

# Integrated Analysis Data Reviewer's Guide

ABC Pharmaceuticals

ABC-MED2020

Integrated Summary of Safety

iADRG Template Version 2023-09-01

# Integrated Analysis Data Reviewer's Guide

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## 1. Introduction

### 1.1 Purpose

This document provides context for the integrated analysis datasets and terminology that benefit from additional explanation beyond the Data Definition document (Define-XML) for integrated studies and a summary of integrated analysis data conformance findings.

### 1.2 Acronyms

Acronym	Definition
ADaM	Analysis Dataset Model
ADRG	Analysis Data Reviewer's Guide
iADRG	Integrated Analysis Data Reviewer's Guide
BDS	Basic Data Structure
DBL	Database Lock
EoT	End of Treatment
IG	Implementation Guide
NA	Not Applicable
SDTM	Study Data Tabulation Model
SAP	Statistical Analysis Plan
TAUG	Therapeutic Area User Guide

### 1.3 Data Standards and Dictionary Inventory for Integrated Datasets

Standard or Dictionary	Versions Used
SDTM Controlled Terminology	SDTM CT 2020-12-18
ADaM	ADaM v2.1/IG 1.1 OCCDS v1.0
ADaM Controlled Terminology	ADaM CT 2020-11-06
Data Definitions	Define-XML v2.0
TAUG	Not Applicable
Medications Dictionary	WHODD Version Global B3 Mar2019

Standard or Dictionary	Versions Used
Medical Events Dictionary	MedDRA v23.1 (includes COVID-19 terminology)
Other Standards	CTCAE v5.0

#### Additional Content of Interest

No additional information.

### 1.4 Source Data Used for Integrated Analysis Dataset Creation

Study Identifier (STUDYID)	Protocol Number	Source Data Standard	Cutoff-Date or DBL-Date/Study Status
ABC09	SAMPLE-9909	ADaM 2.1/IG 1.0	2015-01-01/Completed
ABC08	SAMPLE-9908	ADaM 2.1/IG 1.1	2017-01-01/Completed
ABC07	SAMPLE-9907	ADaM 2.1/IG 1.1	2020-07-01/Ongoing
ABC06	SAMPLE-9906	ADaM 2.1/IG 1.1	2020-08-01/Ongoing

