
# Clinical Data Acquisition Standards Harmonization

CDASH Package-1

Adverse Events
Concomitant Medications
Demographics & Subject Characteristics

Collaborative Group Review

31 May 2007

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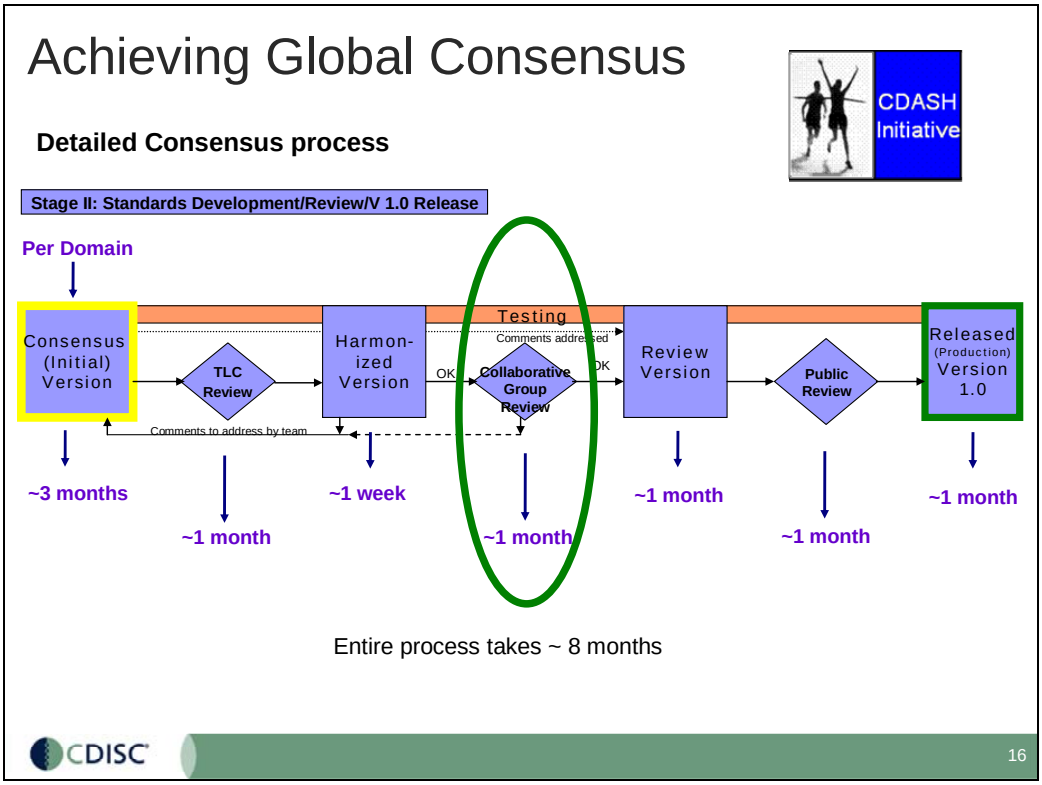
# Section 1. Clinical Data Acquisition Standards Harmonization

## 1. Introduction

This document contains the first of four Clinical Data Acquisition Standards Harmonization (CDASH) Packages to be submitted for Collaborative Group review. CDASH Package-1 consists of Harmonized Versions (HV) for the following domains: Adverse Events, Concomitant Medications (including prior), Demographics & Subject Characteristics domains.

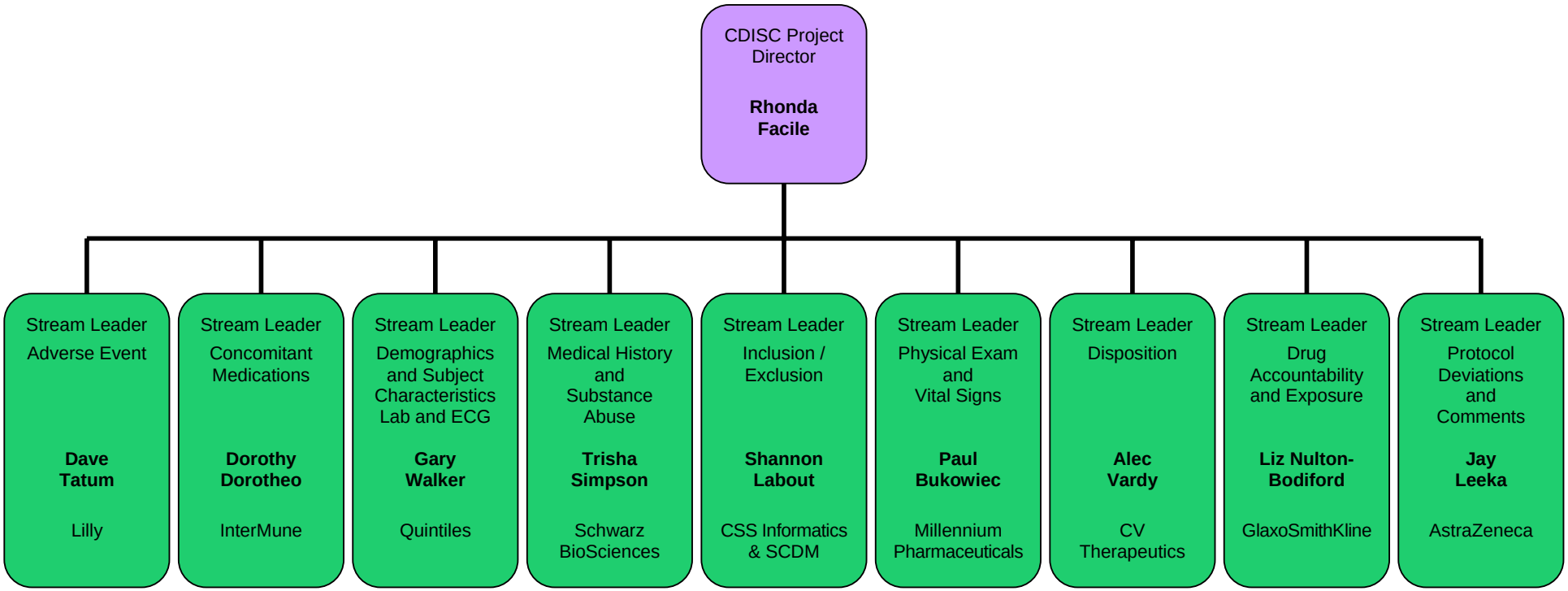
The CDISC Operating Procedure (CDISC-COP-001 Standards Development) was followed in the development of the HVs included in this document. The HVs have been reviewed internally by the CDISC Technical Leadership Committee (TLC), and all comments addressed to produce the Harmonized Versions. The next step in the CDISC consensus process is the external focused review or in this case the Collaborative Group review.




### 1.1 CDASH Core Team

A core team was created to form a qualified, multidisciplinary team of 9 members. Please see the organizational chart on the next page for the members of the CDASH core team. The core team executes the project plan, holds regular conference calls and face-to-face meetings, as appropriate, to achieve the objectives. Each core team member led a steam (or sub-group) of volunteer participants. Volunteers for each stream were recruited via an open invitation and selection process. Effort was made to ensure that representation on each stream was from relevant and diverse companies that included industry, CROs, academia and government.

# CDASH Core Team



## 2. CDASH Project Background

CDASH is in follow-up to Critical Path Opportunity # 45, and is now a CDISC-led project, originally initiated by ACRO (Association of Clinical Research Organizations). CDASH strategy and resources are the responsibility of a Collaborative Group.

