and results obtained from local laboratories. Identify all reference ranges used for specific populations in the SDRG and ADRG.

SI unit: International System of Units

Submitting the LC Upfront or On Request

1. Does the sponsor have to submit the LC domain or only when asked?

- The sponsor is now expected to prospectively submit both the LB and LC domain to the FDA. Not only if requested by an FDA review division.

sdTCG 5.7 (2024-03)

For clinical studies, please submit two separate domains for lab results.

- In earlier versions of the sdTCG sponsors were informed of the potential for a request for conventional units and requested to discuss with the review division.

sdTCG 4.7 (2021-03)

FDA may require laboratory data using conventional units for reviewing submissions and labeling. Sponsors should discuss with the review divisions what laboratory data should utilize conventional units prior to submission.

Copying Records From LB to LC

LBSEQ	LBTESTCD	LBTEST	LBORRES	LBORRESU	LBSTRESC	LBSTRESU
1	SODIUM	Sodium	136	mmol/L	136	mmol/L
2	GLUCOSE	Glucose	3.9	mmol/L	3.9	mmol/L
3	CO2	Carbon Dioxide	25	mEq/L	25	mmol/L
4	CREAT	Creatinine	1.025	mg/dL	90.61	umol/L
5	PH	pH	7.5		7.5	
6	HCG	Choriogonadotropin Beta	-		NEGATIVE	
7	ABO	ABO Blood Group	A		A	
8	TSH	Thyrotropin	2.235	mIU/L	2.235	mIU/L

SI

Conventional

Unitless

Nominal

Same Unit in SI and Conventional

LCSEQ	LCTESTCD	LCTEST	LCORRES	LCORRESU	LCSTRESC	LCSTRESU
1	SODIUM	Sodium	136	mmol/L	136	mEq/L
2	GLUCOSE	Glucose	3.9	mmol/L	70.27027	mg/dL
3	CO2	Carbon Dioxide	25	mEq/L	25	mEq/L
4	CREAT	Creatinine	1.025	mg/dL	1.025	mg/dL
5	PH	pH	7.5		7.5	
6	HCG	Choriogonadotropin Beta	-		NEGATIVE	
7	ABO	ABO Blood Group	A		A	
8	TSH	Thyrotropin	2.235	mIU/L	2.235	mIU/L

All records should be repeated with conversions performed as/if necessary to keep the LB/LCSEQ Key consistent

来源：https://www.cdisc.org/sites/default/files/2024-04/2024_CDISC_Europe%20-%20Submitting%20Laboratory%20Data%20in%20Multiple%20Standard%20Units%20V1.2.pdf

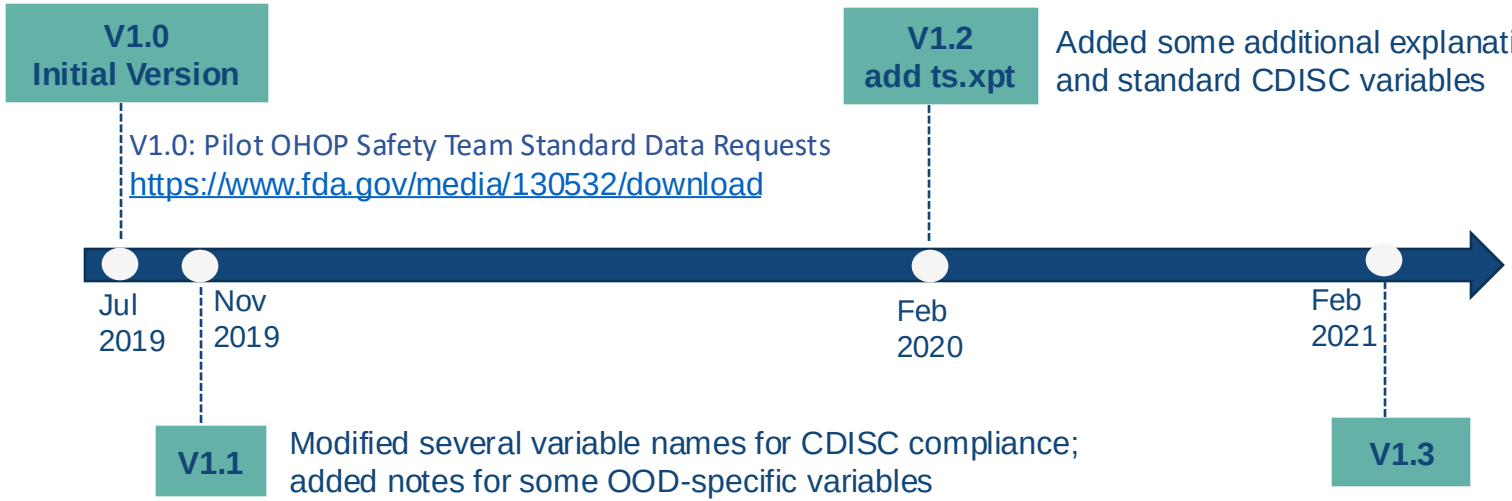
Pilot OCE/OOD Standard Safety Data Requests简介