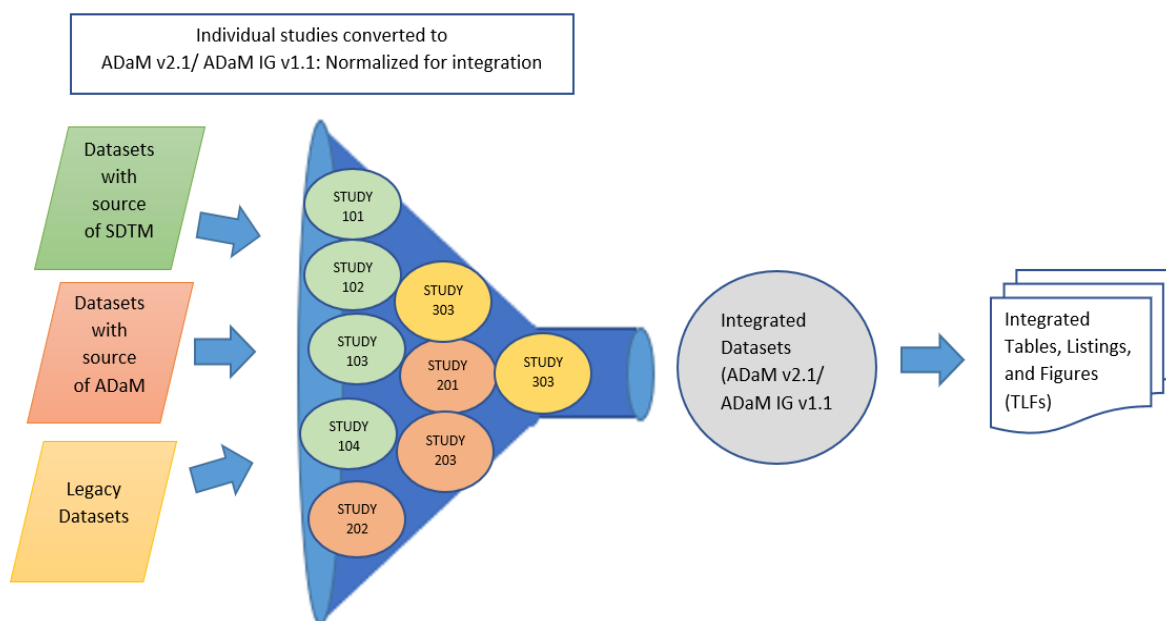
#### Additional Content of Interest

The sponsor clinical group provided AEOSI (Adverse Events of Special Interest) data containing standardized MedDRA queries (SMQs). This is used for ADAE.AESI1 (AECAT1 Category) and AESI2 (AECAT2 Category) variable derivations. The AEOSI dataset has a sponsor-defined data structure, does not contain subject-level information, and does not qualify as an ADaM dataset. Hence, this dataset in SAS Version 5 Transport Format (aeosi.xpt) is placed in the “misc” subfolder under Module 5 (m5) of the eCTD folder structure (m5 > datasets > misc).

The study ABC07 data was cut off to perform the 90-day safety analysis for a regulatory agency safety data update.

The study ABC06 data was cut off to perform the interim analysis, as per the protocol.

## 1.5 Traceability Flow Diagram



## 2. Description of Protocols Used in the Integrated Datasets

### 2.1 Protocol Numbers and Titles

Protocol Number	Indication(s)/Protocol Title	Phase	Treatment ARM(s)
SAMPLE-9909	Phase Ib/II Open-Label Dose-Escalating Clinical Study of the Safety, Tolerability and Pharmacokinetic Profiles of GoodDrug (ABC-MED2020) in Subjects with Prostate Cancer	I/II	Cohort 1/Trt 1, Cohort 2/Trt 2, Cohort 3/Trt 3
SAMPLE-9908	Open-Label, Randomized Study of GoodDrug (ABC-MED2020) Dose 1 vs Dose 2 for Safety and Efficacy in Subjects with Prostate Cancer	II	Trt A, Trt B
SAMPLE-9907	Open-Label Randomized Study of GoodDrug vs Placebo for Safety and Efficacy in Subjects with Prostate Cancer	III	Trt A, Trt C
SAMPLE-9906	Open-Label Extension for Subjects Continuing on GoodDrug (ABC-MED2020) with Prostate Cancer	III	Trt A

**Additional Content of Interest**

The placebo treatment arm in the SAMPLE-9907 study was not included in the integrated datasets.

**2.2 Integrated Analysis Strategy and Design in Relation to ADaM Concepts**

The integration plan defined in the SAP required pooling the safety data in ADAE, ADTTAE, ADLB and ADVS datasets. Integrated ADSL and ADEX datasets were created to support the analyses. Integrated ADMH and ADCM datasets were created for potential subsets or sensitivity analyses.

ADSL contains the safety population flag (SAFFL) to identify all subjects treated with any amount of study drug (GoodDrug ABC-MED2020), combination or control in their respective study and Intent-To-Treat Population flag (ITTFL) that includes subjects randomized to the study. For integrated analysis, the actual treatment group (TRT01A) is defined as the treatment received if the patient received treatment. Planned treatment is defined as the treatment assigned through randomization (TRT01P). A few subjects were randomized but not dosed, so their actual treatment variable (TRT01A) is blank. A population flag identifying high-risk prostate cancer subjects is defined as IND1FL, for subset safety analyses.

Additional flag variables and analysis parameters that come from multiple analysis datasets and have a non-standard format are documented in a supplemental data definition file; a separate PDF file linked to the Define-XML.

- 1) ADSL has Prior History of ACV disease flag (PRACVFL) and is based on individual study ADMH datasets. ACV Event flag (ACVEVFL) is defined as Grouping of Terms for AEs of Interest created in ADAE and used for subgroup analysis.
- 2) ADTTAE has the Time to First ACV Adverse Event (AETTACV) parameter defined as:  
Start date of first occurrence of the adverse event – date of first dose of treatment drug +1 and is used for time to event analysis.  
  
Subjects not experiencing qualifying events will be censored at the end of the treatment-emergent period.

