Clinical Data Acquisition Standards Harmonization (CDASH)

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Revision History

Document Number	Release Date	Updates
CDASH_STD-1.0	01/OCT/2008	Initial release.

Note: See "7.8 Representations and Warranties, Limitations of Liability, and Disclaimer."

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1. Orientation

1.1. Purpose

The aim of the Clinical Data Acquisition Standards Harmonization (CDASH) Standard Version 1.0 is to describe recommended basic standards for the collection of clinical trial data. This document is intended to be used by those functions involved in the planning, collection, management and analysis of clinical trials and clinical data, for example, Clinical Investigators, Medical Monitors, Clinical Research Associates (Monitors), Clinical Research Study Coordinators, Clinical Data Managers, Clinical Data and Statistical Programmers, Biostatisticians, Drug Safety, Case Report Form (CRF) designers and other functions tasked with the responsibility to collect, clean and ensure the integrity of clinical trial data.

Sponsors will need to determine what additional data fields will need to be added to address study-specific requirements based on regulatory and applicable business practices. Until therapeutic area (TA) specific data fields have been standardized, sponsors will need to add these fields to the CDASH recommendations to fulfill their protocol-specific requirements.

The CDASH standards are part of the Clinical Data Interchange Standards Consortium (CDISC) Technical Road Map that is designed to realize the vision of a set of harmonized standards that meet the CDISC Mission and Strategy. The set of standards has been, and will continue to be, developed to support the streamlining of processes within medical research from the production of clinical research protocols through to reporting and/or regulatory submission, warehouse population and/or archive and post-marketing studies/safety surveillance. For more information, click on the following link: http://www.cdisc.org/downloads/CDISC_Road_Map_Spring2008.pdf.

1.2. Organization of this Document

This document has been organized into the following sections:

- **Section 1: Orientation—**This section provides an overall introduction to the purpose and goals of the CDASH project as well as describes the organization of CDASH Standard Version 1.0.
- **Section 2: CDASH Alignment with Other Standards—**This section describes the relationship of CDASH Standard Version 1.0 to the Study Data Tabulation Model Implementation Guide (SDTMIG), controlled terminology and other non-CDISC standards.
- **Section 3: Best Practice Recommendations—**This section introduces the Best Practice recommendations and methodologies for creating data collection instruments. There is also a Frequently Asked Questions (FAQs) section on best practices for creating data collection instruments.
- **Section 4: Overview of CDASH Domain Tables—**This section contains a preview of the new ideas and approaches recommended by the CDASH Domain Teams, introduces data collection fields noted not necessary to collect, defines the core designations used throughout CDASH Standard Version 1.0 and explains the table headers used in the domain tables.
- **Section 5: CDASH Domain Tables—**This section describes the approach taken regarding common identifier and timing variables and contains metadata tables and/or recommendations for the following domains:

  - Adverse Events (AE)
  - Comments (CO)
  - *Prior and* Concomitant Medications (CM)
  - Demographics (DM)
  - Disposition (DS)
  - Drug Accountability (DA)
  - ECG Test Results (EG)
  - Exposure (EX)
  - Inclusion and Exclusion Criteria (IE)
  - Laboratory Test Results (LB)
  - Medical History (MH)
  - Physical Examination (PE)
  - Protocol Deviations (DV)
  - Subject Characteristics (SC)
  - Substance Use (SU)
  - Vital Signs (VS)

- **Section 6: Change Control and the Process for Creating New CDASH Domains—**This section describes the procedure for change control and maintenance of CDASH Standard Version 1.0 as well as the procedure for creating new CDASH domains.
- **Section 7: Appendices—**This section provides additional background material regarding the CDASH project as well as references and supplemental information relevant to implementation of CDASH Standard Version 1.0.

1.2.1. General Notes

- **Paper CRFs vs Electronic CRFs:** The term "CRF" used throughout this document refers to both paper and electronic formats, unless otherwise specified.
- **Fields vs Variables:** The term data collection "fields" refers to fields that are commonly seen on the CRF. The term data collection "variables" refers to what is seen in a clinical database.
- **Study Treatment vs Investigational (Medicinal) Product:** The phrase "study treatment" has been used instead of "investigational (medicinal) product" in order to include all types of study designs and products.
- **Mechanisms for Data Collection:** Different data collection mechanisms can be used to control how data are collected, e.g., tick boxes, check boxes, radio buttons, drop-down lists, etc. For the purposes of this document, these terms will be used interchangeably.

2. CDASH Alignment with Other Standards

2.1. The Study Data Tabulation Model (SDTM)

The CDASH project identifies the basic data collection fields needed from a clinical, scientific and regulatory perspective to enable more efficient data collection at the investigative sites. The SDTM and the SDTMIG provide a standard for the submission of data based on collected data. CDASH moves upstream in the data-flow and identifies a basic set of highly recommended and recommended/conditional data collection fields that are expected to be present on the majority of CRFs. The CDASH data collection fields (or variables) can be mapped to the SDTM structure. When the data are identical between the two standards, the SDTMIG variable names are presented in the CDASH domain tables. In cases where the data are not identical, CDASH has suggested new variable names. As part of this mapping, SDTMIG variable names have been provided under the "Additional Information for Sponsors" column where applicable as an aid.

The CDASH recommendations are based on the SDTMIG version 3.1.1. Where appropriate and possible, forward compatibility with SDTMIG version 3.1.2 has been incorporated, as in the case of the DA domain.

SDTM and CDASH are clearly related. All SDTMIG "Required" variables have been discussed and either included in the CDASH standard, determined to be derivable or can be obtained from data sources other than the CRF. Therefore, there are instances where the variables do not exactly match due to their different purposes (i.e., data submission vs. data collection).

Derived Data
The SDTM standard contains some derived data whereas CDASH data collection fields are not derived at the data acquisition stage.

Data Collection Fields not Included in the SDTM
The CDASH recommendation also includes some data collection fields that are not included in the SDTMIG (e.g., "Were there any adverse events?" or "Were any concomitant medications taken?"). These collection fields are intended to assist in the cleaning of data and in confirming that no data are missing. To facilitate the use of these types of fields, suggested variable names are provided (e.g., AEYN, CMYN, CMONGO) in the Variable Name column and are shaded to denote that they are CDASH-suggested data collection variable names and not SDTMIG variable names.

