STUDY DATA REVIEWER'S GUIDE

NONCLINICAL

(nSDRG)

Testing Facility Study Number: CBER-POC

Sponsor Study Number: ZYX-CBA001

An Intramuscular Repeated Dose of 456a Vaccine in New Zealand White Rabbits with a 3 Week Recovery Period

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1. nSDRG Introduction

This document provides context for the SEND datasets for Testing Facility Study Number CBER-POC, in addition to what is provided in the define.xml file, to facilitate the FDA Reviewer's and Data Manager's use of the SEND datasets. This document also includes a summary of SEND dataset conformance findings.

1.1. Study Protocol Title, Number and Report Version

Study Title	An Intramuscular Repeated Dose of 456a Vaccine in New Zealand White Rabbits with a 3 Week Recovery Period
Testing Facility Study Number	CBER-POC
Report Version	Final Report, no report amendments

1.2. Summary of SEND Dataset Creation Process

The data collection systems utilized are included in the study report. Submit™ was used to generate SEND datasets. Terminology was converted to SEND Controlled Terminology during SEND dataset creation.

All data were processed by the Submit™ SEND solution (Instem) to produce one integrated SEND dataset package. The define.xml file was created using DataDefine (Instem).

1.3. SEND Dataset Verification

Data in the SEND datasets are an accurate representation of the data for Testing Facility Study Number CBER-POC. Any differences between the datasets and the study report are described in Section 6.2.

2. Study Design

2.1. Study Design Summary

The following diagram illustrates the Experimental Design copied from the study report:

Experimental Design

Group No.	Treatment	Dosage	Dose Volume	Animal Numbers			
				Main Study		Recovery Study	
				Males	Females	Males	Females
1	Control	0	1 mL	1001-1005	1501-1505	1006-1010	1506-1510
2	456a	$1x10^{11}$ VP	1 mL	2001-2005	2501-2505	2006-2010	2506-2510

VP = Virus particles

Injection Site Location and Days of Dosing

Group No.	Treatment	Dosing days (dosing site)		
		1	15	29
1	Control	Site 1	Site 2	Site 3
2	456a	Site 1	Site 2	Site 3

Site 1: Day 1= right thigh (posterior)
Site 2: Day 15 = left thigh
Site 3: Day 29 = right thigh (anterior)

2.2. Trial Design Domain Overview

The following diagram illustrates the trial design.

Each color represents a different trial element.

ETCD	Element
ACCL	Acclimation
D_1	0 vp/dose every two weeks
D_2	1x10^11 vp/dose every two weeks
RECOVERY	Recovery

			EPOCH		
SPGRPCD	ARMCD	ARM	Acclimation	Treatment	Recovery
1	1	Control 0 vp/dose	Acclimation	0 vp/dose every two weeks	
	1R	Control 0 vp/dose Recovery	Acclimation	0 vp/dose every two weeks	Recovery
2	2	1x10^11 vp/dose 456a	Acclimation	1x10^11 vp/dose every two weeks	
	2R	1x10^11 vp/dose 456a Recovery	Acclimation	1x10^11 vp/dose every two weeks	Recovery

SPGRPCD	SETCD	SET	SET LABEL
1	1M	Control 0 vp/dose Main	Group 1 - Control 0 vp/dose Main
	1R	Control 0 vp/dose Recovery	Group 1 - Control 0 vp/dose Recovery
2	2M	1x10^11 vp/dose 456a Main	Group 2 - 1x10^11 vp/dose 456a Main
	2R	1x10^11 vp/dose 456a Recovery	Group 2 - 1x10^11 vp/dose 456a Recovery

3. Standards, Formats, and Terminologies and their Versions

3.1. Standards Used

Dataset Component	Standard or Dictionary	Versions Used
Tabulation Datasets	CDISC SEND Implementation Guide	3.1
Tabulation Datasets, Data Definition File	FDA Technical Conformance Guide	4.1
Controlled Terminology	CDISC SEND Controlled Terminology	2018-06-29
Data Definition File	CDISC DEFINE.XML	2.0

3.2. Rationale for Standards Selection

SEND Implementation Guide (IG) v3.1 is the current version required by the FDA Study Data Standards Catalog for studies of this type and study start date. The version of Controlled Terminology (CT) selected was the most recent version available in the Submit SEND solution as implemented at Charles River Laboratories at the time of dataset generation. Define.xml v2.0 is the current specification for data definition files listed in the FDA Data Standards Catalog. Any FDA Business Rules that are not yet implemented and relevant for this study are explained in Section 5.5.

