Submitting Clinical Trial Datasets to Evaluate the Impact of Immunogenicity on the Pharmacokinetics of a Drug

Guidance for Industry

Technical Specifications Document

For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov.

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Contains Nonbinding Recommendations

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Guidance for Industry
Technical Specifications Document[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

1.0 INTRODUCTION

This guidance is intended to assist industry in the submission of datasets from clinical studies that evaluate immunogenicity and its impact on the pharmacokinetics of a drug. In this document, FDA provides detailed information and specifications for these datasets. These specifications may elicit discussions between the sponsor[2] and reviewers regarding issues with trial design or conduct that may affect the content of the analysis datasets. These specifications were built to support the data standards and processes described in the technical specification document *Study Data Technical Conformance Guide* (March 2026).[3] Refer to other related FDA guidance documents for the general recommendations on evaluation of immunogenicity.[4,5]

[1] This guidance has been prepared by the Office of Clinical Pharmacology in the Center for Drug Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2018-D-1216 (available at https://www.regulations.gov/docket?D=FDA-2018-D-1216) (see the instructions for submitting comments in the docket).

[2] For the purposes of this guidance, the term *sponsor* refers to both sponsors and applicants.

[3] For the most recent version of a technical specification document, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[4] See the draft guidance for industry *Immunogenicity Information in Human Prescription Therapeutic Protein and Select Drug Product Labeling--Content and Format* (February 2022). When final, this guidance will represent FDA's current thinking on this topic. We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[5] See the guidances for industry *Immunogenicity Testing of Therapeutic Protein Products —Developing and Validating Assays for Anti-Drug Antibody Detection* (February 2019) and *Immunogenicity Assessment for Therapeutic Protein Products* (August 2014).

For questions regarding a specific submission, the sponsor should contact the applicable review division. For questions about a particular data standard implementation issue, contact cder-edata@fda.hhs.gov. For more general recommendations on the use and submission of standardized study data, refer to the technical specification document *Study Data Technical Conformance Guide* (March 2026).

This document provides detailed data specifications for the following datasets:

- Analysis Dataset for Immunogenicity Specimen (ADIS)
- Analysis Dataset for Pharmacokinetic Concentrations (ADPC)
- Subject-Level Analysis Dataset (ADSL)

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, the guidance describes the Agency's current thinking on a topic and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended but not required.

Not every data element included in a standard's underlying data model is fit for purpose for every clinical trial. The use of the word *required* in this document generally indicates a requirement by the Agency and not any external organization. Any use of the word *required* that would have a different meaning will be explained in the text. For example, the Study Data Tabulation Model Implementation Guide (SDTMIG)[6] classifies variables as required, expected, or permissible. This use of the word *required* by the Standards Data Organization does not necessarily indicate an Agency requirement.

2.0 OVERVIEW OF THE DATASET SPECIFICATION

The sections below describe the desired content of the datasets, ADIS, ADPC, and ADSL. The variable names and associated metadata are based on current Clinical Data Interchange Standards Consortium (CDISC)[6] standards for Study Data Tabulation Model (SDTM) and Analysis Data Model (ADaM), where possible. Each specification includes a column (i.e., the Comment column) that contains information about the variables, such as the expected content, derivation considerations, or assumptions. If any variable is unclear, sponsors are encouraged to discuss expectations with the FDA via the applicable review division.

Some variables may not be appropriate for all clinical trials. If a sponsor's trial did not collect the data necessary to create a specified variable, then it is acceptable to omit the variable in the datasets. It is acceptable to include additional variables to capture information about the study design, the immunogenicity results, etc. when needed. Variables that have been omitted or added should be documented in the Define.xml file and itemized in the Analysis Data Reviewer Guide as a separate table.

[6] See https://www.cdisc.org/.

Sponsors should also submit programs that were used to create these datasets (see technical specification document *Study Data Technical Conformance Guide* (March 2026), section 4.1.2.10). Consistency in controlled terminology across SDTM and ADaM as well as across ADaM datasets is important to facilitate traceability and support analyses. Use of standard controlled terminology is preferred where applicable (e.g., Medical Dictionary for Regulatory Activities (MedDRA), CDISC-controlled terminology). For variables without standard controlled terminology, where appropriate and to the degree possible, sponsor-defined controlled terminology should also be consistent across SDTM and ADaM datasets.