The CDASH Findings domain (i.e., DA, EG, IE, LB, SU, and VS) tables are presented in a structure that is similar to the SDTM submission model, which is to list the variable names and some examples of the tests. It is expected that implementers will need to modify to include protocol specific tests in a CRF presentation layout. Sponsors should use the CDASH recommendations to identify the types of data to collect while referring to the SDTM and CDISC Controlled Terminology for additional metadata, (e.g., labels, data type, controlled terminology, etc.).

The CDASH Domain Teams have intentionally not reproduced other sections of the SDTM standard and implementers are asked to refer to the SDTM and SDTMIG on the CDISC website for additional information (http://www.cdisc.org/standards/index.html).

2.2. CDISC Controlled Terminology

Terminology applicable to CDASH data collection fields is either in production or under development by the CDISC Terminology Team. Production terminology is published by the National Cancer Institute's Enterprise Vocabulary Services (NCI EVS) and can be accessed via the following link: http://www.cancer.gov/cancertopics/terminologyresources/CDISC.

In cases where a CDASH field has associated controlled terminology, the code list is referenced in the Definition column in the domain tables.

In addition, the Commonly Used CDISC Controlled Terminology appendix includes subsets of controlled terminology for selected data collection fields. Although users may access directly the full EVS code lists (via the link above), we have identified the most commonly used terms as an aid for implementers.

2.3. Other Standards (Beyond CDISC)

The landscape of healthcare-related standards is large and complex and there are numerous players in this arena. Fortunately, CDISC has a "niche" in the development of standards for clinical/medical research. CDISC has initiated a collaboration with a leading healthcare standards development organization, Health Level Seven (HL7), to harmonize the CDISC clinical research with the HL7 healthcare standards. CDISC and HL7 have had a Charter Agreement since 2001; this agreement has been renewed every 2-3 years and includes a commitment to harmonize the CDISC and HL7 standards. In fact, the Biomedical Research Integrated Domain Group (BRIDG) model was initiated through the efforts of CDISC to ensure such harmonization between the CDISC standards for medical research and the HL7 Reference Information Model (RIM) and also to ensure that the CDISC standards themselves are harmonized among each other. The BRIDG model is currently a collaborative project of CDISC, HL7, NCI and FDA. In addition, the BRIDG model has been accepted by the HL7 Regulated Clinical Research Information Management (RCRIM) Work Group as their domain analysis model, to form the basis for interoperability for HL7 messages that are developed within the HL7 RCRIM Work Group.

There is growing recognition around the globe that proprietary standards prevent data interchange, which is essential to effective partnering and information exchange between and among clinicians and researchers. Clinical care can reap benefits through medical research findings, and more clinicians will be interested in conducting research if we can streamline the research process by integrating it into their clinical care workflow. CDISC encourages the adoption of its global standards for clinical research, which should continue to be harmonized with healthcare standards, to provide a means for interoperability among healthcare and research systems such that medical research can support informed healthcare decisions and improve patient safety.

CDISC has a long-time principle of working with others through productive collaboration and not duplicating efforts. Hence, in addition to HL7, CDISC has many and varying relationships with other standards developing organizations (SDOs) and alliance partners. With Health Level 7 (HL7), the relationship is close and the standards are being harmonized. With others, the relationships are more recent and, therefore, not as well-defined or mature. CDISC was approved for Liaison A status with ISO in 2007. This status allows the CDISC standards to be brought to ISO through a fast-track procedure versus starting at the ground level. More recently, to harmonize healthcare standards, ISO, CEN and HL7 formed the Joint Initiative Council. CDISC was accepted into the Joint Initiative Council (JIC) in July 2008. CDISC has also been involved with the U.S. Health Information Technology Standards Panel (HITSP) and the HITSP Board since it was initiated in 2006, with a goal to ensure that these national harmonization steps do not diverge from the global work being done by CDISC and HL7 and JIC.

3. Best Practice Recommendations

3.1. Introduction to Best Practices

The Best Practice recommendations are included in CDASH Standard Version 1.0 as a help to implementers. Although outside the original scope of the project charter, the CDASH Core Team decided that these recommendations would encourage consistent implementation and the most optimal use of the CDASH standard. These Best Practices comprise the Recommended Methodologies for Creating Data Collection Instruments, a Suggested CRF Development Workflow and a section of FAQs about Best Practices for Creating Data Collection Instruments. CRF layout is out of scope for the CDASH project, however, the Best Practices section includes some concepts related to layout because these concepts are important to consider when developing CRFs.

"There is arguably no more important document than the instrument that is used to acquire the data from the clinical trial, with the exception of the protocol, which specifies the conduct of that trial. The quality of the data collected relies first and foremost on the quality of that instrument. No matter how much time and effort go into conducting the trial, if the correct data points were not collected, a meaningful analysis may not be possible. It follows, therefore, that the design, development and quality assurance of such an instrument must be given the utmost attention." [1]