The project goal is to develop a set of 'content standards':

- Variable Names
- Definitions
- Related metadata
- Implementation instructions

for a basic set of global data collection field (i.e., case report form variables) that will support clinical research studies. The initial scope of the project is the 'safety data domains' (i.e., Adverse Events, Concomitant Medications (including prior), Demographics and Subject Characteristics, Medical History, etc.). These safety domains cut across all therapeutic areas, beginning with 14 domains. The overarching goal of this project is to provide for a standard format for collecting data at investigative sites, across applications and study sponsors.

### 2.1 CDASH Project Process

The project is comprised of 9 Streams (sub-groups) each containing from 10 to 40 volunteers representing industry, CROs, academia and government. Each stream held bi-weekly teleconferences to review and discuss the identification of basic data collection variables.

Starting with Study Data Tabulation Model (SDTM) variable tables volunteers were asked to collect CRF samples currently used by industry, evaluate commonalities/differences of CRF samples and the SDTM, document data points included/excluded with justifications.

*Guiding principles: variables should –

- Ensure that SDTM "required" elements are addressed directly or indirectly
- Be "standard" but flexible to allow customization within defined limits
- Limit variables to required and necessary
- Comply with regulatory requirements
- Reduce redundancies; Not duplicate information found elsewhere in CRFs
- Increase collection of meaningful data
- Facilitate use of standards by all users
- Be appropriate for use both pre and post approval studies
- Allow consistent and efficient data collection/storage/transmission and analysis

**ACRO presentation: 2006-10-18 CDASH Kick-off Meeting*

Streams were then asked to reach agreement on basic data collection variables, map these variables to SDTM, add definitions and write completion and/or implementation guidelines/instructions.

The Streams began by reviewing CRF samples supplied by ACRO (where available), CDASH, as well as other CRF samples collected by stream members that are currently used by industry. Within each Stream sub-groups

were assigned and given the action items of scanning CRF samples and QC of CRF examples and then achieved consensus on administrative details (team members, meeting, etc.).

The streams collected feedback from numerous functional areas within their respective companies (including ex-US affiliates) to identify the purpose for their respective streams' data collection focus (i.e., Adverse Events, Concomitant Medication (including prior), Demographics and Subject Characteristic data). The Streams then focused the group discussions on CDASH project scope, category terminology – mandatory/conditional/optional, variable labels and definitions. The SDTM submission variables served as a target for deliverable data. Data collection variables were mapped to the SDTM variables as applicable.

## 3. General Recommendations and Observations Applicable to all Domains

### 3.1 Compliance

It is assumed that Sponsors will add or delete data collection variables as needed to meet protocol specific and other data collection requirements (e.g. therapeutic specific data variables and others as required per protocol, business practice and operating procedures).

Mandatory data collection variables must be present on the CRF to be compliant with the CDASH project, however, it is assumed that sponsors will determine which data variable will be collected based on TA specific data requirement, protocol and other considerations.

### 3.2 Recommended Date and Time Format

The CDASH project recommends the use of the DD/MMM/YYYY format on CRFs. Any needed time fields should use the HH:MM format. For use in a submission, the two fields will be concatenated to form the ----DTC variable, using the ISO 8601 (YYYY-MM-DDTHH:MM) format.

### 3.3 Terminology

Production Terminology developed by the Controlled Terminology Team will be incorporated in the CDASH documents as it becomes available. Terminology used by the CDASH project is published by the National Cancer Institute's Enterprise Vocabulary Services (NCI EVS). CDISC Controlled Terminology is listed where appropriate. Where feasible, complete codelists have been provided in this document to aid the reviewers. The final document, however, will only list the name of the codelist stored in NCI's EVS. Terminology proposed by the CDASH project will be forwarded to the CDISC Controlled Terminology team for consideration and vetting via their consensus process.

During the course of the CDASH development process, proposed terminology has been identified in some of the streams for data collection variables. Terminology proposals will be sent to the CDISC Terminology Team for inclusion in the consensus process.

### 3.4 Basic Identifiers (Study, Site, Investigator, Subject)

Site, Investigator and Patient/Subject identification data variables (STUDYID, COUNTRY, SITEID, INVID, and SUBJID) may be collected in the demographics domain. In the case of paper CRFs, these data collection variables may be collected on each case report form page as required, according to standard practice, local regulation, etc.

### 3.5 Data Collection Variables Considered Not Necessary to Collect

This section contains a brief representation of examples of other variables (including SDTM variables) that were discussed by the streams and were not considered data collection variables applicable to most clinical research. This representative list is not exhaustive, and it is included to give the reviewer an idea of what data collection variables were discussed within the stream during their deliberations.

## 4. SDTM (Submission) and CDASH (Acquisition)

The SDTM and the CDASH project have two different purposes. The SDTM is for reporting data collected to regulatory authorities. The CDASH project seeks to identify the basic data collection variables needed from a clinical, scientific and regulatory data collection perspective, to enable efficient data collection at the investigative sites. Data collection variables identified on the CDASH project will be mapped into the SDTM, as applicable and appropriate.

## 5. CDASH Categories for Data Collection Variables

In order to facilitate classification of the types of data collection variables, the CDASH core team agreed on the following categories:

### 5.1 Mandatory

Mandatory = A data collection variable that must be on the CRF (e.g., a regulatory requirement (if applicable)).

### 5.2 Conditional

Conditional = A data collection variable that must be collected on the CRF for specific cases (may be recorded elsewhere in the CRF or from other data collection sources).

### 5.3 Optional

Optional = A data collection variable that is available for use if needed (may be recorded elsewhere in the CRF or from other data collection sources).

## 6. CDISC SDTM Core Variables*

Within the SDTM all variables are assigned an SDTM "Core Variable" category, this assignment of categories (Required, Expected and Permissible) reflects the expectation of inclusion in an SDTM submission.

### 6.1 Required

Required = Any variable that is basic to the identification of a data record (i.e. essential key variables) or is necessary to make a record meaningful. Required variables should always be included in the dataset and cannot be null for any record.

### 6.2 Expected

Expected = Any variable necessary to make a record useful in the context of a specific domain. Columns for Expected variables are assumed to be present in each submitted dataset even if some values are null.

### 6.3 Permissible

Permissible = A variable that should be used in a domain as appropriate when collected or derived. All timing variables and any Qualifier variable specified in a domain model are permissible for use in that domain. Null values are allowed, but the Sponsor can decide whether a Permissible variable should be included as a column when all values for that variable are null.

** CDISC SDTM Implementation Guide: Human Clinical Trials (Version 3.1.1)*

# 7. Collaborative Group Review Process and Instructions

## 7.1 CDASH Package-1

Data collection variables for the Adverse Events, Concomitant Medications, Demographics & Subject Characteristics domains.

Each Harmonized Version contains the following sections:

- Introduction and Background
- Table 1: Mandatory Data Collection Variables
- Table 2: Conditional/Optional Data Collection Variables
- Data Collection Variables Considered Not Necessary to Collect

## 7.2 Review Process

The review of the following basic data collection variable tables should answer the following questions:

- Do the proposed data variables cover the basic variables common to most clinical research?
- Is the document, taking into account the above, appropriate for broader public review?

## 7.3 Comments Process

A package consisting of 3 Harmonized Versions and an Excel comments spreadsheet will be sent to each CG member for distribution within their respective organizations.

Each Collaborative Group member is requested to consolidate all comments from their respective organization into one Excel spreadsheet. Please complete the Commenter Name, Stream and variable name you wish to comment on.

Consolidated comments spreadsheets should be returned to scamhi@cdisc.org no later than **03 July 2007**.

Comments will be addressed and a "Reviewed Version" achieved within 1 month of receipt of the consolidated comments.