The ability to efficiently analyze or trace data can depend on the use of consistent controlled terminology across datasets. For this reason, the specifications explicitly identify certain parameters and variables where consistent controlled terminology across datasets is expected. For example, to support analyses, the sponsor-defined controlled terminology for variables such as AVISIT, ATPT, and others should be consistent across ADIS and ADPC or, to support traceability between SDTM and ADaM, the value of PARAM in ADIS should be equivalent to the value of the corresponding ISTEST for parameters that are not derived. In all cases, the variable labels and the variable type noted in the specifications should be used.

3.0 DESCRIPTION OF ANALYSIS VARIABLES AND DATA SPECIFICATIONS

3.1 Analysis Dataset of Immunogenicity Specimen

The ADIS contains one record per subject per parameter per time point and provides a comprehensive set of variables pertaining to the subject and their antidrug antibody (ADA) measures. This dataset is based on the ADaM Basic Data Structure (BDS) and derived from Immunogenicity Specimen Assessments (IS) domain described in the SDTMIG v3.4 of the CDISC.

Each test type for the ISTEST variable with the test details (ISTSTDTL or ISTSTOPO) in the IS dataset should be represented under the PARAM variable in the ADIS dataset. Examples of PARAM variables are "ADA screening,"[7] "ADA confirmatory," "ADA titer," "neutralizing antibodies," and "neutralizing antibodies titer." Under the PARAM variable, "ADA conclusion" is an additional parameter recommended for reporting the ADA status of each sample. Each immunogenicity test result described under the ISTRESC variable in the IS dataset should be represented under the AVALC variable in the ADIS dataset. Examples of AVALC variables may include character strings (e.g., such as "negative," "positive," "missing," or floating text (e.g., for "ADA titer" and "neutralizing antibody titer")). Each numerical result of the immunogenicity test described in the ISTRESN variable in the IS dataset should be represented under the AVAL variable in the ADIS dataset.

Each immunogenicity specimen (sample) should have a final ADA status based on the results from "ADA screening" and "ADA confirmatory" tests. The final ADA status should be reported

[7] Quotation marks are used in this guidance to indicate that the enclosed text represents the exact character result or test type values, as opposed to a description or characterization. See AVALC and PARAM entries in Table 1.

as "ADA conclusion." See Table 1 for the proposed definition for "ADA conclusion" which aligns with the whitepaper by Shankar et al.[8] Each "ADA screening" result should have an associated "ADA conclusion" result, therefore, the total number of samples with "ADA conclusion" status should be the same as the total number of samples with "ADA screening" status. The output of "ADA conclusion," AVALC, should take only a definitive value in floating text of either "negative" or "positive" when the assay has an adequate drug tolerance relative to the drug concentration. If the assay drug tolerance is not adequate, the AVALC value should be reported as "inconclusive." The "ADA conclusion" output should not contain numerical results, but rather, "blank," "NA," etc. If the "ADA conclusion" output cannot be determined, the AVALC value should be reported as "missing," and the reason should be provided under the ISSTAT variable. The ADA status reported in the "ADA conclusion" will be used to assess the impact of ADA on pharmacokinetics. When it is necessary to provide further details of a positive finding for "ADA conclusion," a derived character variable (AVALC2) may be used. See Table 1 for potential utility of AVALC2.

The variable ADASUBJ in the dataset is for reporting subject-level ADA status, which is derived from the status of all ADA samples. Typically, each subject would have the same value for this variable at all visits (e.g., ADA negative, ADA positive, ADA inconclusive), unless otherwise called for by specific study design features. Definition of the ADASUBJ results (i.e., the derivation of ADASUBJ from the "ADA conclusion" results of all ADA samples of each subject) should be provided in the Define.xml file. For example, the definition of the ADASUBJ results can be one of the following:

1. ADA negative when a given subject reported negative for all post-dose samples under the parameter of ADA conclusion,

2. ADA positive when at least one post-dose sample reported positive and baseline is negative under the parameter of ADA conclusion, or

3. ADA inconclusive when one or more samples reported ADA inconclusive and the remaining sample or samples are negative under the parameter of ADA conclusion.

Table 1 shows typical variables and specific derivations from the standard IS domain in the ADaM-compliant ADIS dataset.

[8] Shankar G, S Arkin, L Cocea, V Devanarayan, S Kirshner, A Kromminga, V Quarmby, S Richards, CK Schneider, M Subramanyam, S Swanson, D Verthelyi, S Yim, 2014, Assessment and reporting of the clinical immunogenicity of therapeutic proteins and peptides-harmonized terminology and tactical recommendations, AAPS J, 16(4):658–673.