3.2. Recommended Methodologies for Creating Data Collection Instruments

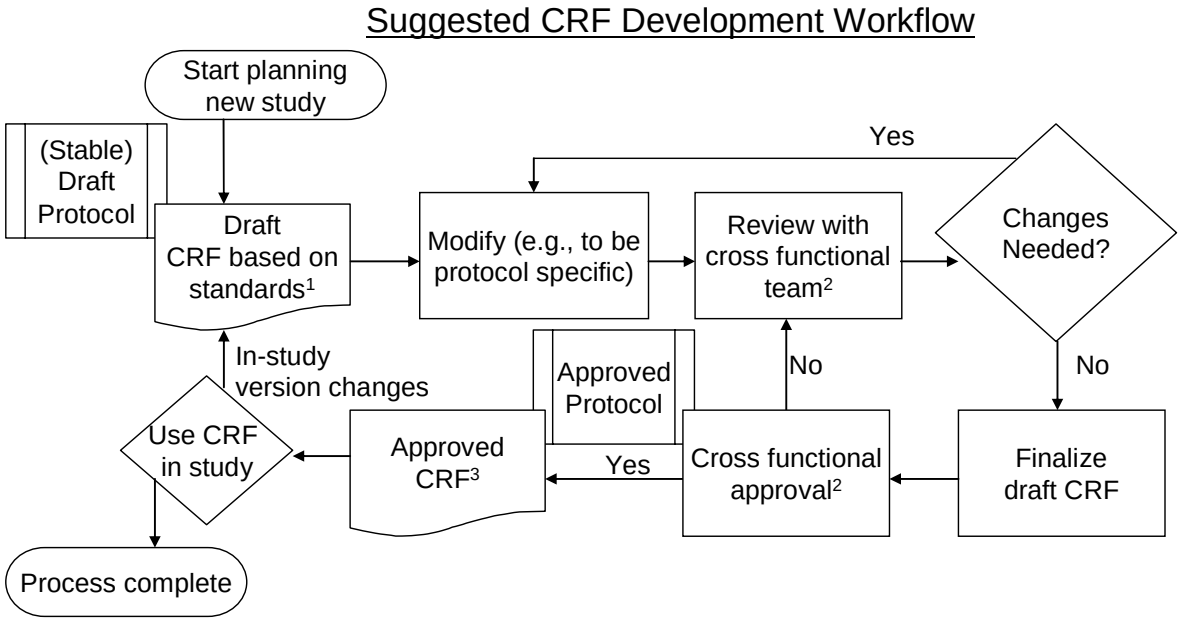
Ref	Methodology	Rationale
1	**Necessary Data Only** CRFs should avoid collecting redundant data and should instead focus on collecting only the data needed to answer the protocol questions and to provide adequate safety data.	• Usually, only data that will be used for analysis should be collected on the CRF due to the cost and time associated with collecting data. Data that is collected should generally be reviewed and cleaned. • When available, the Statistical Analysis Plan (SAP) needs to be reviewed to ensure that the parameters needed for analysis are collected and can be easily analyzed. The Statistician is responsible for confirming that the CRF collects all of the correct data.
2	**Control** The process of designing, printing, distributing CRFs, and accounting for unused CRFs must be controlled. • The CRF development lifecycle should be a controlled process using a formalized, documented process that incorporates design, review, approval and versioning steps. • The CRF development process should be controlled by SOPs covering, at a minimum, design, development, QA, approvals, version control and site training.	• A controlled process for developing CRFs will help ensure that CRFs comply with company standards and processes.

[1] Good Clinical Data Management Practices, Version 4, October 2005, Society for Clinical Data Management

Ref	Methodology	Rationale
3	**Adequate Review** The team that designs the data collection instruments for a study needs to be involved in the development of the protocol and should have appropriate expertise represented on the CRF design team *(e.g., statistics, programming, data management, clinical operations, science, regulatory, pharmacovigilance).* • Staff involved in CRF design should review the protocol to ensure that it is possible to collect the proposed data. • Statisticians should review the CRF against their planned analyses to make sure all required data will be collected in an appropriate form for those analyses. • Clinical Operations staff should review the CRF to make sure the questions are unambiguous and that it is possible to collect the data being requested. • Programmers should review the CRF to ensure that the manner in which the data are collected on the CRF will not adversely affect the programming function. • Scientific experts should provide input on the efficacy and/or safety data collection fields, and educate the Clinical Data Management (CDM) staff on the type and methods of collecting those data. • Regulatory experts should review the CRF for compliance with all applicable regulations. • Data Entry is an important "user" of the CRF and their perspective should be included in the review as well. • Pharmacovigilance should review to ensure appropriate data capture and process to support expedited reporting. Ideally, the CRF should be developed in conjunction with the protocol and SAP. All research-related data on the CRF should be addressed in the protocol to specify how and when it will be collected.	• The CRF design team should perform an adequate review of the CRF to ensure that the CRF captures all of the data needed for analysis. Furthermore, the team needs to ensure that the data are collected in a manner consistent with the sponsor's processes and should also be easy for the site to complete.
4	**Site Workflow** The team developing the data collection instruments needs to consider the workflow at the site and the standard of care.	• The CRF needs to be quick and easy for site personnel to complete. • Clinical Operations staff should review the CRF for compatibility with site workflow and site procedures. • Although CDM may make the final decisions about CRF design, those decisions should be informed by study and user requirements.

Ref	Methodology	Rationale
5	**Employ Standards** Within the data collection environment, standards should be employed to collect consistent data across compounds and TAs. CDASH standards should be used wherever possible and sponsor standards developed as needed.	• Using data collection standards across compounds and TAs saves time and money at every step of drug development. • Using standards: - reduces production time for CRF design and reduces review and approval time. - reduces site re-training and queries and improves compliance and data quality at first collection. - facilitates efficient monitoring, reducing queries. - improves the speed and quality of data entry due to familiarity with standards and reduces the training burden in-house. - enables easy reuse and integration of data across studies and facilitates "data mining" and the production of integrated summaries. - reduces the need for new clinical and statistical programming with each new study. - addresses FDA Critical Path Opportunities 45.
6	**Clarity** CRF questions and completion instructions should not "lead" the site.	Data need to be collected in a way that does not introduce bias or errors into the study data. Questions should be clear and unambiguous. This includes making sure that the options for answering the question are complete *(i.e., may need to include options such as "Other", "None").*
7	**Translations** Translations of CRFs into other languages should be a parallel process following the same set of steps with separate reviews and approvals by the appropriate experts.	CRFs that are translated into other languages should follow the same development process as the original CRF to ensure the integrity of the data collected. Cultural and language issues should be addressed appropriately during the process of translating CRFs to ensure the CRF questions have consistent meaning in all languages.
8	**CRF Completion Guidelines** CRF questions should be as self-explanatory as possible, thereby reducing the need for separate instructions. When instructions are needed, prompts and short instructions may be placed on the CRF page. More detailed instructions may be presented in a CRF completion guideline for paper CRFs, or in a context-sensitive help file for electronic CRFs (eCRFs). All instructions should be concise. Instructions should be standardized along with the CRF as much as possible. This promotes standardization in that all sites will use the same conventions for completing the fields.	Putting short instructions and prompts on the CRF increases the probability that they will be read and followed and can reduce the number of queries and the overall data cleaning costs. Well designed completion guidelines will also enhance the flow of the CRF. Providing short instructions and prompts on the CRF, and moving long instructions to a separate instruction booklet, facing page or checklist will decrease the number of pages in the CRF, with the following benefits: • Decreased CDM costs *(e.g., decreased data entry costs).* • Allows CRF to be formatted so that the reader can easily identify the fields to be completed. • The format of the page is less cluttered which makes it easier for site personnel and monitors to identify fields with missing responses.