3.3. Nonstandard Terminology

No nonstandard terminology was used.

4. Description of Study Datasets

4.1. Dataset Summary

Dataset Name	Dataset Label	Supplemental Qualifiers?	Related Records?	Observation Class
TS	Trial Summary			Trial Design
TE	Trial Elements			Trial Design
TA	Trial Arms			Trial Design
TX	Trial Sets			Trial Design
CO	Comments			Special Purpose
DM	Demographics			Special Purpose

Dataset Name	Dataset Label	Supplemental Qualifiers?	Related Records?	Observation Class
SE	Subject Elements			Special Purpose
EX	Exposure			Interventions
DS	Disposition			Events
BW	Body Weight			Findings
CL	Clinical Observations			Findings
FW	Food and Water Consumption			Findings
LB	Laboratory Test Results			Findings
MA	Macroscopic Findings	X	MI	Findings
MI	Microscopic Findings	X	MA	Findings
OM	Organ Measurements			Findings
VS	Vital Signs			Findings

4.2. Dataset Explanation

4.2.1. All Domains

- Baseline flag (--BLFL) is populated with the last non-missing value prior to the first dose in applicable domains.

4.2.2. DM-Demographics

- RFSTDTC is populated with the date of the first dose for that animal.
- Individual animal birth dates were not available in the data collection system; the AGETXT variable is populated with the actual age as per study report.

4.2.3. TS-Trial Summary

- TSVAL is populated with planned information from the study protocol with the following exceptions:
    - STENDTC is populated with the date the final report was approved.
    - EXPENDTC is populated with the Experimental Completion Date in the report.
    - EXPSTDTC is populated with the Experimental Start Date in the report.
    - DOSENDTC is populated with the date prior to necropsy.
    - DOSSTDTC is populated with the first day of dosing.

4.2.4. EX-Exposure

- Contains the actual dose administered.
- Contains one record per animal per dose.

4.2.5. CL-Clinical Observation

- In addition to clinical observations, the CL domain also includes ophthalmology results.
- Dermal scoring collected using a scoring scale are not presented within CL as these data are outside the scope of SENDIG v3.1.

4.2.6. LB-Laboratory Test Results

- For calculated endpoints, if all values needed to perform the calculation are not done or excluded these incalculable results are not included.
- The collected results, 1+, 2+, 3+, and 4+ cannot be decoded in LBSTRESC due to system limitations that do not allow for different decodes based on the LBTEST value.
- Complete scoring scales are included in the study report.
- LBDTC is populated with the actual dates/times of analysis and not the sample collection date/time.

4.2.7. MA-Macroscopic Findings

- MALAT is only populated when a paired tissue is examined unilaterally. When paired tissues are examined together, laterality is not documented in the data collection system.
- Any text after the second colon ":" in MAORRES is a comment and is also presented in the CO domain.

4.2.8. MI-Microscopic Findings

- MILAT is only populated when a paired tissue is examined unilaterally. When paired tissues are examined together, laterality is not documented in the data collection system.
- Any text after the second colon ":" in MIORRES is a comment and is also presented in the CO domain.
- MIDTHREL is populated for all non-normal findings for all subjects regardless of disposition status.

4.2.9. OM-Organ Measurements

- OMLAT is only populated when a paired tissue is examined unilaterally. When paired tissues are examined together, laterality is not documented in the data collection system.
- For calculated endpoints, if all values needed to perform the calculation are excluded these incalculable results are not included.

4.3. Use of Supplemental Qualifiers

Dataset Name	Variable Name (QNAM)	Variable Label (QLABEL)	Description
SUPPMA	Macroscopic Findings	MARESMOD	Contains modifiers that were part of MAORRES for which SEND variables have not yet been developed.
SUPPMI	Microscopic Findings	MIRESMOD	Contains modifiers that were part of MIORRES for which SEND variables have not yet been developed.

4.4. Data Not Included in SEND Datasets

Data	Reason
Immunology Assessments	Out of scope for SENDIG v3.1
Dermal Scoring	Out of scope for SENDIG v3.1

5. Data Standards Validation Rules, Versions, and Conformance Issues

The SEND datasets were evaluated for conformance using the SEND Checker functionality within the Submit system (Instem) and the Pinnacle 21 Community dataset validation tool.

The define.xml file was evaluated for conformance using the Pinnacle 21 Community dataset validation tool.