Table 1. Analysis variables metadata for ADIS

Variable Name	Variable Label	Type	Comments
STUDYID	Study Identifier	Char	Unique identifier for a study.
USUBJID	Unique Subject Identifier	Char	Unique identifier for a subject across all studies for all applications or submission involving the products.
AVISIT	Analysis Visit	Char	Derived. Data source is SDTM.IS.VISIT. Protocol-defined description of a clinical encounter. It should be coded consistently to allow the mapping of time-matched measures between ADIS and ADPC datasets. For example, AVISIT may be described as a protocol visit number, a treatment cycle number and day number, or any other character value logically related to a clinical encounter.
AVISITN	Analysis Visit N	Num	Derived. Data source is SDTM.IS.VISITNUM. Numeric version of AVISIT that represents the time point associated with the visit. The value should be unique for each AVISIT. It helps with the plotting and interpretation of the values.
ADY	Study Day of Visit/ Collection Time	Num	Derived. Data source is SDTM.IS.ISDY. Actual study day of visit/collection/exam expressed in integer days relative to sponsor-defined Subject Reference Start Date/Time (RFSTDTC) in Demographics.
ATPT	Analysis Time Point	Char	Derived. Data source is SDTM.IS.ISTPT. ADIS.ATPT and ADPC.ATPT should be coded in a consistent fashion.
ATPTN	Analysis Time Point N	Num	ATPTN provides a numeric representation of ATPT. Defining ATPTN so that its values represent the planned time point in a consistent unit. It helps with the plotting and interpretation of values. ATPTN should have a one-to-one relationship with ATPT.
ISDTC	Date/Time of Collection	Char	Derived. Data source is SDTM.IS.ISDTC. Collection date and time of an observation.

Continued

Table 1, Continued

Variable Name	Variable Label	Type	Comments
PARAM	Parameter: Immunogenicity Test or Examination Name	Char	Derived. Data source is SDTM.IS.ISTEST and the test details are provided in SDTM.IS.ISTSTDTL or SDTM.IS.ISTSTOPO. For records with a corresponding record in Immunogenicity Specimen Test (ISTEST), the test details are provided in ISTSTDTL/ ISTSTOPO based on the multi-tiered approach to evaluate immunogenicity. PARAM may take one of the following values: • "ADA screening" • "ADA confirmatory" • "ADA conclusion" • "ADA titer" • "neutralizing antibodies" • "neutralizing antibodies titer" For example, when ISTEST = ADA, ISTSTDTL / ISTSTOPO can take the value of "screening," "confirmatory," or "titer" and the corresponding PARAM value would be "ADA screening," "ADA confirmatory," and "ADA titer," respectively. "ADA conclusion" is further derived from the combined results of "ADA screening," and "ADA confirmatory." See AVALC for additional description.
PARAMCD	Parameter Code: Immunogenicity Test/ Exam Short name	Char	Derived. The base data source is SDTM.IS.ISTESTCD. The assignment of PARAMCD should consider SDTM.IS.ISTSTDTL or SDTM.IS.ISTSTOPO. Each PARAM should have a unique PARAMCD. PARAMCD should be abbreviated up to a maximum length of 8 characters.

Continued

Table 1, Continued

Variable Name	Variable Label	Type	Comments
AVAL	Analysis Value	Num	Derived. Data source is SDTM.IS.ISSTRESN. It is a numeric value for reporting the immunogenicity test results under PARAM (e.g., PARAM = "ADA titer" or "neutralizing antibodies titer").
AVALC	Analysis Value (C)	Char	Derived. Data source is SDTM.IS.ISSTRESC. Character result is in the standard format for reporting the immunogenicity test results under PARAM. The preferred response can be "positive" or "negative" or "inconclusive" (for "ADA screening," "ADA confirmatory," "ADA conclusion," and "neutralizing antibodies"), or titer value (for "ADA titer" and "neutralizing antibodies titer"). The reason for an inconclusive result should be explained in the Define.xml file. "ADA conclusion" is assigned "positive" or "negative" or "inconclusive" based on the combined results of "ADA screening" and "ADA confirmatory." (See Appendix section for an example derivation of "ADA conclusion.")
AVALU	Standard Units of Analysis Value	Char	Derived. Data source is SDTM.IS.ISSTRESU. These are standardized units for AVAL and AVALC and should have the same value as those used for ISSTRESC and ISSTRESN.
PKADAFL	IS Matching Pharmacokinetic Flag	Char	Populate with "Y" if there is a matching nominal pharmacokinetic sample time point for the nominal IS time point (e.g., if there are time-matched pharmacokinetic measures in ADPC) or null otherwise.
CISANLFL	Concentration IS Analysis Flag	Char	Character flag variable set to "Y" if the record is used in the concentration-IS analysis or null otherwise.