3.3. Suggested CRF Development Workflow



High Level Overview of CRF Development Best Practices:

- [1]Develop as early as possible with a stable draft Protocol, based on CDASH and internal standards
- [2]Develop as a cross-functional team, reviewing from the perspective of the respective disciplines, including:
  - Is all data for analysis collected?
  - Is it possible to collect this way at the site?
  - Are we collecting appropriate data to address safety?
- [3]CRF is approved after Protocol is approved

3.4. FAQs on Best Practices for Creating Data Collection Instruments

Ref	Question	CRF Type	Best Practice Recommendation	Rationale
1	Should "Yes/No" questions be preferred over "Check all that apply" questions?	Paper and electronic	• If an assessment can have composite responses *(e.g., presence or absence of two or more symptoms)*, "Yes/No" questions for each component response *(e.g., symptom)* are preferred to "Check all that apply" questions. • One exception to this recommendation might be assessments where the majority of options would be answered "No". An example would be the collection of ECG abnormality data where approximately 45 abnormalities may be listed but only a few will apply. • Another exception is the "Check if ongoing" question. This is a special use case of "Yes/No" where the question is usually presented as a single possible response of "Yes" in conjunction with an end date. In this case, if the box is checked, the field will contain "Yes" and if it is blank and there is an end date present, it can be mapped to "No".'	• "Yes/No" questions provide a definite answer. The absence of a response is ambiguous as it can mean "No", "None" or that the response is missing.
2	Should there be a standard order for "Yes/No" response boxes and other standardized lists?	Paper and electronic	• It is recommended that a consistent order of "Yes/No" responses be used.	• A standard order of "Yes/No" response boxes promotes ease of use of the CRF. • Presenting "Yes/No" responses in a standard order is "one tool" that can be used to reduce bias, but questions should also be carefully worded so they don't introduce bias or lead the investigator to a desired response.
3	What date format should be used for subject and site-completed CRF data?	Paper and electronic	• CDASH recommends the unambiguous format DD-MMM-YYYY where "DD" is the day as a 2-digit numeric value, "MMM" is the month as a 3-character letter abbreviation in the local language, and "YYYY" is the year as a 4-digit numeric value. For example for an English CRF, the second day of February 2008 would be "02-FEB-2008", whereas for a French CRF it would be "02-FEV-2008". • For electronic data capture (EDC), the user may be able to select a date from a calendar, and this would also meet the recommendation for an unambiguous date.	• Using the CDASH-recommended collection date format *(i.e., DD-MMM-YYYY)* will provide unambiguous dates and will be seen as the same date by anyone who reads them. For example, the date "06/08/02" is ambiguous because it can be interpreted as "June 8, 2002" or "August 6, 2002". • *Note: If subject-completed CRF pages are translated into a local language, the CDASH recommended date format for collection may make it easier to translate the documents.* • Dates are collected in a user-friendly format, but transformed and stored in the database as ISO 8601 format and submitted as ISO 8601.

Ref	Question	CRF Type	Best Practice Recommendation	Rationale
4	What time format should be used for subject and site-completed CRF data?	Paper and electronic	CDASH recommends the use of a 24-hour clock using the HH:MM:SS format for recording times. 00:00:00 would indicate midnight with the next day's date.	• As many of the HH:MM:SS elements should be used as are needed for a particular field. • Subject-completed times may be recorded using a 12-hour clock and an A.M. or P.M. designation. The time would then be transformed to a 24-hour clock in the database. • Times are collected in a 24-hour format which eliminates the need to convert to the ISO 8601 format for submission.
5	Should manually-calculated data items be recorded on the CRF?	Paper and electronic	• Manually-calculated fields should not typically be recorded within the CRF when the raw data on which the calculation is based are recorded in the CRF. • An exception is when a treatment and/or study conduct decision needs to be made based on those calculations. In those cases it may be useful for the calculated field to be recorded within the CRF. • It may also be useful to provide the site a step-by-step worksheet to calculate this data.	• Data items which can be calculated from other data captured within the CRF are more accurately reported if they are calculated programmatically in-house using validated algorithms. • Capturing both the source data items and the calculated field would be a duplication of data. • If the calculated field is used to make a treatment and/or study conduct decision, the results of the calculation would be required on the CRF to explain the decision made.
6	Should all data collected on CRFs be databased?	Paper	• Data that are collected on CRFs should usually be databased. • If data are not required for reporting or analysis, but collecting the data aids the investigator or monitor, it is recommended that data be collected on a worksheet. Worksheets used at the investigator's site are not typically brought in-house and will not subsequently be databased *(e.g., an entry criteria worksheet or a dose titration worksheet).* • Some fields, such as "Were there any Adverse Events – Yes/No" may need to be databased, but will not be reported with submission data. • Some fields, such as Investigator's Signature, can be verified by the data entry staff, but cannot actually be databased. • *Note: All such worksheets should be considered source documents or monitoring tools, and should be maintained at the site with the study files.* • *Note: Worksheets should be developed in a parallel process to ensure consistency*.	• Although the data recorded on worksheets are supporting documentation for key information collected elsewhere in the CRF, these data are not needed in the clinical database and do not need to be recorded on the CRF.