# ADVERSE EVENT STREAM

Harmonized Version

Stream Leader: Dave Tatum

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# Section 2. Adverse Event Stream Harmonized Version

## 1. Introduction and Background

The Adverse Event Stream was comprised of 34 members representing the following organizations: Boston Scientific Corporation, GSK, Harvard CRI, Othera Pharmaceuticals, Inc, Genzyme Corp., Novartis Pharmaceuticals Corporation, Stellar Systems, University of Utah Health Science Ctr, ZymoGenetics, NCI Enterprise Vocabulary Services (EVS), University of Pennsylvania, Kos Pharmaceuticals, Inc., Schwarz BioSciences, ArisGlobal, LLC, Teva Neuroscience, Abbott, Boston Scientific, PharmaNet, Inc, Schering Plough Research Institute, Ofni Systems Inc., Abbott, Eli Lilly and Company, Teva Neuroscience, Amgen, CV Therapeutics and Millennium Pharmaceuticals.

## 2. Table 1: Mandatory Data Collection Variables

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 1 | Adverse Event | AETERM *(required)* | Verbatim description of the adverse event. | *not applicable* | ICH-E2A | Using accepted medical terminology, enter only the diagnosis (if known); otherwise enter a sign or symptom. If a diagnosis subsequently becomes available, then this diagnosis should be entered on the AE form, replacing the original entries, where appropriate.<br><br>Death should not be recorded as an event but should be recorded as the outcome of the event. The condition that resulted in the death should be recorded as the event.<br><br>Record only one diagnosis, sign or symptom per event. For example, nausea and vomiting should not be recorded in the same entry, but as 2 separate entries.<br><br>Do not use abbreviations. | |
| 2 | Start Date | AESTDTC *(expected)* | Date when the adverse event started. | *not applicable* | ICH-E2A | Record the date that the AE began. | SDTM Variable AESTDTC: Concatenate Start Date and Time (if time is collected) into AESTDTC using the ISO 8601 format (YYYY-MM-DDTHH:MM:SS). |
| 3 | Stop Date | AEENDTC *(expected)* | Date when the adverse event resolved. | *not applicable* | ICH-E2A | Record the date that the AE ended.<br><br>If the AE is ongoing, leave the space blank. | SDTM Variable AEENDTC: Concatenate Start Date and Time (if time is collected) into AEENDTC using the ISO 8601 format (YYYY-MM-DDTHH:MM:SS). |

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 4 | Serious Event? | AESER *(expected)* | Indicates whether or not the adverse event is determined to be "serious" according to the protocol. | Y, N | ICH E2B<br><br>CRF 312.32 Serious, Guidance (Sections 12.3.1 & 12.2.4) | Assess if an adverse event should be classified as serious. | |
| 5 | Relationship | AEREL *(expected)* | Indication of whether the investigational product had a causal effect on the adverse event. | *not available* | ICH E6 4.11.2<br><br>ICH E2A, E2B, 321CFR 312.64(b), 21 CFR 312.55(b)<br><br>Federal Register: Vol. 61, No. 138, Sec 12.2.1; Vol. 60, No. 40, Sec.II.A.2<br><br>21CFR 312.64(b), 21 CFR 312.55(b),<br><br>Devices:<br><br>21 CFR , part 803, sections 803.32, 803.42, 803.52 (item number 5<br><br>Description of event or problem, including a discussion of how the device was involved, nature of the problem, patient follow-up or required treatment, and any environmental conditions that may have influenced the event.) | Select "No" if data are available to identify a clear alternative cause for the adverse event other than the investigational product.<br><br>Select "Yes" if the cause of the adverse event is related to the investigational product and cannot be reasonably explained by other factors (such as the subject's clinical state, concomitant therapy, and/or other interventions) OR if the cause of the adverse event is unknown. | The AE Stream proposes the use of Yes / No on the CRF. This mirrors the recommendation on ACRO's initial Adverse Events CRF.<br><br>While the SDTM indicates that this variable may be subject to sponsor-defined terminology, the following examples are given in the CDISC Notes column of the define table:<br><br>NOT RELATED<br><br>UNLIKELY RELATED<br><br>POSSIBLY RELATED<br><br>RELATED |

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 6 | Action Taken | AEACN *(expected)* | Action(s) taken with the investigational product in response to the adverse event. | Action Taken with Study Treatment Text Type<br>Dose Increased<br>Dose Not Changed<br>Dose Reduced<br>Drug Interrupted<br>Drug Withdrawn<br>Not Applicable<br>Unknown | ICH E2B<br>Data Elements for Transmission of Individual Case Safety Reports: B.4.K.16 – Action(s) taken with Drug | Record the action(s) taken resulting from the event (e.g., if the subject's treatment is ultimately withdrawn due to an event, then the choice Treatment Withdrawn should be recorded). | |
| 7 | Outcome | AEOUT *(permissible)* | Description of the subject's status associated with an event using a controlled terminology list. | Adverse Event Outcome Text Type<br>Fatal<br>Not Recovered/Not Resolved<br>Recovered/Resolved<br>Recovered/Resolved with Sequelae<br>Recovering/Resolving<br>Unknown | ICH E2B, E2C<br>21 CFR 314.82 a.;<br>Data Elements for Transmission of Individual Case Safety Reports: B.2.i.8 Outcome of reaction/ event at the time of last observation. | Select the appropriate outcome. | |

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 8 | AE Severity | AESEV<br><br>*And/or*<br><br>AETOXGR *(both are permissible)* | A description of the severity of the adverse event using a controlled terminology list. | Severity/Intensity Scale for Adverse Events Name<br><br>Mild<br><br>Moderate<br><br>Severe<br><br>*And/or*<br><br>Common Terminology Criteria for Adverse Events Number Code<br><br>1 = Mild Adverse Event<br><br>2 = Moderate Adverse Event<br><br>3 = Severe Adverse Event<br><br>4 = Life-Threatening or Disabling Adverse Event<br><br>5 = Death Related to Adverse Event | ICH E3, E9<br><br>Fed Register: Vol. 63, No.179, Sec. 6.3; Vol. 61, No.138, Sec 12.2.1<br><br>Per CTEP, NCI guidelines: Adverse Event Reporting Requirements, January 1, 2005.<br><br>2.7. Grade CTC/CTCAE are the foundation of the CTEP, NCI guidelines: Adverse event reporting requirements for CTEP, NCI Investigational agents. Grade is an essential element of the guidelines and, in general, relates to seriousness for purposes of regulatory reporting to CTEP. | Severity: The reporting physician/healthcare professional will be asked to assess the severity of the adverse drug/biologic event using the established categories. This assessment is subjective and the reporting physician/ healthcare professional should use medical judgment to compare the reported Adverse Event to similar type events observed in clinical practice. Severity is not equivalent to seriousness.<br><br>*And/or*<br><br>Severity Toxicity Grade: The reporting physician/healthcare professional will be asked to assess the severity of the adverse event using the toxicity grades. | Either AESEV or AETOXGR must appear on the CRF. Some studies may mandate the collection of both.<br><br>Note: Completion of Toxicity grade is a mandatory field for cancer studies. In all other types of studies this is an optional field. |