- **发布机构：** OCE/OOD
- **发布原因：** There is tremendous variability and inconsistency in the use of the CDISC ADaM data standard in safety datasets for oncology NDA/BLA applications submitted to FDA. This variability leads to inefficiency in review for the FDA and multiple information requests to applicants during the course of the review to resolve inconsistencies in analyses between FDA and applicants.
- **最新版本：** v1.3(2021-02)

OCE(OHOP)： Oncology Centre of Excellence（肿瘤卓越中心）
https://www.fda.gov/about-fda/fda-organization/oncology-center-excellence

OOD： Office of Oncologic Diseases（肿瘤疾病办公室）
https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-oncologic-diseases-ood

Pilot OCE/OOD Standard Safety Data Requests简介



- V1.3: Pilot OCE/OOD Safety Team Standard Data Requests
https://www.fda.gov/media/133252/download
- v1.3里涉及到ADSL, ADAE, ADEX, ADEXSUM, ADCRSNT, ADLB, TS

Pilot OCE/OOD Standard Safety Data Requests-ADLB

Pilot OCE/OOD Standard Safety Data Requests v1.3

ADLB Variable Name	Variable Label	Type	Codelist/ Controlled Terms	CDISC Core	OCE/OOD Core (SDTM or ADaM)	CDISC Variable (ADaMIG v1.1 or SDTM v3.3 or OCE/OOD v1.3=FDA)	OCE/OOD Additional Information
TRxxSDT	Date of First Exposure in Period xx	Num		Cond	Cond	ADaM	Required if there are multiple treatment periods
TRxxEDT	Date of Last Exposure in Period xx	Num		Cond	Cond	ADaM	Required if there are multiple treatment periods
AVISIT	Analysis Visit	Char		Cond	Cond	ADaM	Required if there are multiple treatment periods
ADT	Analysis Date	Num		Perm	Req	ADaM	
ADY	Analysis Relative Day	Num		Perm	Req	ADaM	
APERIOD	Period	Num		Perm	Req	ADaM	
PARAM	Parameter	Char		Req	Req	ADaM	
PARAMCD	Parameter Code	Char		Req	Req	ADaM	
AVAL	Analysis Value	Num		Cond	Req	ADaM	
AVALC	Analysis Value (C)	Char		Cond	Cond	ADaM	
AVALU	Analysis Value Unit	Char		N/A	Req	FDA	Include even if unit is included in PARAM description.

OCE/OOD和CDISC里面core不一样的变量

OCE/OOD要求的新变量

Pilot OCE/OOD Standard Safety Data Requests-ADLB

- 和sponsor的命名规则不一样的变量

Pilot OCE/OOD Standard Safety Data Requests v1.3

ADLB Variable Name	Variable Label	Type	Codelist/ Controlled Terms	CDISC Core	OCE/OOD Core (SDTM or ADaM)	CDISC Variable (ADaMIG v1.1 or SDTM v3.3 or OCE/OOD v1.3=FDA)	OCE/OOD Additional Information
BTOXGRHN	Baseline Toxicity Grade High (N)	Num	0, 1, 2, 3, 4, Null	Perm	Req	ADaM	Numeric version of BTOXGRH
EVLLBFL	Evaluable Lab Flag	Char	Y, N	N/A	Req	FDA	Flag baseline and all on-study values for those lab parameters where a subject has both a baseline and at least one on-study value for a specified laboratory test. Only include laboratory values that occur during the period defined for the Treatment Emergent adverse event flag (TRTEMFL) for the adverse event dataset

Pilot OCE/OOD Standard Safety Data Requests-ADLB

对于ADLB的变量要求:

CDISC Core	OCE/OOD Core (SDTM or ADaM)	Variables
Req	Req	USUBJID、TR01SDT、PARAM、PARAMCD、LBSEQ、LBTESTCD、LBTEST
Cond	Cond	TRTxxA、TRxxSDT、TRxxEDT、AVISIT、AVALC、BASE
Perm	Perm	CHG、PCHG
Exp	**Req**	DTHFL、LBSTRESN、LBSTRESC、LBSTRESU
Cond	**Req**	SAFFL、TRT01A、TR01EDT、AVAL、ABLFL
Perm	**Req**	APERIOD、ADT、ADY、ANRLO、ANRHI、ANRIND、ATOXGRL、ATOXGRH、ATOXGRLN、ATOXGRHN、BTOXGRL、BTOXGRH、BTOXGRLN、BTOXGRHN
N/A	**Req**	**AVALU、EVLLBFL**、BNRIND
N/A	**Perm**	**TRTFL**

EVLLBFL(Evaluable Lab Flag)

Table 3. Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in ≥ 5% of Patients in Study 1

Laboratory Abnormality	Grade 3 or 4† (%)*
Chemistry	
Gamma Glutamyl Transferase Increased	[redacted]
Hypophosphatemia	[redacted]
Hyponatremia	[redacted]
Alkaline Phosphatase Increased	[redacted]
Hematology	
Lymphopenia	[redacted]

† Graded according to NCI CTCAE version 4.03.
* Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: [redacted]

1、同时有基线和至少一个治疗期间的LB检查结果；

2、“治疗期间”需要与ADAE.TRTEMFL定义一致

说明书表格中，对于分母的处理和展示

The standard in OCE/OOD for analyses reported in the laboratory abnormalities table in product labeling is to use patients with a baseline and at least one post-baseline laboratory evaluation as the denominator for each test. The denominator will vary from test to test. This is to ensure that all patients who had laboratory evaluations done both pre and post-drug exposure for each test are captured.

有基线并且至少有一次基线后实验室检查的受试者例数作为分母:

- 每个检查项目的分母可能都会不一样
- 为了确保每个药物暴露前后都进行了实验室检查的受试者都被纳入分析

Table 4
Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline with Incidence ≥1% in Worsening to Grade 3 or 4
Safety Analysis Set

Grou

Category Laboratory test	Worsened to Grade 3 or 4 n (%)	Worsened ≥1 Grade from Baseline n (%)
Chemistry		
Gamma Glutamyl Transferase Increased (IU/L) (m=129)	10 (7.8%)	44 (34.1%)
Magnesium Increased (mmol/L) (m=129)	4 (3.1%)	16 (12.4%)
Phosphate Decreased (mmol/L) (m=129)	10 (7.8%)	58 (45.0%)
Potassium Decreased (mmol/L) (m=129)	5 (3.9%)	21 (16.3%)
Sodium Decreased (mmol/L) (m=129)	7 (5.4%)	57 (44.2%)
Triglycerides Increased (mmol/L) (m=128)	4 (3.1%)	46 (35.9%)
Hematology		
Hemoglobin Decreased (g/L) (m=129)	[illegible]	[illegible]
Hemoglobin Increased (g/L) (m=129)	[illegible]	[illegible]
Leukocytes Decreased (10^9/L) (m=129)	[illegible]	[illegible]
Lymphocytes Decreased (10^9/L) (m=129)	[illegible]	[illegible]
Neutrophils Decreased (10^9/L) (m=129)	[illegible]	[illegible]
Platelets Decreased (10^9/L) (m=129)	[illegible]	[illegible]
Liver Function		
Alanine Aminotransferase Increased (IU/L) (m=129)	[illegible]	[illegible]
Alkaline Phosphatase Increased (IU/L) (m=129)	[illegible]	[illegible]
Aspartate Aminotransferase Increased (IU/L) (m=129)	[illegible]	[illegible]
Bilirubin Increased (umol/L) (m=129)	[illegible]	[illegible]

Pilot OCE/OOD Standard Safety Data Requests补充

- Under the RTOR program, when submitting complete ADaM datasets for key efficacy and safety tables/figures for the pivotal study, please refer to OOD Safety standard data specifications for the requested format of safety datasets.
- This document is a pilot, it is not required per standard yet

RTOR (Real-Time Oncology Review) https://www.fda.gov/about-fda/oncology-center-excellence/real-time-oncology-review

Real-Time Oncology Review (RTOR) Guidance for Industry: https://www.fda.gov/media/160186/download

PHUSE (Phmaceutical Users Software Exchange): https://advance.phuse.global/display/WEL/FDA+Oncology+Safety+Data+Standards