5.1. Validation Outcome Summary

Pinnacle 21 Community identified no errors or warnings in the SEND datasets.

Pinnacle 21 Community identified one error and no warnings in the define.xml.

5.2. FDA SEND Validation Rules Version

Rule conformance to SENDIG v3.1 and the define.xml standard were evaluated using Pinnacle 21 Community, Version 3.0, which includes checks for conformance against published FDA Business and Validator Rules.

5.3. Errors

Pinnacle 21 Community identified no errors in the SEND datasets.

Pinnacle 21 Community identified one error in the define.xml file which is explained in the following table.

Define.xml Errors		
Rule	**Message**	**Explanation**
DD0118	NCI Code 'C71620' for Codelist 'Unit' on Variable 'VSORRESU' / 'VSSTRESU' does not match NCI Code 'C66770' for Standard Codelist 'Units for Vital Signs Results' for Variables 'VSORRESU'/'VSSTRESU'	This is a Pinnacle 21 limitation because Pinnacle 21 incorrectly checked these units against "Units for Vital Signs Results" (NCI Code 'C66770'). However, the SENDIG v3.1 states these two variables within " Unit" (NCI Code 'C71620'). Therefore, this is an invalid error.

5.4. Warnings

Pinnacle 21 Community identified no warnings in the SEND datasets or define.xml.

5.5. FDA Business Rules

FDA Business Rules v1.4 were followed.

6. Sponsor Decisions Related to Data Standards Implementations

6.1. Sponsor Defined Standardization Descriptions

The SEND Datasets do not include permissible variables when all values for the variable are null.

The EX domain contains the actual dose administered.

6.2. Differences between SEND Datasets and Study Report

Terminology used during data collection is used in the study report. That terminology was converted to SEND Controlled Terminology during SEND dataset creation.

The SEND datasets may contain different significant digits and/or decimal places than what is presented in the report.

All explanations of abbreviations are included within the study report.

6.2.1. CO-Comments

- The CO domain is populated with comments collected in the data collection system. These comments are not always included in the study report.

6.2.2. BW-Body Weights

- The terminal body weight appears in both the body weight table and in the organ weight report tables in the study report. The terminal body weight only appears in the BW domain in the SEND dataset.

6.2.3. CL-Clinical Observations

- The CL domain contains NORMAL findings, however only animals with positive findings are presented in the study report.
- The time points used in CLTPT correspond to time points used in the study report. The following table lists the timepoints used in study report and CL.

Time Point Used in Study Report	Timepoint Definition	CLTPT
CSO	Cage side observation on non-dosing days	CSO
PreRx	Observation predose	PreRx
PostRx	Observation post dosing	PostRx
PostRx1	1 hour postdose	PostRx1
PostRx5	4 to 8 hours postdose	PostRx5
SIRT	Detailed clinical observations non-dosing days	SIRT

6.2.4. LB-Laboratory Test Results

- LBTEST populated with Specimen Appearance when LBCAT is Coagulation represents the specimen condition.

6.2.5. MA-Macroscopic Findings

- Histopathological observations linked to macroscopic findings are identified in the study report with a (H) designation. These records have a correlation in RELREC to MI.
- Trackable Gross Lesions are identified in the study report with a (TGL) designation. These records have a correlation in RELREC to MI as a correlation to a histopathology observation in that tissue or to “NO CORRELATE” in the report.

6.2.6. MI-Microscopic Findings

- Gross pathological observation linked to histopathological findings in that tissue are identified in the study report with a (G) designation. These records have a correlation in RELREC to MA.
- The study report contains a “NO CORRELATE” specimen which is used to complete verification of a trackable gross lesion in the data collection system. This record is not included in MI.

6.2.7. OM-Organ Measurements

- The organ weight ratios in OM may differ from the ratios presented in the study report because of the rounding methodology used in the calculation of the ratios presented in the study report.

6.2.8. VS-Vital Signs

- The time points used in VSTPT correspond to time points used in the study report. The following table lists the timepoints used in study report and VS.

Time Point Used in Study Report	Timepoint Definition	CLTPT
Pr	Predose	PreRx
p	Body temperature recorded on non-dosing days	PostRx
P6	6 hours postdose	PostRx6

6.3. Nonstandard Electronic Data Submitted

There are no nonstandard electronic data included as part of the submission.

6.4. Legacy Data Conversion

No legacy data was converted as a part of the submission.