## 3. Table 2: Conditional/Optional Data Collection Variables

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 1 | Serious Event Type *(O)* | AESCAN<br>AESCONG<br>AESDISAB<br>AESDTH<br>AEHOSP<br>AELIFE<br>AESOD<br>AESMIE<br>AECONTRT<br>AETOXGR<br>*(above all permissible)*<br>Note: For devices: Requires Intervention – no current SDTM variable exists | Captures the criteria required by regulation for determining if an event is "Serious". | Y, N or NULL | ICH E3<br>Guidance Sections 12.3.1 & 12.2.4) Guidance CRF 312.32 Serious Adverse Events<br>Device Reference:<br>21 CFR 803.32 (user facility) and 21 CFR 803.52 (Manufactures). Part 803 is Medical Device Reporting. | Indicate the category of the adverse event that classified the event as 'serious" Select all that apply. | Select all that apply implies that a field exists for each choice. Corresponding SDTM variables and labels are listed. |
| 2 | Other Action Taken *(O)* | AEACNOTH *(permissible)* | Other Action(s) taken in response to the adverse event. (Does not include investigational products) | *not applicable* | | Action Other: Record all other action (s) taken. | |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 3 | AE Start Time *(O)* | AESTDTC *(expected)* | Time when the adverse event started. | *not applicable* | ICH-E2A | If appropriate, record the time that the AE began using a 24 hour clock in HH:MM:SS format, as needed. Midnight should be recorded as 00:00:00 and starts the new date. | SDTM Variable AESTDTC: Concatenate Start Date and Time (if time is collected) into AESTDTC using the ISO 8601 format (YYYY-MM-DDTHH:MM:SS). |
| 4 | AE End Time *(O)* | AEENDTC *(expected)* | Time when the adverse event resolved. | *not applicable* | ICH-E2A | If appropriate, record the time that the AE resolved using a 24 hour clock in HH:MM:SS format, as needed. Midnight should be recorded as 00:00:00 and starts the new date. | SDTM Variable AEENDTC: Concatenate Start Date and Time (if time is collected) into AEENDTC using the ISO 8601 format (YYYY-MM-DDTHH:MM:SS). |
| 5 | Category for Adverse Event *(O)* | AECAT *(permissible)* | Used to define a category of related records. | *not applicable* | | | See the SDTM Implementation guide for completion instructions. |
| 6 | Subcategory for Adverse Event *(O)* | AESCAT *(permissible)* | A further categorization of adverse event. | *not applicable* | | | See the SDTM Implementation guide for completion instructions. |
| 7 | Event Pattern Code *(O)* | AEPATT *(permissible)* | Time pattern by which Adverse Event occurs. Values: Single Episode, Intermittent, Continuous. | *not available* | | | See the SDTM Implementation guide for completion instructions. |
| 8 | Event Body Location *(O)* | AELOC *(permissible)* | Describes anatomical location relevant for the event (e.g., Left Arm for skin rash). | *not available* | | | See the SDTM Implementation guide for completion instructions. |

## 4. Table 3: Data Collection Variables Considered Not Necessary to Collect on CRF

| | SDTM Variable Name *(SDTM Core)* | Variable Label | Definition | Applicable Regulations | Rationale |
|---|---|---|---|---|---|
| 1 | None | Continuing Flag | Identifies an event that is ongoing at the time of a subject's discontinuation from a study. | | Redundant field used for monitoring or cleaning. |
| 2 | None | Expected Criteria | Representation of the expectedness of the event. | CRF 312.32 Unexpected adverse drug experience. | Handled in Clinical Investigative Brochure. Value of investigator's input. |
| 3 | None | Event Diagnosis | Provides the sender with an opportunity to combine signs and symptoms that were reported into a succinct diagnosis. | | Considered a redundant field. |
| 4 | None | Ongoing as of Date | Gives reference to when the subject was last contacted to determine if the AE was still ongoing. | | Considered a redundant field, captured in other fields: Blank Stop Date and Outcome. |
| 5 | None | Time Course | Helps understand the nature of the AE. | | Derived. |
| 6 | None | Is this AE the reason for withdrawal from the study? | | | Captured elsewhere in the CRF (action taken). |
| 7 | DOMAIN *(required)* | Domain Abbreviation | Two-character abbreviation for the domain most relevant to the observation. (AE) | | Derived. |
| 8 | USUBJID *(required)* | Unique Subject Identifier | Unique subject identifier within the submission. | | Derived. |
| 9 | AESEQ *(required)* | Sequence Number | Sequence number given to ensure uniqueness within a dataset for a subject. Can be used to join related records. | | Derived. |
| 10 | AEGRPID *(permissible)* | Group ID | Used to tie together a block of related records in a single domain to support relationships within the domain and between domains. | | Derived if needed. |
| 11 | AEREFID *(permissible)* | Reference ID | Optional internal or external identifier such as a serial number on an SAE reporting form. | | Not needed. |
| 12 | AESPID *(permissible)* | Sponsor-Defined Identifier | Optional Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database. Example: Line number on an Adverse Event page. | | Not needed. |
| 13 | AEMODIFY *(permissible)* | Modified Reported Term | If AETERM is modified, then AEMODIFY will contain the modified text. | | Derived if needed. |

| | SDTM Variable Name *(SDTM Core)* | Variable Label | Definition | Applicable Regulations | Rationale |
|---|---|---|---|---|---|
| 14 | AEDECODE *(required)* | Dictionary-Derived Term | Dictionary-derived text description of AETERM or AEMODIFY. Equivalent to the Preferred Term (PT in MedDRA). The sponsor should specify the dictionary name and version in the Sponsor Comments column of the Define document. | | Derived. |
| 15 | AEOCCUR *(permissible)* | Adverse Event Occurrence | Used when the occurrence of specific adverse events is solicited to indicate whether an adverse event occurred or not. | | Considered redundant, can be addressed during analysis. |
| 16 | AEBODSYS *(expected)* | Body System or Organ Class | Body system or organ class (Primary SOC) that is involved in an event or measurement from the standard hierarchy (e.g., MedDRA). | | Derived. |
| 17 | AERELNST *(permissible)* | Relationship to Non-Study Treatment | Records the investigator's opinion as to whether the event may have been due to treatment other than study drug. Reported as free text. | | Not needed. |
| 18 | AESTDY *(permissible)* | Study Day of Start of Adverse Event | Study day of start of adverse event relative to the sponsor-defined RFSTDTC. | | Derived. |
| 19 | AEENDY *(permissible)* | Study Day of End of Adverse Event | Study day of end of adverse event relative to the sponsor-defined RFSTDTC. | | Derived. |
| 20 | AEDUR *(permissible)* | Duration | Collected duration and unit of an adverse event. | Yes | Derived. |
| 21 | AEENRF *(permissible)* | End Relative to Reference Period | Identifies the end of the event as being BEFORE, DURING, DURING/AFTER or AFTER the sponsor-defined reference period. | | Derived. |

## 5. Notes

- Study discontinuations caused by Adverse Events: Some companies capture this information on the AE CRF, usually as a Y/N question; others capture this information on the Study Summary or Study Discontinuation page. A decision can only be made on the location of this information after consultation with the Stream handling the Discontinuation CRF.


# CONCOMITANT MEDICATIONS STREAM

Harmonized Version

Stream Leader: Dorothy Dorotheo, InterMune

Co-Stream Leaders: Lauren Shinaberry, PRA Int.,
Carol Bogardus, Amgen

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# Section 3. Concomitant Medications Stream Harmonized Version

## 1. Introduction

The Prior & Concomitant Medication Stream is comprised of 19 members from for the following organizations: NIH/OBA, Genzyme, Amgen, Schwarz BioSciences, PPD, Westat, Intermune, PRA, GSK, Wyeth, CCF, Johnson & Johnson, Percipenz, Novartis, Commitum, CCF, Pharmanet. Job functions represented included Data Management, Statistical Programming, Clinical Programming, Biostatistics, Data Standards Development, Safety Reporting and Clinical Operations.

## 2. Assumptions

The expectation is that the same basic/mandatory data elements will be collected for both General Medications & Medications of Interest and additional fields will be added as applicable for each specific Medication of Interest. The rationale for generally excluding Medications of Interest is that by definition, the collection of data for drugs specifically mentioned in the protocol is likely to change from protocol to protocol and data collection will be at a higher degree of detail and those details can change significantly depending on the exact nature of the Medications of Interest.