Continued

Table 1, Continued

Variable Name	Variable Label	Type	Comments
AVALC2	Analysis Value (C) for sample ADA status relative to baseline ADA sample		Derived character variable. The purpose of this variable is to describe whether a post-dose ADA sample with "ADA conclusion = positive" in AVALC variable belongs to the category of either "treatment-induced ADA" or "treatment-boosted ADA" or "ADA negative." Another categorization could be "treatment-emergent ADA" (for "treatment-induced ADA" and "treatment-boosted ADA" combined) or "non-treatment-emergent ADA" (for samples with "ADA confirmatory = positive" without an increase in ADA titer from baseline greater than the prespecified magnitude). A definition of these results categories should be provided in the Define.xml file. When a post-dose ADA sample has an ADA conclusion of "negative" or "inconclusive" in AVALC variable, AVALC2 will take the same value as AVALC.
ADASUBJ	Subject level	Char	Derived character variable as an indicator of subject-level ADA status;-possible results could be "ADA negative," "ADA positive," "ADA inconclusive," or "not evaluable." Typically, each subject would have the same value for this variable at all visits, unless otherwise called for by specific study design features. A definition of these results categories should be provided in the Define.xml file.
ABLFL	ADA Baseline Record Flag		Derived. Data source is SDTM.IS.ISBLFL. Indicator used to identify a baseline value. Should be "Y" or null.
ISNAM	Vendor name	Char	Derived. Data source is SDTM.IS.ISNAM. Name or identifier of the laboratory or vendor who provided the test results.

Continued

Table 1, Continued

Variable Name	Variable Label	Type	Comments
ISSPEC	Specimen Type	Char	Derived. Data source is SDTM.IS.ISSPEC. Determines the types of specimens used for a measurement.
ISMETHOD	Method of Test or Examination	Char	Derived. Data source is SDTM.IS.METHOD. Method of the test or examination.
TRTP	Planned Treatment	Char	Planned treatment arm.
TRTPN	Planned Treatment N	Num	The numeric code for TRTP. One-to-one mapping within ADIS to TRTP. The mapping should be the same in ADIS and ADPC.
TRTSEQP	Planned Sequence of Treatments	Char	Planned sequence of treatments.
TRTA	Actual Treatment	Char	Actual treatment arm.
TRTAN	Actual Treatment N	Num	The numeric code for TRTA. One-to-one mapping within ADIS to TRTA. The mapping should be the same in ADIS and ADPC.
TRTSEQA	Actual Sequence of Treatments	Char	Actual sequence of treatments.
ISSTAT	Completion Status	Char	Derived. Data source is SDTM.IS.ISSTAT. Used to indicate that a test was not done.
ISLLOQ	Lower Limit of Quantitation	Num	Derived. Data source is SDTM.IS.ISLLOQ. Indicates the lower limit of quantitation.
ISCAT	Category for Immunogenicity test	Char	Derived. Data source is SDTM.IS.ISCAT. Used to define a category of topic variable values across subjects.

Continued

Table 1, Continued

Variable Name	Variable Label	Type	Comments
PARCAT	Parameter Category	Char	Used to group parameters into categories and must have a one-to-many relationship with PARAM. This variable enables multiple groupings of PARAM. Multiple PARCATs, like PARCAT1, PARCAT2, etc., can be created to align with various grouping as needed. It should be defined based on a thorough review of all parameters and the intended analysis grouping. For example, PARCAT can be the name of the analyte, e.g., ADA against the drug and ADA against a specific component of the drug.

3.2 Analysis Dataset for Pharmacokinetic Concentrations

The ADPC contains one record per subject per pharmacokinetic concentration per time point and provides a comprehensive set of variables pertaining to the subject and their quantitative pharmacokinetic measures. This dataset is based on the ADaM BDS and derived from Pharmacokinetics Concentration (PC) domain described in the SDTMIG v3.4 of CDISC.