For ongoing studies:

For subjects still on the study drug at the analysis data cut-off date, the end of the treatment-emergent period will be the analysis data cut-off date. Only adverse events reported within the period and safety measurements taken within the period will be considered treatment-emergent and included in the analysis of safety.

### 3. Analysis Considerations Related to Integrated Analysis Datasets

#### 3.1 Core Variables

Core variables are those that are represented across all integrated analysis datasets.

Variable Name	Variable Description
STUDYID	Study Identifier from Original Study
USUBJID	Unique Subject Identifier from Original Study
SUBJID	Subject Identifier from Original Study
SITEID	Site Number from Original Study
REGION1	Geographic Region 1
SITEIDN	Study Site Identifier (N)
COUNTRY	Country
ARM	Description of Planned Arm
ARMCD	Planned Arm Code
ACTARM	Description of Actual Arm
ACTARMCD	Actual Arm Code
AGE	Age
AGEU	Age Units
AGEGR1	Age Group 1
AGEGR1N	Age Group 1 (N)
SEX	Sex
RACE	Race
ETHNIC	Ethnicity



Variable Name	Variable Description
ICFDT	Informed Consent Date
ENRLFL	Enrolled Population Flag
SAFFL	Safety Population Flag
FASFL	Full Analysis Set Flag
ITTFL	Intent-To-Treat Population Flag
SCRNFCFL	Screen Failure Flag
POOL01FL	Pooled Analysis Set 01 Flag
POOL02FL	Pooled Analysis Set 02 Flag
COMPLFL	Completers Population Flag
DISBLFL	Baseline Disease Flag
ANCUTDT	Analysis Cutoff Date
TRT01P	Planned Treatment for Period 01
TRT01PN	Planned Treatment for Period 01 (N)
TRT01A	Actual Treatment for Period 01
TRT01AN	Actual Treatment for Period 01 (N)
TR01SDT	Date of First Exposure to Treatment in Period 01
TR01EDT	Date of Last Exposure to Treatment in Period 01
LSTALVDT	Date Last Known Alive
ANTISTDT	Subsequent Anti-Cancer Therapy Start Date
ANTICNFL	Subsequent Anti-Cancer Therapy Flag

### 3.2 Treatment Variables

#### ARM versus TRTxxP

Are the values of ARM equivalent in meaning to the values of TRTxxP?

Yes, the meaning is the same, but the ARM values were different across the studies: the values of TRT01P were remapped for consistency in the integrated analysis.

<b>STUDYID</b>	<b>ARM</b>	<b>TRT01P</b>
ABC09	TRT1	Active 100 mg
ABC09	TRT2	Active 200 mg
ABC09	TRT3	Active 500 mg
ABC06, ABC07, ABC08	TRTA	Active 200 mg
ABC08	TRTB	Active 500 mg
ABC07	TRTC	Placebo

#### ACTARM versus TRTxxA

If TRTxxA is used, then are the values of ACTARM equivalent in meaning to the values of TRTxxA?

Yes, the meaning is the same, but the ACTARM values were different across the studies: the values of TRT01A were remapped for consistency in the integrated analysis.

<b>STUDYID</b>	<b>ACTARM</b>	<b>TRT01A</b>
ABC09	TRT1	Active 100 mg
ABC09	TRT2	Active 200 mg
ABC09	TRT3	Active 500 mg
ABC06, ABC07, ABC08	TRTA	Active 200 mg
ABC08	TRTB	Active 500 mg
ABC07	TRTC	Placebo

#### Use of Treatment Variables in Integrated Analysis

Are both planned and actual treatment variables used in integrated analysis?

Yes, TRT01A was used for safety analysis and TRT01P was used for disposition table(s).

## Use of Treatment Grouping Variables in Integrated Analysis

Are both planned and actual treatment grouping variables used in integrated analysis?

Yes

STUDYID	TR01AG1N	TR01AG1	TR01PG1N	TR01PG1
ABC06, ABC07 ABC08, ABC09	1	Active <=200mg	1	Active <=200mg
ABC08, ABC09	2	Active > 200mg	2	Active > 200mg

## Additional Content of Interest

No additional information.