Ref	Question	CRF Type	Best Practice Recommendation	Rationale
7	Should "Was assessment x performed?" questions be collected and/or databased? ***And*** Should "Yes/No" exam completed be preferred over "Check if not done" questions?	Paper and electronic	• The database should contain an indication that an assessment was not performed. The mechanism for this may be different from system to system or from paper to EDC. • In some cases this might be a "Yes/No – assessment completed" question or a "Check if not done" box; in others it might be a blank flag or list of values to indicate why data are missing. The "Yes/No – assessment completed" question is preferred over the "Check if not done" box because the "Yes/No" format helps to ensure that a response is provided where as it is not absolutely clear if the "Not done" box was missed/skipped if not checked.	• This will provide a definitive indicator to both clinical and statistical programmers that a data field has missing data and has not been overlooked. • This will prevent unnecessary data queries to clarify whether an assessment has been performed.
8	Should free text be an option for a response to a specific question? *(Also refer to the Comments Domain for additional information.)*	Paper and electronic	• The general recommendation from CDASH is that the collection of free text comments and general comments pages should be discouraged. Collection of free text should be limited to cases of specific safety or therapeutic need in reporting or analysis, such as Adverse Events, Concomitant Medications or Medical History. • CDASH recommends that questions be specific and clear rather than open-ended. Instead of free text comment fields, CDASH recommends a thorough review of the CRF by the protocol development team to maximize the use of pre-defined lists of responses.	• The collection and processing of free text requires significant resources and is of limited use when analyzing and reporting clinical data. • Sites may enter data into free text fields that should be recorded elsewhere. • Entering text from these fields into the database is time consuming for data entry and requires CDM resources to review the text for safety information and inconsistencies with other recorded data.
9	Should data be pre-populated in the CRF?	Paper or electronic	• In general, study data should be collected and recorded by the site, not pre-populated. • Fields in the database or on the CRF may be pre-populated if the data are known to be the same for all subjects *(e.g., MH CRF collects data for specific body systems - body systems may be pre-populated)*, or if the data are assigned to the subject *(e.g., subject ID, site ID).* • *Note: This recommendation will be revisited once eCRFs are integrated with electronic health records which will result in CRFs populated with data from hospital or healthcare systems.*	• The CRF should be used as a tool to collect unknown study data.
10	Should location of measurement and position of subject *(e.g., oral temperature, blood pressure from right arm, etc.)* be collected for each assessment?	Paper and electronic	• Location data should be collected only when multiple possibilities are present and the location is required to make a meaningful analysis of the data *(e.g., a comparison of blood pressures collected supine, right arm and left arm).*	• Location options are only used when the protocol specifies.

Ref	Question	CRF Type	Best Practice Recommendation	Rationale
11	Should sites be given guidance on how to record verbatim terms for adverse events, concomitant medications or medical history in the CRF?	Paper and electronic	• CDASH recommends not providing actual coding dictionaries to the site for adverse events, concomitant medications or medical history reported terms, as this may bias responses.	• CDASH recommends that guidance be provided to the sites to ensure clear reporting of adverse events, concomitant medications or medical history. • For medications, this may include defining, for example, whether generic or trade names are permissible. • For medical history and adverse events, this may include providing an understanding of the level of detail needed for accurate medical coding *(e.g., "Diabetes" should not be reported without also providing the type)* and sites may be encouraged to record specific, medically correct terminology on the forms *(e.g., "hyperglycemia", instead of "high blood sugar").*

4. Overview of CDASH Domain Tables

4.1. Introduction

The CDASH data collection fields included in the following domain tables are the most commonly used and should be easily identified by most implementers. It is recognized and expected **that sponsors will need to add additional data collection fields** to capture TA-specific data points as well as other data specified in the clinical study protocol or required according to local regulatory requirements.

Use the CDASH recommendations when developing company standards on the sponsor level, taking into consideration the requirements of the stage of clinical development and the individual therapeutic area requirements, and NOT on a trial-by-trial basis within the sponsor organization.

The CDASH domain tables are arranged in alphabetical order. CRF layout was not within the scope of the CDASH project so as a help to implementers, the data collection fields are presented in the order they commonly appear on a basic CRF.

The CO, IE, PE and DV domains contain new approaches that we would specifically like to point out. These recommendations came about within the respective Domain Teams and reflect the current thinking and standard practice taken by a significant number of organizations/companies.

- **Comments:** Avoid the creation of a General Comments CRF to collect unsolicited comments. Solicited comments linked to specific data collection fields is the recommended approach.
- **Inclusion/Exclusion Criteria:** Use the IE form to collect only the criterion or criteria NOT MET.
- **Physical Examination:** Record only whether or not an exam was done on the PE form. Clinical sites are asked to record baseline abnormalities on a Medical History, Targeted Medical History or Baseline Conditions CRF. Post baseline abnormalities or baseline conditions that worsened during the clinical study are to be recorded on the Adverse Event CRF.
- **Protocol Deviations:** Avoid creating a Protocol Deviations CRF if this information can be derived from other domains or system functionalities.

For a more detailed discussion regarding these recommendations please see the individual domain tables.

4.2. Data Collection Fields Generally Considered Not Necessary to Collect on the CRF

As part of the development process each Domain Team reviewed sample CRFs currently in use by the Domain Team members' respective companies. After close review and much discussion, the Domain Teams determined that some data collection fields were not necessary to collect (i.e., not recommended for inclusion) on CRFs. These fields were organized by domain and compiled into tables called "Data Collection Fields Generally Considered Not Necessary to Collect on the CRF". The "Rationale" column within the tables contains the reasons(s) the Domain Teams determined the fields to be generally not necessary to collect. In most cases it was because these fields would be derived or would be collected elsewhere in the CRF. Sponsors are free to use these fields if deemed appropriate for the type of study they are conducting and/or phase of development their respective project is in. The tables are available for review on the CDISC website: www.cdisc.org.

4.3. Core Designations for Basic Data Collection Fields

In order to facilitate classification of the different types of data collection fields, the following categories were used:

- **Highly Recommended:** A data collection field that should be on the CRF (e.g., a regulatory requirement).

- **Recommended/Conditional:** A data collection field that should be collected on the CRF for specific cases or to address TA requirements (may be recorded elsewhere in the CRF or from other data collection sources).
- **Optional:** A data collection field that is available for use if needed.

It is assumed that sponsors will determine which data collection fields will be collected based on TA-specific data requirements, protocol and other considerations.

4.4. Explanation of Table Headers

1	2	3	4	5	6
Data Collection Field	**Variable Name (CDASH variable name shaded)**	**Definition**	**Case Report Form Completion Instructions**	**Additional Information for Sponsors**	**CDASH Core**

1. **Data Collection Field:** Basic data to be collected.