For the purposes of this effort, General Medications were considered the primary focus, NOT Medications of Interest, where

> *General Medications* are any medications spontaneously reported by a subject when asked if they have taken any medications in an open-ended way that does not ask about any specific drug.
>
> *Medications of Interest* are any medications or classes of drugs specifically mentioned in the protocol. Examples are excluded medications, drugs requiring a washout period prior to dosing in study, or rescue medications.

The following assumptions were made:

- Among the many reasons to collect General Medications are:
  - Identification of unanticipated drug-drug interaction signals,
  - To assess the use of medications that may mask or enhance efficacy
  - To provide details regarding the possible cause or course of adverse events.
- "Prior" refers to medications that were started prior to study participation.

## 3. Table 1: Mandatory Data Collection Variables

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 1 | Reported Name of Drug, Med or Therapy | CMTRT *(required)* | Verbatim drug name that is either pre-printed or collected on a CRF | *not applicable* | ICH-E6 (Section 6.6.2) | The trade or proprietary name of the drug is recommended; otherwise the generic name may be recorded. | It is assumed that the verbatim drug names will be coded to a standard dictionary such as WHO Drug at some point after the data has been collected on the CRF.<br><br>For the collection of verbatim drug name, the recommendation is to ask the sites to provide the trade name since it is more exact then the generic. The trade name provides the base generic and the appropriate salt for that particular drug. In addition, for coding purposes it helps with ATC coding. |

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 2 | Start Date | CMSTDTC *(permissible)*<br>or<br>*CMSTRF *(permissible)* | Date or relative time frame that the medication was first taken | * CMSTRF:<br>Before<br>During<br>After | | *(If collecting the date)* Record the date the medication was first taken in DD-MMM-YYYY format. If the subject has been taking the medication for a considerable amount of time prior to the start of the study, it is acceptable to have an incomplete date. Medications started during the study are expected to have a complete date.<br>*(If collecting the relative time frame)* Indicate if this medication was started before/prior to the study or during the study. | Recommending that either the Start Date **or** categorizing the medication as starting BEFORE, PRIOR or DURING the study should be provided by the clinical sites.<br>If Start Date is collected it should be stored in the CMSTDTC variable. If BEFORE, PRIOR or DURING is collected it should be stored in the CMSTRF variable.<br>Information such as, "Prior", "Before", "Continuing from previous visit" is considered to be related to CRF layout and is an intermediate step to determining the start of the medication. The preferred method is to collect a Start Date. Partial dates for medications started prior to the study are acceptable.<br>If the sponsor wishes to collect medications at the visit level, the assumption is that the first time a medication was reported, a Start Date will be collected. Subsequent references to the medication do not need to collect the Start Date again numerous times.<br>SDTM Variable CMSTDTC: Concatenate Start Date and Time (if time is collected) into CMSTDTC using the ISO YYYY-MM-DDTHH:MM.<br>* SDTM Variable CMSTRF:<br>Please refer to the SDTM Implementation Guidelines for details. |

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 3 | End/Stop Date | CMENDTC *(permissible)* | Date that the subject stopped taking the medication. | *not applicable* | | Record the date the subject stopped taking the medication in DD-MON-YYYY format. If the subject has not stopped taking the medication leave this item blank. | The assumption is that sponsors should either have a complete stop date or will indicate that the medication was ongoing at the end of the study.<br><br>SDTM Variable CMENDTC: Concatenate End/Stop Date and Time (if time is collected) into CMENDTC using the ISO date format YYYY-MM-DDTHH:MM |
| 4 | Ongoing/ Continuing | *CMONGO (Note: this is a data collection variable and not an SDTM variable.)*<br><br>*CMENRF *(permissible)* | Timing info--use of the medication is ongoing/continuing at the point of data collection | * CMENRF:<br><br>Before<br><br>During<br><br>After<br><br>During/After<br><br>Unknown | | If subject has not stopped taking the medication at the time of data collection, check the Ongoing/Continuing box and leave the Stop Date blank. | This box will be marked to indicate that the subject has not stopped taking the medication at the time of data collection. Upon study completion, it is expected that every reported medication should have either a Stop Date or be marked as Ongoing/continuing, but not both.<br><br>This is not a direct mapping to CMENRF. The date of data collection would determine in conjunction with stop date and the ongoing/continuing check box how CMENRF will be populated.<br><br>CMENRF has to be derived using the end/stop date or the check box if continuing.<br><br>* SDTM Variable CMENRF: Please refer to the SDTM Implementation Guidelines for details. |