### 3.3 Subject or Protocol Considerations that Require Special Integrated Analysis Rules

Were any additional updates (e.g., codelists, value-level metadata, dictionaries) performed when integrating?

Yes.

- Recoding for study ABC06 included updating AESEV = 0,1,2 to CDISC standard ASEV = 1,2,3 and Race variable re-coding to the CDISC standard rather than the CRF coding.

Subject issues that were considered for analysis:

- Subjects ABC06-101-138, ABC08-502-322 were rescreened subjects. The subjects were randomized in error since they took prohibited medications within the 7 days prior to screening; they were screen failures and were not dosed. These subjects were rescreened 30 days later, enrolled, and given new subject IDs. Their original subject IDs were not included in the total counts of randomized subjects.
- Subjects from site 141 in study ABC08 were excluded from the integrated safety analyses. After database lock, observations in study led to concerns about data integrity at this site, leading to the exclusion of both safety and efficacy data from the site. For more details, see SAP section 3.

## Additional Content of Interest

No additional information.

### 3.4 Use of Visit Windowing, Unscheduled Visits and Record Selection

Was windowing used in one or more integrated analysis datasets?

Yes. Visit windowing was used for ADLB and ADVS integrated datasets. Refer to the integrated SAP for more details.

Analysis visit windows were defined in a similar way across studies ABC09, ABC08 and ABC07, with the following differences:

- The EoT analysis visit window ranged up to 7 days after last dose of study drug in ABC09 and ABC08 and up to 10 days after last dose of study drug in ABC07.
- The FU analysis visit window started at 8 days after last dose of study drug in ABC09 and ABC08 and at 11 days in ABC07.

Because these differences are considered minor and to ensure consistency with the individual study reports, analysis visit windows will not be redefined in the ISS, but re-used from the individual studies, with the following exceptions for studies ABC06 and ABC07:

- If a week 4 value is missing, it will be imputed by a non-missing week 2 value.
- If a week 4 and a week 2 value are missing, the week 4 value will be imputed by a non-missing week 1 value.
- The EoT value, 7 days post last dose as derived in study ABC09, will also be used for all studies as the EoT value in the ISS database.

Were unscheduled visits included in any integrated analysis datasets?

Yes. All unscheduled laboratory data in the integrated ADLB were used for the evaluation of the worst result. Both scheduled and unscheduled visits were used in ADVS for assessing consecutive post baseline visits for vital signs measured at the investigator site.

Were rules used for record selection in one or more integrated analysis datasets?

Yes. ANL01FL was used to define the record selection across all studies for the integrated analysis of laboratory (ADLB) and vital signs (ADVS) datasets. ANL01FL is defined as the assessment closest to the target day when the subject has more than one visit with a measurement within a visit window. In the case of ties between observations located on different sides of the target day, the later assessment will be used in the analyses.

#### **Additional Content of Interest**

No additional information.

### **3.5 Imputation/Derivation Methods**

If date imputation was performed, were there rules that were used in multiple integrated analysis datasets?

Yes. For ADAE and ADCM datasets that may contain partial onset or start dates, imputation rules are as follows:

- If the day is missing and the year and month are the same as the year and month of the first date of study drug dosing, then the date is imputed as the first dosing date.
- Otherwise, if month and day are missing and year is present, the date is imputed as the

first day of the year. For AEs, a missing onset date was imputed according to the conventions mentioned in SAP section 7.5.

No imputation of missing dates for other variables was done.

#### **Additional Content of Interest**

Data derivation methods:

DTYPE was used in the datasets listed in the table below.

<b>ADaM Variable</b>	<b>Controlled Terminology</b>
ADLB.DTYPE	AVERAGE, LOCF, MAX, MIN, WORST
ADVS.DTYPE	AVERAGE, LOCF, WORST