The ADaM-compliant ADPC dataset allows for an analysis of changes in concentration over time. The information, combined with immunogenicity information in the ADIS dataset, allows for stratification to inform the impact of immunogenicity on a drug's pharmacokinetics. Thus, to allow for proper mapping of time-matched pharmacokinetics and IS rows, the time variables presented in both ADIS and ADPC (e.g., AVISIT) should be coded consistently. The variables and specific derivations from the standard ADaM-compliant ADPC dataset are described in Table 2.

Table 2. Analysis variables metadata for ADPC

Variable Name	Variable Label	Type	Comments
STUDYID	Study Identifier	Char	Unique identifier for a study.
USUBJID	Unique Subject Identifier	Char	Unique identifier for a subject across all studies for all applications or submissions involving the products.

Continued

Table 2, Continued

Variable Name	Variable Label	Type	Comments
AVISIT	Analysis Visit	Char	Derived. Data source is SDTM.PC.VISIT. Protocol-defined description of a clinical encounter. It should be coded consistently to allow the mapping of time-matched measures.
AVISITN	Analysis Visit N	Num	Derived. Data source is SDTM.PC.VISITNUM. Numeric version of AVISIT. Because study visits are usually defined by certain time points, defining AVISITN so that it represents the time point associated with the visit can facilitate plotting and interpretation of the values. Alternatively, AVISITN may be a protocol visit number, a cycle number, an analysis visit number, or any other number logically related to AVISIT or useful for sorting that is needed for analysis (see ADaM Implementation Guide, (ADaM IG)).
AVISITN	Analysis Visit N	Num	Derived. Data source is SDTM.PC.VISITNUM. Numeric version of AVISIT. Because study visits are usually defined by certain time points, defining AVISITN so that it represents the time point associated with the visit can facilitate plotting and interpretation of the values. Alternatively, AVISITN may be a protocol visit number, a cycle number, an analysis visit number, or any other number logically related to AVISIT or useful for sorting that is needed for analysis (see ADaM Implementation Guide, (ADaM IG)).
ATPT	Analysis Planned PC Time Point	Char	Derived. Data source is SDTM.PC.PCTPT. Text description of the time when specimen should be taken. This could be represented as an elapsed time of last dose. Examples: "start," "5 min post." IS. ISTPT and PC. PCTPT and the corresponding ADIS.ATPT and ADPC.ATPT should be coded in a consistent fashion so mapping of time-matched measures can be performed.

Continued

Table 2, Continued

Variable Name	Variable Label	Type	Comments
ATPTN	Analysis PC Time Point Number	Num	Derived. Data source is SDTM.PC.PCTPTNUM. ATPTN provides a numeric representation of ATPT. Defining ATPTN so that its values represent the planned time points in a consistent unit (e.g., minutes or hours after dosing) is not required but can facilitate plotting and interpretation of the values. There should be a one-to-one mapping between ATPT and ATPTN (see ADaM IG). As for ATPT, the coding of ATPTN should be the same for ADIS.ATPTN and ADPC.ATPTN.
ADY	Analysis Relative Day	Num	Derived. Data source is SDTM.PC. PCDY. Study day of specimen collection, measured as integer days.
PARAM	Analyte Name	Char	Analyte name. Derived. Data source is SDTM.PC.PCTEST. Pharmacokinetic Test short name: short name of the analyte or specimen characteristic.
PARAMCD	Parameter Code	Char	Derived. Data source is SDTM.PC.PCTESTCD. Parameter code with a maximum length of 4 characters. One-to-one correspondence with PCTEST.
AVAL	Analysis Value	Num	Derived. Data source is SDTM.PC.PCSTRESN. PCSTRESN should store all numeric test results or findings.
AVALC	Analysis Value (C)	Char	Derived. Data source is SDTM.PC.PCSTRESC.
AVALU	Unit of Analysis Value	Char	Derived. Data source is SDTM.PC.PCTRESU. Standard unit for PCSTRESN and PCSTRESC.
PCLLOQ	Lower Limit of Quantitation	Num	Indicates the lower limit of quantitation for an assay. Units should be those used in PCSTRESU.
PCCAT	Sub-category of PC Test	Char	A further categorization of a test category.
PCSTATUS	Analysis Status	Char	Indicate the status of sample analysis.
PCSPEC	PC Specimen Material Type	Char	Define the type of specimen used for a measurement.