## 4. Table 2: Conditional/Optional Data Collection Variables

| | CRF Data Collection Variable *(C: Conditional O: Optional)* | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 1 | Indication *(C)* | CMINDC *(permissible)* | The reason for administration of a concomitant (non-study) medication.<br><br>Examples: Nausea, Hypertension.<br><br>This is not the pharmacological /therapeutic classification of an agent (antibiotic, analgesic, etc.), but the reason for its administration to the subject. | *not applicable* | | Record the reason the medication was taken. If a diagnosis is known, that is what should be reported. Otherwise, record the symptoms. If taken as prophylaxis, we recommend reporting as "Prophylaxis for…". | This additional information is collected on the CRF when the sponsor would want to capture the reason(s) why a subject took a medication. This information can then be used as deemed appropriate for coding, analysis (i.e., in the classification of medications), for reconciling the medications taken by a subject with their provided medical history and/or AEs/SAEs as part of the data clean-up and monitoring process, etc. |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 2 | Start Time *(O)* | *CMSTTM (Note: this is a data collection variable, if collected will be derived into CMSTDTC)* | Time the medication was started. | *not applicable* | | Optionally, if appropriate, record the time that the medication was started using a 24 hour clock in HH:MM format, as needed. Midnight should be recorded as 00:00 and starts the new date.<br><br>SS seconds may be collected where deemed appropriate. | Collecting the time a medication was started is only appropriate if it can be realistically determined and if there is a scientific reason for needing to know this level of detail. Typically, it is not recommended that a start time be collected unless the subject is under the direct care of the site at the time a medication is taken.<br><br>SDTM Variable CMSTDTC: Concatenate Start Date and Time (if time is collected) into CMSTDTC using the ISO date format YYYY-MM-DDTHH:MM:SS<br><br>SDTM Variable CMSTDTC: For further details regarding this variable, please refer to the SDTM Implementation Guidelines. |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 3 | Stop/End Time *(C)* | *CMENTM (Note: this is a data collection variable, if collected will be derived into CMENDTC)* | Time that the subject stopped taking the medication. | *not applicable* | | Optionally, if appropriate, record the time that the medication was stopped using a 24 hour clock in HH:MM format, as needed. Midnight should be recorded as 00:00 and starts the new date.<br><br>SS seconds may be collected where deemed appropriate. | Collecting the time a medication was started is only appropriate if it can be realistically determined and if there is a scientific reason for needing to know this level of detail. Typically, it is not recommended that a start time be collected unless the subject is under the direct care of the site at the time a medication is taken.<br><br>SDTM Variable CMENDTC: Concatenate End/Stop Date and Time (if time is collected) into CMENDTC using the ISO date format YYYY-MM-DDTHH:MM:SS<br><br>SDTM Variable CMENDTC: For further details regarding this variable, please refer to the SDTM Implementation Guidelines. |
| 4 | Route of administration *(C)* | CMROUTE *(permissible)* | Identifies the route of administration of the drug. | Route of Administration Name | | Provide the route of administration for the drug. | This additional information is collected on the CRF when the sponsor would want to capture a medication's route of administration for purposes such as coding. Some companies may use route in coding medications to be able to choose a precise preferred name and ATC code. |
| 5 | Were any medications taken? *(O)* | *CMYN (Note: This is a data collection variable and not an SDTM variable.)* | General prompt question to aid in monitoring and data cleaning. | | | Indicate if the subject took any medications. If yes, include details where indicated. | It is understood that in SDTM this field will not be part of the submitted data. For the purposes of data collection, the intent is to help with data cleaning and monitoring. |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 6 | Medication Sequence Number *(O)* | CMSPID *(permissible)* | A unique identifier (such as a line number on a paper CRF) that may be used to reference a specific record on the CRF | *not applicable* | | | For paper CRFs which collect medications it can be beneficial to use a sequence number in a data query to clearly communicate to the site the specific record in question.<br><br>A sequence number may also be used to link data on another CRF to a specific medication.<br><br>Some CRF designs (such as a single medication per page, or in an EDC system) can manage to address these issues without needing a pre-printed or pre-assigned sequence number. |
| 7 | AE Number *(O)* | AESPID *(permissible for AE domain)* | Identifier for the adverse event that is the indication for this medication. | *not applicable* | | | A link between the adverse event and the medication to mitigate that event is desirable, but there may be other ways to collect this type of information.<br><br>Utilizing this variable to maintain a link to a sequence number associated with an AE may result in unnecessary data cleaning work. For example, if the AE number gets reassigned or deleted due to a query response or a correction by the clinical site.<br><br>We acknowledge that AESPID will not be included in the CM domain in submissions. |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 8 | Dose Form *(O)* | CMDOSFRM *(permissible)* | Name of the pharmaceutical dosage form (e.g., tablets, capsules, syrup) of delivery for the drug. | Pharmaceutical Dosage Form Name | | | We recognize that some drugs have multiple forms and this field may be needed to code the drug to an ATC level. However, in general, this level of detail should not be necessary except for medications of interest.<br><br>If this field is not on the CRF, but a medication that happens to need the formulation for coding purposes is recorded, the site could be queried to add the formulation as part of the drug name. |
| 9 | Dosing Frequency per interval *(O)* | CMDOSFRQ *(permissible)* | How often the medication was taken. For example, BID, every other week, PRN. | *not available* | | | When collected, the recommendation is to collect dosing information in separate fields for specific and consistent data collection. See below for the rest of the dosing information components (Dose per administration, and dose unit.) |
| 10 | Dose per Administration (Strength) *(O)* | CMDOSTXT *(permissible)* | The dose of medication taken per administration. | *not applicable* | | | If there is a scientific reason for needing dosing information this may be included.<br><br>This SDTM variable was chosen instead of CMDOSE (a numeric variable) to allow for flexibility in capturing text entry, e.g., range of dosing 200-400. |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 11 | Dose Unit *(O)* | CMDOSU *(permissible)* | Within structured dosage information, the unit associated with the dose (e.g., "mg" in "2mg three times per day). | *not available* | | | If there is a scientific reason for needing dosing information this may be included. |
| 12 | Intended Dose Regimen *(O)* | CMDOSRGM *(permissible)* | Within structured dosage information, the number of units for the interval (e.g., i.e., in oncology where drug is given 1 week on, and 3 weeks off. | *not applicable* | | | If there is a scientific reason for needing dosing information this may be included. |

## 5. Table 3: Data Collection Variables Considered Not Necessary to Collect on CRF

| | SDTM Variable Name | Variable Label | Definition | Applicable Regulations | Rationale |
|---|---|---|---|---|---|
| 1 | None | Generic Dispensed | An indicator that the drug name provided is a generic name. | | Assuming drug names are coded to a dictionary, this is redundant and should not also be a field on the CRF |
| 2 | None | Response | Did the condition for which the medication was taken respond to treatment | | Applies to Medications of Interest |
| 3 | None | Prescription or OTC | Indicate whether the drug required a prescription or if the subject obtained it OTC | | This level of detail not required for General Medications. |
| 4 | None | Device used to admin drug | For some drugs, such as asthma medications, the delivery device can affect the response | | Applies to Medications of Interest |
| 5 | None | Was drug admin for exacerbation | Used to identify medications taken for a specific indication which has worsened | | Applies to Medications of Interest |
| 6 | None | Was drug admin as a rescue Medication | Used to identify medications taken for a specific indication which has worsened | | Applies to Medications of Interest |
| 7 | None | Cumulative dose used | Calculated total exposure over a specified duration | | Applies to Medications of Interest, alternatively, can be calculated from other fields. |
| 8 | None | Total Duration Unit | Unit of time for subject exposure (i.e. minutes, hours, days, etc.) | | If needed, can be derived. |
| 9 | None | Was Medication stopped due to toxicity | Did the medication reach toxic levels, requiring it to be discontinued? | | Applies to Medications of Interest |
| 10 | None | General Comments | | | The team assumes that comments will be collected on a Comment CRF. Alternatively Concomitant Medication comments may also be captured within the appropriate Concomitant Medications CRF. |
| 11 | None | None Taken | A single box that can be marked to indicate that no concomitant medications were taken | | Instead of this question, a Y/N question “Were any drugs taken?” is recommended to avoid ambiguity if this box is not marked, but no medication details are present. This recommended option is listed on Table 3. |
| 12 | None | Type of Medication | | | Applies to Medications of Interest |
| 13 | DOMAIN *(required)* | Domain Abbreviation | Two-character abbreviation for the domain most relevant to the observation. (CM) | | Derived. |

| | SDTM Variable Name | Variable Label | Definition | Applicable Regulations | Rationale |
|---|---|---|---|---|---|
| 14 | USUBJID *(required)* | Unique Subject Identifier | Unique subject identifier within the submission. | | Derived. |
| 15 | CMSEQ *(required)* | Sequence Number | Sequence number given to ensure uniqueness within a dataset for a subject. Can be used to join related records. | | Derived. |
| 16 | CMGRPID *(permissible)* | Group ID | Used to tie together a block of related records in a single domain to support relationships within the domain and between domains. | | Derived if needed. |
| 17 | CMMODIFY *(permissible)* | Modified Reported Name | If CMTRT is modified, then CMMODIFY will contain the modified text. | | Derived if needed. |
| 18 | CMDECODE *(required)* | Standardized Medication Name | Standardized or dictionary-derived text description of CMTRT or CMMODIFY. Equivalent to the generic medication name in WHO Drug. The sponsor should specify the dictionary name and version in the Sponsor Comments column of the Define document. If an intervention term does not have a decode value in the dictionary then CMDECODE will be left blank. | | Derived. |
| 19 | CMCAT *(permissible)* | Category for Medication | Used to define a category of medication/treatments. | | Derived, if needed. Applies to Medication of Interest. |
| 20 | CMSCAT *(permissible)* | Subcategory for Medication | A further categorization of medication/treatment. | | Derived, if needed. |
| 21 | CMOCCUR *(permissible)* | Concomitant Medication Occurrence | Used when the use of specific medications/treatment is solicited to indicate whether a medication was taken or not. | | Applies to Medication of Interest. |
| 22 | CMSTAT *(permissible)* | Concomitant Medication Status | The status indicates that the question was not asked. | | Not needed. |
| 23 | CMREASND *(permissible)* | Reason Medication Not Collected | Describes the reason concomitant medication was not collected. Used in conjunction with CMSTAT when value is NOT DONE. | | Not needed. |
| 24 | CMCLAS *(permissible)* | Medication Class | Use only when the dictionary used codes to a single class. If using a dictionary that allows links to multiple classes, then omit CMCLAS from the dataset. | | Derived. |
| 25 | CMCLASCD *(permissible)* | Medication Class Code | Use only when the dictionary used codes to a single class. | | Derived. |
| 26 | CMDOSE *(permissible)* | Dose per Administration | Amount of CMTRT taken. | | CMDOSTXT should be used to populate CMDOSE if a numeric dose is needed. |