## **4. Integrated Analysis Data Creation and Processing Issues**

### **4.1 Split Datasets**

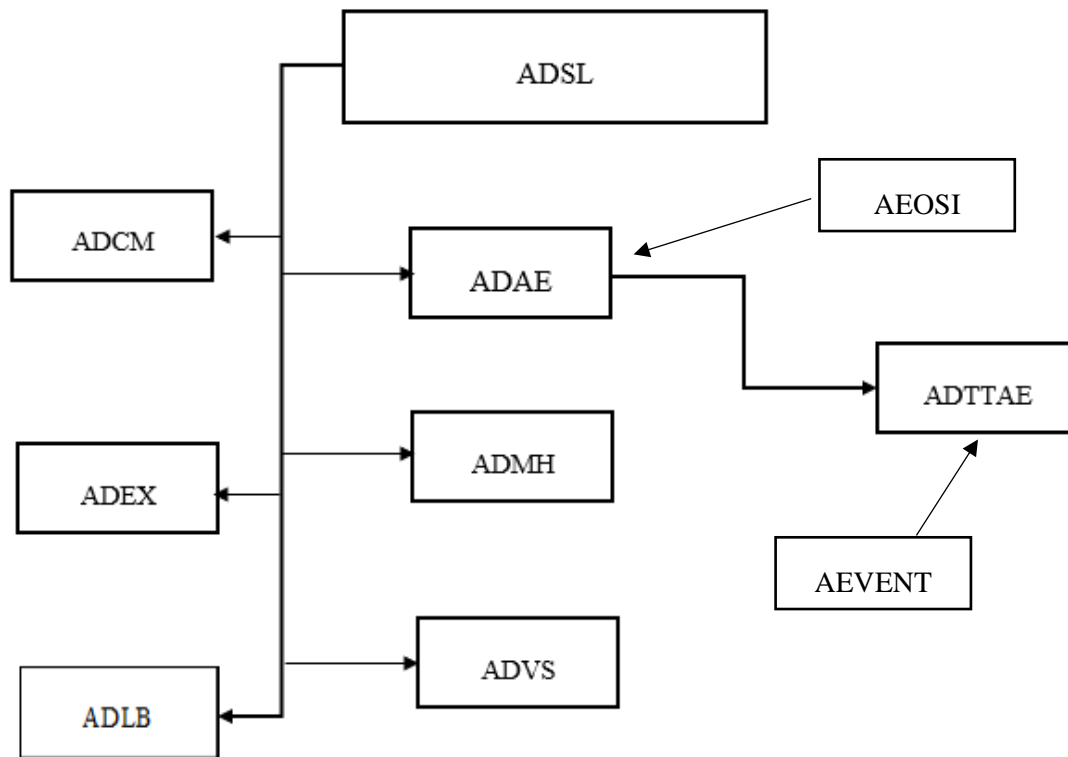
ADLB was split into ADLB1 (for chemistry test results) and ADLB2 (for hematology test results) when integrated from study-level ADLB datasets due to size constraints. The dataset was split based on the value of PARCAT1.

As per the Study Data Technical Conformance Guide, v4.7.1, June 2021, Section 3.3.2 Dataset Size, split datasets are included in the submission in addition to the larger non-split datasets. Non-split datasets are included in the Define-XML. The split datasets are placed in a subdirectory “split” under Module 5 (m5) of the eCTD folder structure.

### **4.2 Data Dependencies**

ADSL was used in the creation of all other integrated analysis datasets, mostly for the purpose of deriving subject-level variables that were carried into individual datasets. Additionally, ADTTAE is derived from ADSL and ADAE. See Figure 4.2 for data dependency information for integrated datasets.

The sponsor clinical group provided AEOSI (Adverse Events of Special Interest) data containing standardized MedDRA queries (SMQs). Refer to section 1.4 for further information. AEVENT, an intermediate dataset used in the ADTTAE dataset creation, is explained in section 4.3.

**Figure 4.2: Data Dependencies**

### 4.3 Intermediate Datasets

AEVENT was created during the trial to compute dates and time to event duration for AE time to event analyses. Because it doesn't qualify as an ADaM dataset, this dataset in SAS Version 5 Transport Format (aevent.xpt) is placed in the "misc" subfolder under Module 5 (m5) of the eCTD folder structure (m5 > datasets > iss > misc).

#### Additional Content of Interest

No additional information.

## 5. Integrated Analysis Datasets Descriptions

### 5.1 Overview

Is an integrated statistical analysis plan included in the submission?

Yes. Refer to the analysis plan document: "ABC-MED2020 Integrated Safety Statistical Analysis Plan".