OCE/OOD关于两个方向CTCAE等级的检查项目的规定及行业内的一些做法

Method 1： Two columns for toxicity grade should be populated for consistency in evaluation to account for labs with bidirectional grading (e.g. potassium)

Table 4.9.1 Example of Bi-Directional Lab Toxicity Variables

	USUBJID	PARAMCD	AVISITN	AVAL	BASE	ABLFL	ANRLO	ANRHI	ATOXDSCL	ATOXGRL	BTOXGRL	ATOXDSCH	ATOXGRH	BTOXGRH
1	001-0001	HGB	1	7.4	7.4	Y	11	16.1	Anemia	Grade 3	Grade 3	Hemoglobin increased	Grade 0	Grade 0
2	001-0001	HGB	2	20.5	7.4		11	16.1	Anemia	Grade 0	Grade 3	Hemoglobin increased	Grade 3	Grade 0
3	001-0001	AST	1	33	33	Y	5	25				Aspartate aminotransferase increased	Grade 1	Grade 1
4	001-0001	AST	2	55	33		5	25				Aspartate aminotransferase increased	Grade 1	Grade 1
5	001-0001	AST	3	60	33		5	25				Aspartate aminotransferase increased	Grade 1	Grade 1
6	001-0001	AST	4	77	33		5	25				Aspartate aminotransferase increased	Grade 2	Grade 1
7	001-0001	PLAT	1	250	250	Y	150	450	Platelet count decreased	Grade 0	Grade 0			
8	001-0001	PLAT	2	100	250		150	450	Platelet count decreased	Grade 1	Grade 0			
9	001-0001	PLAT	3	99	250		150	450	Platelet count decreased	Grade 1	Grade 0			
10	001-0001	PLAT	4	75	250		150	450	Platelet count decreased	Grade 1	Grade 0			
11	001-0001	PLAT	5	49	250		150	450	Platelet count decreased	Grade 3	Grade 0			
12	001-0002	HGB	1	21.1	21.1	Y	11	16.1	Anemia	Grade 0	Grade 0	Hemoglobin increased	Grade 3	Grade 3

Method 2：

To assign grades for parameters with bi-directional criteria, our current approach is to create different parameter codes, eg, low/high hemoglobin are "HGBL" and "HGBH" with the lab data provided on both records. Would this be an acceptable approach as well?.

SHIFTy变量是否需要加到ADLB数据集中？

Should a change or shift variable for grades be added? An example (FDA request): Provide a shift column that describes the change from baseline grade to post treatment grade. For example, for change from grade 1 hyperkalemia to grade 1 hypokalemia post-treatment, the shift column for potassium would specify "+1 to -1", indicating treatment-emergent hypokalemia.

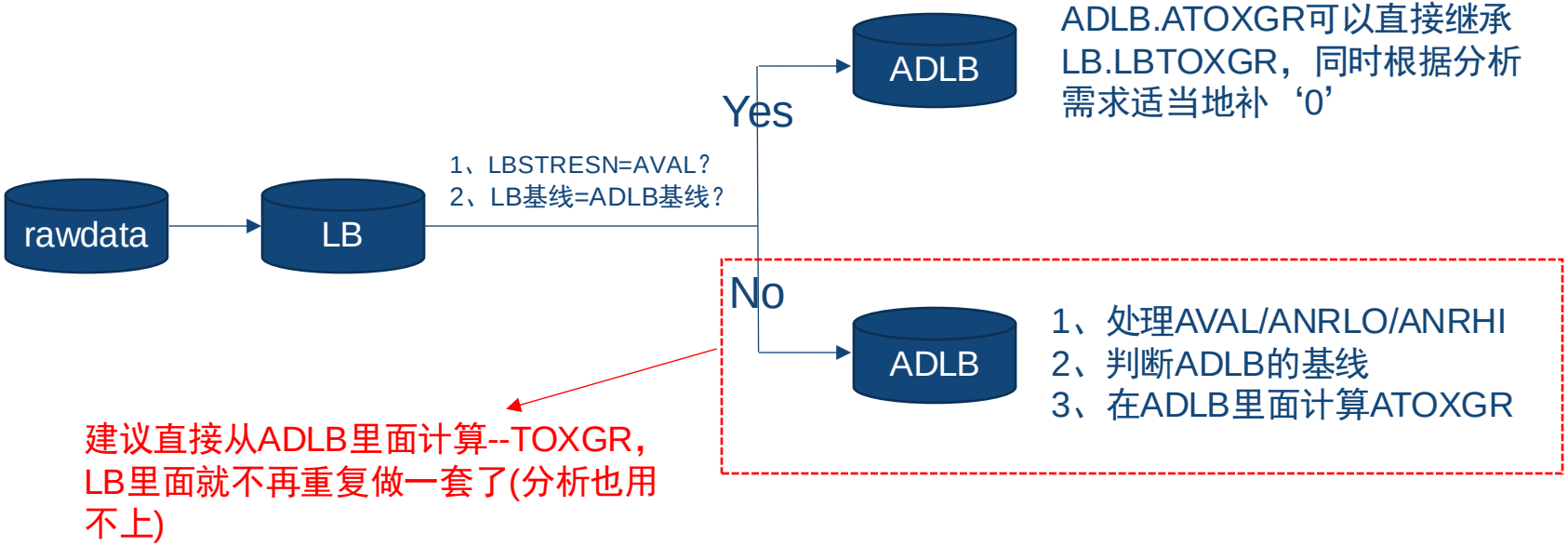
Table 4.9.2 Example Use of Shift Variables