Continued

Table 2, Continued

Variable Name	Variable Label	Type	Comments
PCDTC	Date/Time of Specimen Collection	Char	Date/time of specimen collection represented in ISO 8601character format.
TRTA	Actual Treatment	Char	Actual treatment arm.
TRTAN	Actual Treatment N	Num	The numeric code for TRTA. One-to-one mapping within ADPC to TRTA. The mapping should be the same in ADIS and ADPC.
TRTSEQA	Actual Sequence of Treatments	Char	Actual sequence of treatments.
TRTP	Planned Treatment	Char	Planned treatment arm.
TRTPN	Planned Treatment N	Num	The numeric code for TRTP. One-to-one mapping within ADIS to TRTP. The mapping should be the same in ADIS and ADPC.
TRTSEQP	Planned Sequence of Treatments	Char	Planned sequence of treatments.
PCSEQ	Sequence Number	Num	Derived. Data source is SDTM.PC.PCSEQ. Sequence number given to ensure uniqueness of subject records with a domain. May be any valid number.
PCADAFL	IS Matching Pharmacokinetic Flag	Char	Populate with "Y" if there is a matching ADA sample time point for the nominal pharmacokinetic time point (e.g., if there are time-matched ADA measures in ADIS).
CISANLFL	Concentration IS Analysis Flag	Char	Character flag variable set to "Y" if the record is used in the concentration-IS analysis or null otherwise.

3.3 Subject-Level Analysis Dataset

The Subject-Level Analysis Dataset (ADSL) contains one record per subject and provides variables such as subject-level population flags, planned and actual treatments for each period, demographic information, stratification and subgrouping variables, important dates, etc. This dataset should be an ADaM-compliant ADSL as described in the ADaM Implementation Guide (ADaM IG) and discussed in the technical specification document *Study Data Technical Conformance Guide* (March 2026), Section 4.1.2.4.

The variables and specific derivations from the standard ADaM-compliant ADSL dataset are described in Table 3. The treatment assignments contained in this dataset are essential for the analysis of immunogenicity data from clinical trials in which subjects may receive a different

dosing regimen. The dosing regimen can influence the immunogenicity incidence and its impact on the drug's pharmacokinetics.

Table 3. Analysis variables metadata for ADSL

Variable Name	Variable Label	Type	Comments
STUDYID	Study Identifier	Char	Unique identifier for a study.
USUBJID	Unique Subject Identifier	Char	Unique identifier for a subject across all studies for all applications or submission involving the products.
ARM	Description of Planned Arm	Char	Name of the arm to which the subject was assigned.
ARMCD	Planned Arm Code	Char	Short name for arm.
ARMNRS	Reason Arm and/or Actual Arm is Null	Char	A coded reason that arm variables (ARM and ARMCD) and/or actual arm variables are nulls.
SITEID	Study Site Identifier	Char	Unique identifier for a site within a study.
ACTARMCD	Actual Arm Code	Char	Code of actual arm.
ACTARM	Description of Actual Arm	Char	Description of actual arm.

APPENDIX

All dataset examples in this appendix contain illustrative data from a single subject and a subset of variables expected in a complete dataset for a clinical trial that would be submitted for review by the FDA.

Example Schedule of Assessments

Table A contains an illustrative example of the schedule of assessments for pharmacokinetic and immunogenicity data in a hypothetical clinical study (Study A). The example schedule provided the basis for the example Immunogenicity Specimen Assessments (IS) dataset in Table B, the example Analysis Dataset for Immunogenicity Specimen (ADIS) in Table C, and the example Analysis Dataset for Pharmacokinetics Concentrations (ADPC) in Table D. The subset of variables included in this table serves the purpose of illustrating the derivations of certain variables and how some variables across these datasets relate to each other.

Table A. Example Schedule of Assessments

Activity	Visit					
	Cycle 1			Cycle 2	Cycle 3	Cycle 4
	Day 1			Day 29	Day 57	Day 85
	Pre-dose	1-hr post-dose	2-hr post-dose	Pre-dose	Pre-dose	Pre-dose
Pharmacokinetics	X	X	X	X	X	X
Immunogenicity	X			X	X	X

Example Study Data Tabulation Model Immunogenicity Specimen Assessments Dataset

Table B is an example a of study data tabulation model (SDTM) dataset for a single subject following the IS domain specifications to illustrate how to report the results from immunogenicity assessments using the multi-tiered approach as described in the draft guidance for industry *Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products* (January 2025).[1] Character Result/Finding in Standard Format (ISSTRESC) and Numeric Results/Findings in Standard Units (ISSTRESN) are provided for illustrative purposes. Scenarios displayed in Table B include:

[1] When final, this guidance will represent FDA's current thinking on this topic. We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

- The IS sample obtained from Cycle 1 had a negative result in the antidrug antibody (ADA) screening test (row 1).
- The IS sample obtained from Cycle 2 had a positive result in the ADA screening test (row 2) and a negative result in the ADA confirmatory test (row 3).
- The IS sample obtained from Cycle 3 had a positive result in both the ADA screening test (row 4) and the ADA confirmatory test (row 5), a negative result in the neutralizing antibody confirmatory test (row 6), and a value for the ADA titer (row 7) that did not account for the minimum required dilution.
- The IS sample obtained from Cycle 4 had positive results in the ADA screening test (row 8), ADA confirmatory test (row 9), and neutralizing antibody confirmatory test (row 10), and values for ADA titer and neutralizing antibody titer (rows 11 and 12) that did not account for the minimum required dilution.

Table B. Illustrative SDTM.IS Dataset

Row	STUDYID	USUBJID	VISIT	ISTPT	VISITDY	ISTEST	ISTSTDTL or ISTSTOPO	ISSTRESC	ISSTRESN
1	1	1	Cycle 1 day 1	Pre-dose	1	Antidrug Antibody	Screening Test	Negative	
2	1	1	Cycle 2 day 1	Pre-dose	29	Antidrug Antibody	Screening Test	Positive	
3	1	1	Cycle 2 day 1	Pre-dose	29	Antidrug Antibody	Confirmatory Test	Negative	
4	1	1	Cycle 3 day 1	Pre-dose	57	Antidrug Antibody	Screening Test	Positive	
5	1	1	Cycle 3 day 1	Pre-dose	57	Antidrug Antibody	Confirmatory Test	Positive	
6	1	1	Cycle 3 day 1	Pre-dose	57	Neutralizing Antidrug Antibody	Confirmatory Test	Negative	
7	1	1	Cycle 3 day 1	Pre-dose	57	Antidrug Antibody	Titer	2*	2
8	1	1	Cycle 4 day 1	Pre-dose	85	Antidrug Antibody	Screening Test	Positive	
9	1	1	Cycle 4 day 1	Pre-dose	85	Antidrug Antibody	Confirmatory Test	Positive	

Continued

Table B, Continued

10	1	1	Cycle 4 day 1	Pre-dose	85	Neutralizing Antidrug Antibody	Confirmatory Test	Positive	
11	1	1	Cycle 4 day 1	Pre-dose	85	Antidrug Antibody	Titer	16*	16
12	1	1	Cycle 4 day 1	Pre-dose	85	Neutralizing Antidrug Antibody	Titer	8*	8

* Titer values did not account for the minimum required dilution factor (value = 20).

Example Immunogenicity Specimen Analysis Dataset

Table C is an example ADIS dataset corresponding to the IS dataset described in Table B of the Appendix. Note that this table only shows a subset of variables in the ADIS dataset described in Table A. In this example, outputs of immunogenicity assessment are derived from the IS dataset for each assessment time point in Table B. Additionally, it illustrates how to obtain the derived values when the ADA status of PARAM is "ADA conclusion." The characters values (AVALC) and numeric values (AVAL) are provided for illustrative purposes only. Results displayed in Table C include the following:

- Rows 1-12 correspond to the results of individual IS specimen tests that are in the SDTM IS dataset in Table B.
- Rows 13-16 have the final status value "ADA conclusion" for the variable PARAM. For AVALC:
  - Cycle 1: "ADA conclusion" is negative because the ADA screening result is negative.
  - Cycle 2: "ADA conclusion" is negative because the ADA screening result is positive, and the ADA confirmatory result is negative.
  - Cycle 3 and Cycle 4: "ADA conclusion" is positive because the ADA screening result and ADA confirmatory results are both positive.