2. **Variable Name:** Lists the SDTM-based variable name defined in the SDTMIG.

   (CDASH variable name shaded): This column also provides suggested variable names (e.g., CMONGO and CMTTIM). These variable names are "SDTM-like variables" and can help facilitate the derivation of SDTMIG variables needed for submission.

3. **Definition:** Describes the purpose of the data collection field. The text may or may not mirror the text in the SDTMIG (in the "Variable Label" or "CDISC Notes" columns). Where applicable, CRF text examples are presented in italics. When an available code list better describes the text, a reference to the code list will be provided, in the format {*code list name*} (see Section 2.2 for information about controlled terminology).

4. **Case Report Form Completion Instructions:** Contains information for the clinical site on how to enter collected information on the CRF.

5. **Additional Information for Sponsors:** Contains further information, such as rationale and implementation instructions, on how to implement the CRF data collection fields.

6. **CDASH Core:** Contains the CDASH core designations for basic data collection fields (see Section 4.3 for definitions of core designations).

5. CDASH Domain Tables

5.1. Common Identifier Variables

The following apply across all of the data collection domains.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Protocol/Study Identifier	STUDYID	Unique Identifier for a study within a submission.	Not applicable.	This is typically pre-printed/pre-populated.	Highly Recommended
2	Site Identifier Within a Study	SITEID *Or* **SITENO**	Unique identifier for the study site; however, SITEID is also unique within a submission.	Record your clinical site's identifier as defined by the sponsor.	**Paper:** This is typically pre-printed in the header of each CRF page for single site studies. For studies with multiple sites, this field is typically left blank so that the number can be recorded by the site. **EDC:** This should be pre-populated. If SITEID is not used, SITENO should be used to derive SITEID for SDTM, depending upon sponsor's site identification scheme.	Highly Recommended
3	Subject Identifier	SUBJID	Subject identifier for the study.	Record the identifier for the subject.	**Paper:** This is typically recorded in the header of each CRF page. **EDC:** The subject identifiers may be provided to the site using a pre-populated list in the system.	Highly Recommended
4	Unique Subject Identifier	USUBJID	Unique subject identifier within a submission.	Record the identifier for the subject.	**Paper:** This is typically recorded in the header of each CRF page. **EDC:** The subject identifiers may be provided to the site using a pre-populated list in the system.	Optional
5	Investigator Identifier	INVID	Investigator identifier.	Record the sponsor-defined identifier for your site investigator.	Study level – Not needed if SITEID is equivalent to INVID.	Optional
6	Sponsor-Defined Identifier	--SPID	Optional sponsor-defined reference number. Perhaps pre-printed/pre-populated as an explicit line identifier or defined in the sponsor's operational database *(e.g., line number on a Disposition page).*	Not applicable.	When used, this is typically pre-printed/ pre-populated.	Optional

5.2. Common Timing Variables

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Visit	VISIT / VISITNUM	Visit Name / Visit Number.	When applicable *(e.g., on paper CRFs)*, record the visit name and/or visit number.	This is typically pre-printed/pre-populated.	Optional
2	Date of Visit	**VISDAT**	Date the visit took place.	Record the date the visit took place.	This may be recorded in either the header of the CRF or in the body of the CRF.	Highly Recommended
3	Time of Visit	**VISTIM**	Time the visit took place.	Record the time the visit took place.	This may be useful for Phase I trials.	Optional