| | SDTM Variable Name | Variable Label | Definition | Applicable Regulations | Rationale |
|---|---|---|---|---|---|
| 27 | CMDOSTOT *(permissible)* | Total Daily Dose using CMDOSU | Total daily dose of CMTRT using the units in CMDOSU. | | Should this level of detail be needed for a general medication, it is recommended that it be calculated or derived from other fields such as Dosage Units, Dosage Amount and Dosage Interval to avoid confusion and calculation by the clinical site. |
| 28 | CMSTDY *(permissible)* | Study Day of Start of Adverse Event | Study day of start of adverse event relative to the sponsor-defined RFSTDTC. | | Derived. |
| 29 | CMENDY *(permissible)* | Study Day of End of Adverse Event | Study day of end of adverse event relative to the sponsor-defined RFSTDTC. | | Derived. |
| 30 | CMDUR *(permissible)* | Duration of Medication | Collected duration and unit of treatment. | | If needed, can be calculated from Start Date/Time and Stop Date/Time. |

# DEMOGRAPHICS
# &
# SUBJECT CHARACTERISTICS STREAM

Harmonized Version

Stream Leader: Gary Walker, Quintiles

# Table of Contents

# Section 4. Demographics & Subject Characteristics Stream Harmonized Version

## 1. Introduction

The DM & SC Stream was comprised of 24 members representing many job functions from across the industry and government. Using SDTM as the basis, demographics CRF samples were compared, consistently collected variables were identified, missing variables were noted, the necessity of each variable was determined and regulatory and safety compliance were confirmed. The reason for inclusion/exclusion of variables was documented.

The SDTM variables served as a target for deliverable data. Categories for identify those data that needed to be collected (mandatory), might be collected (optional) and some variables which, under certain circumstances, would be needed (conditional) in order to get to the SDTM data were agreed and are being used consistently across all streams.

The team noted that many of the variables collected have a one-to-one mapping to SDTM variables for delivery. Privacy concerns surround the DM & SC data have been noted and discussed by the team. Some of the variables collected may map in a many-to-one fashion (i.e. many collected components map to one SDTM variable). This perspective provided flexibility in categorizing some variables to help us solve thorny “regulatory” (privacy) issues.

Note: There was discussion regarding which to include, birth date or age, as a required variable. While the age is required for SDTM, it is seen as less exact a scientific value as an imprecise birth date, so the DM stream felt that mandating the collection of BRTHDTC components would provide a better solution to balance known patient privacy requirements, with the ability to provide the best meaningful data for reporting and analysis. From the imprecise birth date data an age can be calculated for analysis and reporting.

## 2. Table 1: Mandatory Data Collection Variables

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 1 | Protocol/Study Identifier | STUDYID *(required)* | Unique Identifier for a study within a submission. | *not applicable* | | | This is typically collected in the header of each CRF page. |
| 2 | Site Identifier | SITEID *(required)* | Unique identifier for the study site. | *not applicable* | | Record your clinical site's site identifier as defined by the sponsor. | This is typically collected in the header of each CRF page. |
| 3 | Subject | SUBJID *(required)* | Subject identifier used within a study. | *not applicable* | | Record the subject identifier as defined for this study. | This is typically collected in the header of each CRF page. |
| 4 | Year of Birth | BRTHDTC *(permissible)* | Year of subject's birth. | YYYY (four-digit year, may collect only last two digits) | | Record the subject's year (e.g., YYYY, a four digit year, or collect only the last two digits) of birth as required for the form. | A collected variable used for recording the year component of the "Date of Birth". |
| 5 | Month of Birth | BRTHDTC *(permissible)* | Month of subject's birth. | MMM (JAN-DEC) | | Record the subject's month MMM (JAN-DEC) of birth. | A collected variable used for recording the month component of the "Date of Birth". |
| 6 | Sex | SEX *(required)* | The assemblage of physical properties or qualities by which male is distinguished from female; the physical difference between male and female; the distinguishing peculiarity of male or female. (NCI – CDISC Definition) | Sex Text Code<br>Female (F)<br>Male (M)<br>Unknown (U)<br>Intersex (UN) | | Check (only one) the appropriate sex (i.e., female, male, etc.) as required on this form. | As reported by subject or caretaker. Defined by HL7 as "Administrative Sex". |

| | CRF Data Collection Variable | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 7 | Race of Subject | RACE *(expected)* | An arbitrary classification based on physical characteristics; a group of persons related by common descent or heredity. | *not available* | Guidance for Industry: Collection of Race and Ethnicity in Clinical Trials *(September 2005)* | Study participants should self-report race and ethnicity whenever feasible, with ethnicity being asked about before race.<br><br>The FDA guidance "that individuals be permitted to designate a multiracial identity/". "Check all that apply" at the time of collection. | The categories listed in the FDA Guidance are as follows:<br><br>American Indian or Alaska Native<br><br>Asian<br><br>Black or African American*<br><br>Native Hawaiian or Other Pacific Islander<br><br>White<br><br>*For ex-US, the recommended categories are the same except for Black instead of Black or African American<br><br>If more detailed characterizations of race or ethnicity are collected to enhance data quality and consistency, it is recommended that they be "collapsible" up to the five minimum designations for ethnicity, as needed for reporting to FDA under its guidance. When more detailed categorizations are desired, the use of race and vocabulary tables located within Health Level Seven's Reference Information Model Structural Vocabulary Tables is recommended, as they are designed to collapse up in this manner. |