Table C. Illustrative ADIS Dataset with Corresponding Variables in the SDTM.IS Dataset Related to Derived ADA Status for Each Specimen

Row	Variable names in SDTM.IS dataset										
	STUDYID	USUBJID		VISIT		ISTPT	VISITDY	ISTEST / ISTSTDTL or ISTSTOPO	ISSTRESC	ISSTRESN	
	Variable names in ADIS dataset										
	STUDYID	USUBJID	TRTA	AVISIT	AVISITN	ATPT	ADY	PARAM	AVALC	AVAL	ABLFL
1	1	1	Drug X	Cycle 1 day 1	1	Pre-dose	1	ADA Screening	Negative		Y
2	1	1	Drug X	Cycle 2 day 1	2	Pre-dose	29	ADA Screening	Positive		
3	1	1	Drug X	Cycle 2 day 1	2	Pre-dose	29	ADA Confirmatory	Negative		
4	1	1	Drug X	Cycle 3 day 1	3	Pre-dose	57	ADA Screening	Positive		
5	1	1	Drug X	Cycle 3 day 1	3	Pre-dose	57	ADA Confirmatory	Positive		
6	1	1	Drug X	Cycle 3 day 1	3	Pre-dose	57	Neutralizing Antibodies	Negative		
7	1	1	Drug X	Cycle 3 day 1	3	Pre-dose	57	ADA Titer	2	40*	
8	1	1	Drug X	Cycle 4 day 1	4	Pre-dose	85	ADA Screening	Positive		
9	1	1	Drug X	Cycle 4 day 1	4	Pre-dose	85	ADA Confirmatory	Positive		
10	1	1	Drug X	Cycle 4 day 1	4	Pre-dose	85	Neutralizing Antibodies	Positive		
11	1	1	Drug X	Cycle 4 day 1	4	Pre-dose	85	ADA Titer	16	320*	
12	1	1	Drug X	Cycle 4 day 1	4	Pre-dose	85	Neutralizing Antibodies Titer	8	160*	
13	1	1	Drug X	Cycle 1 day 1	1	Pre-dose	1	ADA Conclusion	Negative		
14	1	1	Drug X	Cycle 2 day 1	2	Pre-dose	29	ADA Conclusion	Negative		
15	1	1	Drug X	Cycle 3 day 1	3	Pre-dose	57	ADA Conclusion	Positive		
16	1	1	Drug X	Cycle 4 day 1	4	Pre-dose	85	ADA Conclusion	Positive		

* Titer values have been adjusted by the minimum required dilution factor of 20.

Example Analysis Data Model Pharmacokinetics Concentrations Analysis Dataset

Table D shows an example ADPC dataset for the same patient and scenario descriptions as those provided in Tables A and B. Note that this table only shows a subset of variables to be submitted in the ADPC dataset; the subset of variables serves the purpose of illustrating how certain variables in the ADPC dataset are related to variables in ADIS dataset. The character values (AVALC) and numeric values (AVAL) are provided for illustrative purposes only.

As Table A shows, there are more pharmacokinetic samples than immunogenicity samples in the schedule of assessment, and several time points have both immunogenicity samples and pharmacokinetic samples (i.e., time-matched pharmacokinetics and ADA samples). Merging of the ADIS dataset and ADPC dataset is necessary to facilitate the evaluation of ADA effect on pharmacokinetics at individual timepoints (i.e., using time-matched data). Therefore, time information for both ADA and pharmacokinetic samples should be consistent in the ADIS and ADPC definitions (e.g., using the same variable names and the same value for each time point either in character or numeric format). Additionally, the format allows for time points without both ADA and pharmacokinetic samples that may be necessary for other types of analyses outside of the scope of this guidance.

Table D. Illustrative ADPC Dataset with Data to Demonstrate the Corresponding Time-Related Variables in the ADIS Dataset

Corresponding variables in ADIS dataset with time-related variables in *italic* font											
USUBJID	TRTA	*AVISIT*	*AVISITN*	*ATPT*	*ATPTN*	*ADY*					
ADPC data variables											
USUBJID	TRTA	*AVISIT*	*AVISITN*	*ATPT*	*ATPTN*	*ADY*	PARAM	AVALC	AVAL	PCSTATUS	PCLLOQ
1	Drug X	Cycle 1 Day 1	1	Pre-dose	1	1	Drug X	BLQ<0.25	0.125		0.25
1	Drug X	Cycle 1 Day 1	1	1-hr post-dose	2	1	Drug X	100	100		0.25
1	Drug X	Cycle 1 Day 1	1	2-hr post-dose	3	1	Drug X	NA		NOT DONE	0.25
1	Drug X	Cycle 2 Day 1	2	Pre-dose	1	29	Drug X	10	10		0.25
1	Drug X	Cycle 3 Day 1	3	Pre-dose	1	57	Drug X	30	30		0.25
1	Drug X	Cycle 4 Day 1	4	Pre-dose	1	85	Drug X	80	25		0.25