5.3. Adverse Event – AE (Events)

These recommendations are for non-solicited or pre-specified adverse events. As with all the data collection variables recommended in CDASH Standard Version 1.0, it is assumed that sponsors will add other data variables as needed to meet protocol-specific and other data collection requirements (e.g., TA-specific data elements and others as required per protocol, business practice and operating procedures). Sponsors should define the appropriate collection period for adverse events.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Were any Adverse Events experienced?	**AEYN**	General prompt question regarding whether or not any AEs were experienced during the study. This provides verification that all other fields on the CRF were deliberately left blank. *Were any Adverse Events experienced?* {NY} (See Section 2.2.)	Indicate if the subject experienced any adverse events. If yes, include the appropriate details where indicated on the CRF.	The intent/purpose of collecting this field is to help with data cleaning and monitoring. It provides verification that all other fields on the CRF were deliberately left blank. Note: AEYN will not be included as part of the SDTMIG AE Domain for submission.	Optional
2	Line #	AESPID	A sponsor-defined reference number associated with each unique AE record.	• Record sequential numbers for each adverse event, beginning with "1". • Number sequence for all following pages should not be restarted.	Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database (derived) *(e.g., line number on an Adverse Event page).* For paper AE CRFs, it can be beneficial to use a sequence number in a data query to clearly communicate to the site the specific record in question.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
3	Adverse Event	AETERM	Verbatim *(i.e., investigator-reported term)* description of the adverse event.	• Record only one diagnosis, sign or symptom per line *(e.g., nausea and vomiting should not be recorded in the same entry, but as 2 separate entries)*. • Using accepted medical terminology, enter 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. • 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. • Do not use abbreviations.	In most cases, the verbatim term *(i.e., investigator-reported term)* will be coded to a standard medical dictionary such as MedDRA, WHO ART, after the data have been collected on the CRF. The coding data will be stored in field(s) not defined by CDASH.	Highly Recommended
4	Start Date	**AESTDAT**	Date when the adverse event started.	Record the date that the AE began using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	**For the SDTM-based dataset,** the SDTMIG variable AESTDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into AESTDTC using the ISO 8601 format.	Highly Recommended
5	Start Time	**AESTTIM**	Time when the adverse event started.	If appropriate, record the time (as complete as possible) that the AE began. For more detail see the Best Practice section.	Collecting the time an AE 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. An example would be in an early phase study where the subject is under the direct care of the site at the time the event started and the study design is such that it is important to know the AE start time with respect to dosing. **For the SDTM-based dataset,** the SDTMIG variable AESTDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into AESTDTC using the ISO 8601 format.	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	End Date	**AEENDAT**	Date when the adverse event resolved.	Record the date that the AE resolved using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section. If the AE is ongoing, leave the field blank.	**For the SDTM-based dataset**, the SDTMIG variable AEENDTC is derived by concatenating CDASH End Date and Time (if time is collected) into AEENDTC using the ISO 8601 format.	Highly Recommended
7	End Time	**AEENTIM**	Time when the adverse event resolved.	If appropriate, record the time (as complete as possible) that the AE resolved. For more detail see the Best Practice section.	Collecting the time an AE resolved is only appropriate if it can be realistically determined and if there is a scientific reason for needing to know this level of detail. An example would be in an early phase study where the subject is under the direct care of the site at the time the event resolved and the study design is such that it is important to know the AE end time with respect to dosing. **For the SDTM-based dataset**, the SDTMIG variable AEENDTC is derived by concatenating CDASH End Date and Time (if time is collected) into AEENDTC using the ISO 8601 format.	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
8	Ongoing	AEONGO	Indicates AE is ongoing when no End Date is provided. {NY} (See Section 2.2.)	Check the box if the adverse event has not resolved at the time of data collection; leave the End Date blank.	This field will be completed to indicate that the AE has not resolved at the time of data collection. Upon study completion, it is expected that every reported AE should have either an End Date or the Ongoing field will be completed, but not both. The purpose of collecting this field is to help with data cleaning and monitoring, since this field provides further confirmation that the End Date was deliberately left blank. The field is a special use case of "Yes/No," containing "Yes" if the box is checked and "No" if the box is blank and an end date is present. This is not a direct mapping to the SDTMIG variable AEENRF. The date of data collection in conjunction with End Date and the Ongoing CDASH fields would determine how the SDTMIG variable AEENRF will be populated. In some cases this information may be determined from AE Outcome.	Optional
9	Severity	AESEV ***And/or*** AETOXGR	Description of the severity of the adverse event. {AESEV} (See Section 2.2.) {TOXGR} (See Section 2.2.)	Severity: The reporting physician/healthcare professional will assess the severity of the adverse drug/biologic event using the sponsor-defined 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. ***And/or*** Severity CTCAE Grade: The reporting physician/healthcare professional will 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. Note: Completion of CTCAE grade is a mandatory field for cancer studies. In all other types of studies this is an optional field.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
10	Serious Event	AESER	Indicates whether or not the adverse event is determined to be "serious" based on what is defined in the protocol. *Is the Adverse Event serious?* {NY} (See Section 2.2.)	Assess if an adverse event should be classified as serious based on the "serious" criteria defined in the protocol.	This field is related to the individual serious adverse event type fields, which may or may not be reported on the CRF.	Highly Recommended
11a	Serious Event Type - Congenital Anomaly or Birth Defect	AESCONG	Indicates if a "serious" adverse event was associated with a congenital anomaly or birth defect. *Is the AE associated with a congenital anomaly or birth defect?* {NY} (See Section 2.2.)	Record if the "serious" adverse event was associated with congenital anomaly or birth defect.	If the details regarding a Serious AE need to be collected in the clinical database, then it is recommended that a separate Yes/No variable be defined for each Serious AE type. In many cases sponsors will only collect the AESER field because the individual serious adverse event types might be collected in a separate pharmacovigilance database and therefore do not need to be collected in the clinical database.	Recommended/ Conditional
11b	Serious Event Type - Persistent or Significant Disability or Incapacity	AESDISAB	Indicates if a "serious" adverse event was associated with a persistent or significant disability or incapacity. *Did the AE result in a persistent or significant disability or incapacity?* {NY} (See Section 2.2.)	Record if the "serious" adverse event resulted in a persistent or significant disability or incapacity.		Recommended/ Conditional
11c	Serious Event Type - Death	AESDTH	Indicates if a "serious" adverse event resulted in death. *Did the AE result in death?* {NY} (See Section 2.2.)	Record if the "serious" adverse event resulted in death.		Recommended/ Conditional
11d	Serious Event Type - Initial or Prolonged Hospitalization	AESHOSP	Indicates if a "serious" adverse event resulted in an initial or prolonged hospitalization for the patient. *Did the AE result in an initial or prolonged hospitalization for the patient?* {NY} (See Section 2.2.)	Record if the "serious" adverse event resulted in an initial or prolonged hospitalization for the patient.		Recommended/ Conditional
11e	Serious Event Type - Life Threatening	AESLIFE	Indicates if a "serious" adverse event was life threatening. *Is the AE Life Threatening?* {NY} (See Section 2.2.)	Record if the "serious" adverse event is life threatening.		Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
11f	Serious Event Type - Other Serious or Important Medical Events	AESMIE	Indicates if a "serious" adverse event is associated with other serious or important medical events. *Is the AE associated with other serious or important medical events?* {NY} (See Section 2.2.)	Record if the "serious" adverse event is associated with other serious or important medical events which may be defined in the protocol or in the Investigator Brochure.	*(See above)*	Recommended/ Conditional
12	Relationship to Study Treatment	AEREL	Indication of whether the study treatment had a causal effect on the adverse event, as reported by the clinician/investigator.	Indicate if the cause of the adverse event is related to the study treatment and cannot be reasonably explained by other factors *(e.g., subject's clinical state, concomitant therapy, and/or other interventions)*.	Sponsored-defined terminology will be used to indicate the relationship between the AE and the study treatment *(e.g., Yes/No or ICH E2B examples: Not Related, Unlikely Related, Possibly Related, Related)*.	Highly Recommended
13	Action Taken with Study Treatment	AEACN	Changes made to the study treatment in response to the adverse event. {ACN} (See Section 2.2.)	Record changes made to the study treatment resulting from the adverse event.	CDISC controlled terminology should be used to indicate the action taken with the study treatment in response to the AE.	Highly Recommended
14	Other Action Taken	AEACNOTH	Describes Other Action(s) taken in response to the adverse event that are unrelated to study treatment dose changes.	Record all other action(s) taken resulting from the adverse event that are unrelated to study treatment dose changes.	This field is usually reported as a free text field. Example: Treatment Unblinded, Primary Care Physician Notified.	Optional
15	Outcome	AEOUT	Description of the subject's status associated with an event. {OUT} (See Section 2.2.)	Record the appropriate outcome of the event in relation to the subject's status.	CDISC controlled terminology should be used to indicate the outcome of the event as it relates to the subject's status. The Outcome controlled terminology includes ICH E2B values.	Highly Recommended
16	Adverse Event that Caused Study Discontinuation	AEDIS	Indication of whether the adverse event caused the subject to discontinue from the study. *Did the AE cause the subject to discontinue from the study?* {NY} (See Section 2.2.)	Record if the AE caused the subject to discontinue from the study.	Since the Action Taken field was defined to only collect the changes made to the study treatment due to the AE, an additional field was created to identify the AE(s) that caused the subject to discontinue from the study. Some sponsors opt to capture this information only on the Subject Disposition CRF while others choose to collect this data on both the Subject Disposition and AE CRFs, so the specific AE term(s) and related data can be identified.	Optional