## 3. Table 2: Conditional/Optional Data Collection Variables (Demographics)

| | CRF Data Collection Variable *(C: Conditional O: Optional)* | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 1 | Country Identifier *(O)* | COUNTRY *(required)* | Country of the investigational site in which the subject participated in the study. | Country Text Code | | | Study level – May be collected on CRF, but site information such as address, city, etc., is kept by the sponsor and the list may be used to populate the SDTM data submitted to regulatory authorities. |
| 2 | Investigator *(C)* | INVID *(permissible)* | An identifier to describe the investigator for a study. | *not applicable* | | Record the sponsor defined identifier for your site investigator. | Study level – Not needed if SITEID is equivalent to INVID. |
| 3 | Investigator Name *(O)* | INVNAM *(permissible)* | Name of the investigator. | *not applicable* | | Record the investigator name. | An investigator is defined as a licensed physician listed as the Principal Investigator on the FDA form 1572 for that study site.<br><br>If collected on the CRF, this is typically found in the header of the CRF. |
| 4 | Date of Evaluation *(C)* | DMDTC / SCDTC *(permissible)* | Date of collection. | *not applicable* | | Record the date evaluation occurred in DD-MMM-YYYY format. A complete date is expected for evaluations that occur during the study. | May be explicitly collected on DM or SC CRFs or may be "inherited" from the same source as other visit dates of collection (such as when Visit Date is collected at the top of a visit page or when a date is generated from an EDC system). One or the other method should be used.<br><br>(May be needed for age calculations in analysis.) |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 5 | Time of Evaluation *(O)* | DMDTC / SCDTC *(permissible)* | Time of collection. | *not applicable* | | Optionally, if appropriate, record the time the evaluation was started, using a 24 hour clock in HH:MM format, as needed. Midnight should be recorded as 00:00 and starts the new date.<br><br>Seconds (SS) may be collected where deemed appropriate. | May be explicitly collected on DM or SC CRFs or may be "inherited" from the same source as other visit dates of collection (such as when Visit Date is collected at the top of a visit page or when a date is generated from an EDC system). One or the other method should be used.<br><br>(Time of collection may be needed for some Phase 1 trials.) |
| 6 | Day of Birth *(C*)* | BRTHDTC *(permissible)* | Day of subject's birth. | DD<br>(two-digit day of the month 01-31) | | Record the subject's day of birth (DD, 01-31). | A collected variable used for recording the day component of the "Date of Birth".<br><br>* If Ethics Committees or local Data Protection Authorities (DPA) disagree with the collection of the complete Date of Birth due to privacy concerns, it might be best to omit this component of the "Date of Birth" to assuage those concerns. |
| 7 | Time of Birth *(O)* | BRTHDTC *(permissible)* | Time of subject's birth, | hh:mm<br>(hours, minutes) | | Optionally, if appropriate, record the time of birth using a 24 hour clock in HH:MM format. Midnight should be recorded as 00:00 and start the new date. | |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 8 | Age *(O)* | AGE<br>*(expected)* | Age of subject | Years, months, days | | | Age needs to be collected as a number and, to be interpreted correctly, needs to be accompanied by the variable Age Unit. It is helpful to know when the age was collected such as by having collected DMDTC is an age may need to be recalculated for analysis.<br><br>While the age is required in SDTM, it is seen as less exact a scientific value as an imprecise birth date, so the DM stream felt that mandating the collection of BRTHDTC components (as described under BRTHDTC) would provide a better solution to balance known subject privacy requirements, with the ability to provide the best meaningful data for reporting and analysis. From the imprecise birth date an age can be calculated for analysis and reporting. |
| 9 | Age Units *(O)* | AGEU<br>*(expected)* | Age units | Age Unit Name<br><br>Days<br><br>Hours<br><br>Months<br><br>Weeks<br><br>Years | | Record the appropriate age unit (e.g., years, months, etc.) as required on the form. | If Age is captured on the CRF, the site must also record age unit(s) to make the "Age" value meaningful. |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 10 | Ethnicity *(O)* | ETHNIC<br>*(permissible)* | A social group characterized by a distinctive social and cultural tradition maintained from generation to generation, a common history and origin and a sense of identification with the group; members of the group have distinctive features in their way of life, shared experiences and often a common genetic heritage; these features may be reflected in their experience of health and disease.<br>(NCI – CDISC Definition) | Patient Ethnic Group Category<br><br>Hispanic or Latino<br><br>Not Hispanic or Latino<br><br>Not reported<br><br>Unknown | Guidance for Industry: Collection of Race and Ethnicity in Clinical Trials *(September 2005)* | Study participants should self-report race and ethnicity whenever feasible, with ethnicity being asked about before race. | If more detailed characterizations of race or ethnicity are collected to enhance data quality and consistency, it is recommended that they be "collapsible" up to the five minimum designations for ethnicity, as needed for reporting to FDA under its guidance. When more detailed categorizations are desired, the use of race and vocabulary tables located within Health Level Seven's Reference Information Model Structural Vocabulary Tables is recommended, as they are designed to collapse up in this manner. |

## 4. Table 3: Conditional/Optional Data Collection Variables (Subject Characteristics)

| | CRF Data Collection Variable *(C: Conditional O: Optional)* | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 1 | Subject Initials *(C*)* | SCTESTCD (REQ/TOPIC) = SUBJINIT | Subject Initials | *not applicable* | | Record the subject's initials (First/Middle/Last) as required on the form. | Ethics Committees or local Data Protection Authorities (DPA) may disagree with the collection of the Subject Initials due to privacy concerns, but it may be argued that this information may be useful for providing critical safety or follow-up information back to the subject at some time in the future. |
| 2 | Eye Color *(O)* | SCTESTCD (REQ/TOPIC) = "EYECD" (value) | Natural eye color | *not applicable* | | Record the subject's eye color. | |
| 3 | Childbearing Potential *(O)* | SCTESTCD (REQ/TOPIC) = "???" (value) | Subject's childbearing potential | *not applicable* | | Check the correct box to indicate the subject's childbearing potential, or postmenopausal or sterilized as required for the form. | |
| 4 | Economic Data *(O)* | SCTESTCD (REQ/TOPIC) = "???" (value) | Subject's (or family's) economic status | *not applicable* | | | Other questions that may contribute to this data may include questions like "Method of payment for medical treatment?" or "Postal code of residence?" |
| 5 | Employment *(O)* | SCTESTCD (REQ/TOPIC) = "???" (value) | Subject's employment status | *not applicable* | | | |

| | CRF Data Collection Variable<br>*(C: Conditional O: Optional)* | SDTM Variable Name<br>*(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 6 | Japanese Ancestry *(O)* | SCTESTCD (REQ/TOPIC) = "???" (value) | Subject's Japanese ancestry | *not applicable* | | | May be collected if RACE is relevant to determine if subject's data may be used in submission destined for Japanese Regulatory Submission.<br>More detailed questions may be needed to determine eligibility such as:<br>a) Born in Japan?<br>b) Number of Japanese-born parent(s)<br>c) Number of Japanese-born grandparent(s) |
| 7 | Family Status *(O)* | SCTESTCD (REQ/TOPIC) = "???" (value) | Current status of family situation. | *not applicable* | | | Possible options to appear on the CRF (list is not exhaustive):<br>Single<br>Married (living together)<br>Separated<br>Divorced<br>Living with Partner<br>Widowed |
| 8 | Education *(O)* | SCTESTCD (REQ/TOPIC) = "???" (value) | Education level achieved at start of study (Reference date) | *not applicable* | | | |

| | CRF Data Collection Variable *(C: Conditional O: Optional)* | SDTM Variable Name *(SDTM Core)* | Definition | CDISC Approved Controlled Terminology | Applicable Regulations | Instruction to Clinical Site | Implementation / Rationale |
|---|---|---|---|---|---|---|---|
| 9 | Sub-study participation *(O)* | SCTESTCD (REQ/TOPIC) = "???" (value) | Sub-study participation information. | *not applicable* | | | For some Phase 1 studies sub-study information is captured, such as "subject is on fasting sub-study" or "subject is on PK sub-study". |

## 5. Table 4: Data Collection Variables Considered Not Necessary to Collect on CRF

| | SDTM Variable Name | Variable Label | Definition | Applicable Regulations | Rationale |
|---|---|---|---|---|---|
| 1 | DOMAIN *(required)* | Domain Abbreviation | Two-character abbreviation for the domain most relevant to the observation. (DM) | | Derived. |
| 2 | USUBJID *(required)* | Unique Subject Identifier | Unique subject identifier within the submission. | | Derived. |
| 3 | RFSTDTC *(expected)* | Subject Reference Start Date/Time | Reference Start Date/time for the subject in ISO 8601 character format. Usually equivalent to date/time when subject was first exposed to study treatment. Required for all randomized subjects; will be null for all subjects who did not meet the milestone the date requires, such as screen failures (if screen failures are submitted). | | Derived. |
| 4 | RFENDTC *(expected)* | Subject Reference End Date/Time | Reference End Date/time for the subject in ISO 8601 character format. Usually equivalent to date/time when subject was determined to have ended the trial, and often equivalent to date/time of last exposure to study treatment. Required for all randomized subjects; null for screen failures (if screen failures are submitted). | | Derived. |
| 5 | ARMCD *(required)* | Planned Arm Code | Short name for ARM (may be up to eight characters). | | Derived. |
| 6 | ARM *(required)* | Description of Planned Arm | Name of the Arm to which the subject was assigned. | | Derived. |
| 7 | DMDY *(permissible)* | Study Day of Collection | Study day of collection measured as integer days. | | Derived. |