Do the integrated datasets support all integrated statistical analysis plan specified objectives?

Yes. The integrated ADaM datasets support the integrated analysis statistical analysis plan specified objectives.

#### Additional Content of Interest

No additional information.

### 5.2 Integrated Analysis Datasets

<b>Dataset Name Dataset Label</b>	<b>Class</b>	<b>Efficacy (E)/ Safety (S)/ Immunogenicity (I)</b>	<b>Baseline or Other Subject Characteristics</b>	<b>All Studies Contribute</b>	<b>Structure</b>
<a href="#">ADSL</a> Subject-Level Analysis Dataset	ADSL		X	X	One record per subject
<a href="#">ADAE</a> Adverse Event Analysis Dataset	OCCDS	S		X	One record per subject per adverse event
<a href="#">ADCM</a> Concomitant Medications Analysis Dataset	OCCDS	S			One record per subject per concomitant medication
ADEX Exposure Analysis Dataset	ADaM OTHER	S		X	One record per subject per visit
<a href="#">ADLB</a> Laboratory Analysis Dataset	BDS	S		X	One record per subject per visit per parameter per derivation type

Dataset Name Dataset Label	Class	Efficacy (E)/ Safety (S)/ Immunogenicity (I)	Baseline or Other Subject Characteristics	All Studies Contribute	Structure
<a href="#">ADMH</a> Medical History Analysis Dataset	OCCDS		X		One record per subject per parameter
<a href="#">ADTTAE</a> Time to Adverse Event Analysis Dataset	BDS	S		X	One record per subject per visit per parameter
<a href="#">ADVS</a> Vital Signs Analysis Dataset	BDS	S		X	One record per subject per visit per parameter

### 5.2.1 ADSL – Subject-Level Analysis Dataset

ADSL has subject-level information that includes all subjects to be analyzed in the integrated datasets. This includes required ADaM variables for demographics, treatment groups and population flags. In addition, it contains other baseline variables, study date and other relevant variables corresponding to the conduct of the study and critical variables used in the analyses. See section 3.1 for the list of core variables.

The USUBJID variable is indicative of either the subject identifier from the parent study if a subject was enrolled in multiple studies or the subject identifier from the single study if a subject was enrolled in only one study.

ADSL contains analysis population flags used in the integrated analysis as described in section 2.2.

Geographic region was defined differently across the study-level CSRs. For the ISS, geographic regions have been redefined (SAP Appendix [Error! Reference source not found.]).

In some countries, race is not allowed to be collected. In these instances, race is left missing and RACEGR1 is set to the category of MISSING.

In some countries only year can be collected for birth date. In these cases, January 1 is used as the month and day for these subjects. BRTHDTF is populated as 'M' for these cases.



See section 3.1 for the list of core variables that are carried into all other analysis datasets. In addition, other variables used in subgrouping summaries were derived, which included demographic grouping variables for age and years since disease onset.

### 5.2.2 ADAE – Adverse Event Analysis Dataset

ADAE contains all adverse events reported during the study and is based on study-level adverse event SDTM data. Subjects who did not report an adverse event are not included in the dataset. ADAE supports all summaries of treatment emergent adverse events and includes system organ class and preferred terms based on coded data using MedDRA, version 23.1. Missing start and stop dates for adverse events were imputed as described by the rules in the ISS SAP. The following variables were used to keep the original dictionary version values:

- LLTORG1 – LLT in Original Dictionary 1
- LLTNORG1 – LLT Code in Original Dictionary 1
- DECDORG1 – PT in Original Dictionary 1
- PTNORG1 – PT Code in Original Dictionary 1
- HLTORG1 – HLT in Original Dictionary 1
- HLTNORG1 – HLT Code in Original Dictionary 1
- HLGTORG1 – HLGT in Original Dictionary 1
- HLGTNOR1 – HLGT Code in Original Dictionary 1
- BDSYORG1 – SOC in Original Dictionary 1
- SOCORG1 – Primary SOC in Original Dictionary 1
- SOCNORG1 – Primary SOC Code in Original Dictionary 1
- AEDICT1 – Original Dictionary Version 1

The sponsor clinical group provided AEOSI (Adverse Events of Special Interest) data containing standardized MedDRA queries (SMQs). Refer to section 1.4 for further information.