	USUBJID	AVAL	BASE	ABLFL	ATOXGRL	BTOXGRL	ATOXGRH	BTOXGRH	SHIFT1	SHIFT2
1	001-0001	7.4	7.4	Y	Grade 3	Grade 3	Grade 0	Grade 0		
2	001-0001	20.5	7.4		Grade 0	Grade 3	Grade 3	Grade 0	Grade 3 to Grade 0	Grade 0 to Grade 3
3	001-0001	33	33	Y			Grade 1	Grade 1		
4	001-0001	55	33				Grade 1	Grade 1		Grade 1 to Grade 1
5	001-0001	60	33				Grade 1	Grade 1		Grade 1 to Grade 1
6	001-0001	77	33				Grade 2	Grade 1		Grade 1 to Grade 2
7	001-0001	250	250	Y	Grade 0	Grade 0				
8	001-0001	100	250		Grade 1	Grade 0			Grade 0 to Grade 1	
9	001-0001	99	250		Grade 1	Grade 0			Grade 0 to Grade 1	
10	001-0001	75	250		Grade 1	Grade 0			Grade 0 to Grade 1	
11	001-0001	49	250		Grade 3	Grade 0			Grade 0 to Grade 3	
12	001-0002	21.1	21.1	Y	Grade 0	Grade 0	Grade 3	Grade 3		

关于LB/ADLB的一些热门问题讨论/分享

- CTCAE毒性等级相关变量的放置位置（SDTM vs ADaM）
- 基线记录的CTCAE毒性等级处理

CTCAE毒性等级变量的放置位置（SDTM vs ADaM）



基线记录的CTCAE毒性等级处理

In CTCAE v5.0, for laboratory tests ALP, ALT, AST, BILI, GGT and Fibrinogen, only post baseline grade derivation is defined based on a Normal or Abnormal value at Baseline，but how to assign grading for baseline values in the ATOXGR-/BTOXGR- variables?

Investigations					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Alkaline phosphatase increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	-
Definition: A finding based on laboratory test results that indicate an increase in the level of alkaline phosphatase in a blood specimen. **Navigational Note:** -					

基线记录的CTCAE毒性等级处理

Method 1：默认基线正常，然后和ULN比较

USUBJID	VISIT	LBBLFL	LBTESTCD	LBSTNRHI	LBSTRESN	LBSTRESU	LBTOX	LBTOXGR
A001	筛选期	Y	ALP	106	110	U/L	Alkaline Phosphatase Increased	1
A001	访视1		ALP	106	150	U/L		
A001	访视2		ALP	106	160	U/L		

- **Key point：**认为基线记录不应该和自身比较，因为和自身比较没有意义
- **不合理之处：**访视1/2的ALP结果比基线值更差，但是从LBTOXGR来看，毒性等级却“变好了”

基线记录的CTCAE毒性等级处理

Method 2： 不特殊处理基线，依然根据基线是否异常来选择和ULN或baseline比较

USUBJID	VISIT	LBBLFL	LBTESTCD	LBSTNRHI	LBSTRESN	LBSTRESU	LBTOX	LBTOXGR
A001	筛选期	Y	ALP	106	110	U/L		
A001	访视1		ALP	106	150	U/L		
A001	访视2		ALP	106	160	U/L		

- 基线正常时，和ULN比较，LBTOXGR给不上；
- 基线异常时，和自身比较，LBTOXGR也给不上；

所以，基线记录的CTCAE毒性等级永远是“0”

Thank You!