For ongoing study ABC06, AE end dates (AEENDTC/AENDT) are cut off up to 2020-08-01 with analysis end date flag (AENDTFF) = Y if the AE end date is greater than the above cutoff date. AE outcome variables (AEOUT/AEOUTN) of these records are set to missing.

For numeric version of action taken with study treatment (AEACNN), both “Dose Delay” and “Dose Interrupted” are grouped into one category – “DRUG INTERRUPTED” – for the listing display.

Treatment-emergent events are attributed to the treatments taken when the event started. TEAEs that start before the first treatment and continue into the study are attributed to the first dose taken in the study. For the integration, adverse events starting within 60 days post treatment and/or prior to the start of secondary treatment are considered treatment emergent. For study ABC09, TEAEs were

captured up to 90 days post dose at the study level. We are using TEAEs within 60 days for integration.

For study ABC09, which was originally coded in MedDRA version 16.0, the MedDRA up-versioning to v23.1 slightly changed adverse event counts for infusion-related reactions. Study ABC08 was also up versioned to v23.1 from v19.1.

### 5.2.3 ADCM – Concomitant Medications Analysis Dataset

This dataset contains data from three different source studies: ABC09, ABC07 and ABC06. Previous and concomitant medications are coded with WHO-DICT. For studies ABC07 and ABC06, the WHO-DD version is MAR2019, and for study ABC09, the WHO-DD version is MAR2014.

No recoding was performed because only limited descriptive analyses of prior and concomitant medications were performed.

### 5.2.4 ADLB – Laboratory Analysis Dataset

This domain was based on laboratory evaluations performed for Phase II/III populations. ADLB was split into two integrated datasets – ADLB1 and ADLB2 – that are included in the submission package. This ADLB dataset contains US conventional units only. The ADLB1 dataset includes selected chemistry tests. The ADLB2 dataset includes selected hematology tests.

Laboratory abnormalities were evaluated based on the potentially clinically significant (PCS) laboratory criteria; the pre-defined values are presented in the ISS SAP. Potentially clinically significant (PCS) laboratory criteria in liver function tests for alkaline phosphatase (ALP), alanine transaminase (ALT), total bilirubin, aspartate transaminase (AST), gamma GT (GGT) and their combination were defined in the ADLB using the following variables:

- CRIT1 – Analysis Criterion 1: Identifies the records with HGB > 4
- CRIT2 – Analysis Criterion 2: Identifies the records with Hy's Law met
- CRIT3 – Analysis Criterion 3: Identifies the records with AST or ALT > 3\*ULN

Visit windowing was defined as per the ISS SAP and available in the ADLB.AVISIT variable. See section 3.4.

DTYPE was used in the ADLB. See the table below listing the DTYPE, derivation rule and controlled terminology used.

ADaM Variable	Derivation Rule	Controlled Terminology
ADLB.DTYPE	<p>ABC09.ADLB.ITYPE: set DTYPE to 'WORST', 'LOCF', respectively, for the derived records</p> <p>ABC08.ADLB.DTYPE: assign 'MAX', 'MIN', respectively, for the derived records</p> <p>ABC07.ADLB.DTYPE contains all derivations as is</p> <p>ABC06.ADLB.DTYPE contains all derivations as is</p>	AVERAGE, LOCF, MAX, MIN, WORST

### 5.2.5 ADMH – Medical History Analysis Dataset

This dataset includes non-prostate medical history. All verbatim terms are coded or up versioned to MedDRA version 23.1. A flag variable (MHONGO) is used to indicate whether the medical history is ongoing.

Study ABC06 does not contribute to the ADMH dataset.

### 5.2.6 ADTTAE – Time to Adverse Event Analysis Dataset

The dataset contains information related to time to event analysis for adverse events (AEs) reported during the study. An intermediate dataset AEVENT was created during the trial to compute dates and time to event duration for AE time to event analyses. [See section 4.3.] ADTTAE was created to support the safety endpoints including:

- Time to first occurrence of a cardiovascular TEAE (Months)
- Time to first occurrence of a grade 3 or higher TEAE (Months)
- Time to first TEAE of second malignancy (Days)
- Time to first occurrence of a serious TEAE (Months).

### 5.2.7 ADVS – Vital Signs Analysis Dataset

The dataset contains information related to systolic and diastolic blood pressure (BP), heart rate, height, weight, temperature, and body mass index collected during the start of the study and at each visit including unscheduled visits. Flags identifying baseline and post baseline records are available for each parameter.

AVALCAT1 was used to categorize the vital sign clinical importance criteria for heart rate and systolic and diastolic BP such as 'Normal', 'Low', 'High' and 'Very High'. AVALCAT2 contains the vital sign PCS (potential clinically significant) criteria for pulse rate, systolic and diastolic BP, weight, and temperature in comparison to the previous visit.

Analysis flags (ANL01FL, ANL02FL) were created to specify vital sign results in various categories to support the table summaries and analysis. See the table below listing the analysis flag and derivation rule used for record selection in ADVS.

ADaM Variable	Derivation Rule
ADVS.ANL01FL	Derived on a parameter basis for subjects with multiple assessments performed during the same analysis visit window, then the visit closest to the analysis is selected
ADVS.ANL02FL	Derived on a parameter basis for subjects with multiple assessments performed during the same analysis visit window, then the worst result for the given vital sign parameter is flagged

DTYPE was used for heart rate, temperature, and blood pressure, which have multiple measurements taken per visit. See the table below listing the DTYPE, derivation rule and any controlled terminology used.

ADaM Variable	Derivation Rule	Controlled Terminology
ADVS.DTYPE	<p>ABC09.ADVS.DTYPE assigned to 'WORST' for derived records if AVISITN=5555</p> <p>ABC08.ADVS.DTYPE replacing the value 'MAXIMUM' by 'WORST'</p> <p>If ABC07.ADVS.DTYPE= ' ' and ABC07.ADVS.DTYPE1 in ('DAYAVG', 'VISAvg'), then assign DTYPE='AVERAGE'</p> <p>ABC06.ADVS.DTYPE contains all derivations as is</p>	AVERAGE, LOCF, WORST

## 6. Data Conformance Summary

### 6.1 Conformance Inputs

Question	Description
Software name and version used for the integrated datasets validation	Pinnacle 21 Enterprise v4.2.1, Validation Engine Version: 2010.1
Version of the validation rules (i.e., CDISC, FDA, PMDA) for the integrated datasets	Used ADaM IG v1.1 individual study validation rules for the FDA as there are no validation rules available for integrated studies
Software name and version for the Define-XML validation	Pinnacle 21 Enterprise v4.2.1, Validation Engine Version: 2010.1, Define-XML v2.0
Version of the validation rules (i.e., CDISC, FDA, PMDA) for the Define-XML	ADaM IG v1.1 for the FDA

Provide any additional compliance evaluation information:

Not Applicable

### 6.2 Issues Summary

The following table summarizes the issues found by the conformance validation:

Dataset	Rule ID	Diagnostic Message	Severity	Count	Explanation
ADLB	AD0130	BASE or BASEC is populated for a unique USUBJID, PARAMCD but no baseline record exists		30	The STUDYID in individual ADaM datasets is designed to represent the study database in which the given record is collected, whereas USUBJID is a unique subject identifier across the parent and extension studies. Hence the ERROR is expected, even though a baseline record exists for a unique USUBJID/PARAMCD/BASETYPE combination.

## 7. Submission of Programs

All programs for the integration of analysis datasets and key safety results are submitted. They were all created on a Linux platform using SAS v9.4. The internal reference date used to create dates in integrated ADaM datasets is 01 January 1960.

### 7.1 Integrated ADaM Programs

Program Name	Dataset	Macro Used
ADSL.txt	ADSL.xpt	
ADAE.txt	ADAE.xpt	
ADCM.txt	ADCM.xpt	
ADLB.txt	ADLB.xpt	viswin.txt

### 7.2 Integrated Analysis Output Programs

Program Name	Output Number	Title	Input
T_14_1_1_dem	14.1.1	Summary of Demographics	ADSL

### 7.3 Macro Programs

Program Name	Purpose
viswin.txt	Visit Windows creation for record selection
sumn.txt	Counts of subjects per population