5.4. Comments – CO (Special Purpose)

5.4.1. Solicited Comments versus Unsolicited Comments

Solicited comments are defined as those entered in free-text data collection fields (such as "Specify" or "Please comment") intentionally included on the CRFs. These data collection fields provide the site with a pre-defined space to further explain or clarify an associated data collection field within the CRF. For example, the Demographics CRF may include a solicited comments data collection field which enables recording of free text, such as "specify" field for "Race – other".

Unsolicited comments are those comments entered outside of pre-defined data collection fields (also referred to as "marginal" comments as they are often written in margins). These may include marginal CRF comments entered by site staff, written by the subject on diaries, or EDC capability to capture comments that are not generally included in any clinical domain. Although such comments may be intended to avoid queries, in practice they often lead to data not being entered into the correct data collection field and cause additional work in the review process.

5.4.2. Considerations Regarding Usage of a General Comments CRF

Solicited comments have also previously been collected using a General Comments CRF. Of the companies represented within the CDASH CO Domain Team, only one company indicated that they continue to collect free text on a General Comments CRF; all others are discontinuing or have discontinued such practices.

The CO Domain Team decided there should be no mandatory data elements for inclusion in a separate Comments CRF. The Team suggests avoiding the creation of a General Comments CRF. This does not pertain to solicited free-text comment data collection fields that may appear within another established domain.

5.4.3. Rationale

Clinical data must be entered in appropriate data collection fields; otherwise, there is a potential for hidden safety events. For example, if an unsolicited general comment of "subject visit was delayed as he had the flu" was captured, this would necessitate that "flu" be entered in the Adverse Event CRF and not left as a comment.

CRF development teams are encouraged to strive for data collection methods maximizing the use of pre-defined lists of responses rather than relying on a General Comments CRF. If there is no mechanism for recording general comments (not related to specific data points), it will be incumbent upon teams to design data collection tools capable of capturing all required data for analysis purposes in dedicated fields. The CO Domain Team suggests that CRF development teams consider what additional information may be needed within a specific CRF. It is better to ask specific questions through creation of well-defined data collection fields that will be more meaningful for analysis rather than inconsistently capturing this information within general comments data collection fields.

General comments are inefficient to program against due to inconsistent wording and frequent misspellings and therefore offer limited or no value for statistical analysis, as they cannot be tabulated. An additional concern is the potential for inappropriate, or sensitive, information to be included within general comments data collection fields. For example, a comment could contain a name or may have unblinding information.

Unsolicited comments which may have been intended to avoid queries, for example “subject visit was delayed due to his holidays”, are not regarded as clinical data. The Investigative site or monitor should be trained to enter the contents of the comments in the appropriate data collection field rather than making marginal notes on the CRF. There is a higher time/cost consideration associated with unsolicited comments and they should be discouraged, as they are labor intensive to data-enter, review and act upon.

5.4.4. Conclusion

The CO Domain Team reviewed ICH E3 & E6 and did not find any requirement that indicate unsolicited comments should be included in a submission dataset. The CO Domain Team consensus and recommendation is that only the parameters captured in appropriate CRF data collection fields are considered clinical study data that is submitted to regulatory parties in datasets; all other comments are considered unsolicited comments.

Individual sponsor companies must determine their own path in handling the situation should unsolicited comments appear on CRFs.

5.5. *Prior and* Concomitant Medications – CM (Interventions)

The same basic data collection variables should be collected for all medications (Prior, General Concomitant Medications and Medications of Interest). It is assumed that additional fields will be added as applicable for each specific Medication of Interest. For the purposes of this effort, Prior and General Concomitant Medications were considered the primary focus, not Medications of Interest. The term "Prior" refers to medications that were started prior to study participation. Sponsors should define the appropriate collection period for prior and concomitant medications.

5.5.1. General Medications

General Medications are defined as any medications 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. Additional information might be sourced by referring to a subject's medical record.

5.5.2. Medications of Interest

Medications of Interest are defined as any medications or classes of drugs specifically mentioned in the protocol, (e.g., excluded medications, drugs requiring a washout period prior to dosing in study, or rescue medications).

Medications of Interest were not the primary focus for this domain due to the fact 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. Among the many reasons for this 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.

As with all the data collection variables recommended in the CDASH draft document, it is assumed that sponsors will add other data variables as needed to meet protocol-specific and other data collection requirements (e.g., TA-specific data elements and others as required per protocol, business practice and operating procedures).

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Were any medications taken?	**CMYN**	General prompt question to aid in monitoring and data cleaning. *Were any medications taken?* {NY} (See Section 2.2.)	Indicate if the subject took any medications. If "Yes", include the appropriate details where indicated.	The intent/purpose of collecting this field is to help with data cleaning and monitoring. *Note: CMYN will not be included as part of the SDTMIG CM Domain for submission.*	Optional
2	Line #	CMSPID	A sponsor-defined reference number.	• Record sequential numbers for each medication, beginning with "1". • Number sequence for all following pages should not be restarted.	Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database (derived) *(e.g., line number on a concomitant medication page).* For paper Prior & Concomitant Medication CRFs, it can be beneficial to use a sequence number in a data query to clearly communicate to the site the specific record in question.	Optional
3	Medication / Therapy Name	CMTRT	Verbatim drug name or therapy (type of therapies that has similar data collection characteristics as medications.)	• Record only one medication per line. • Provide the full trade or proprietary name of the drug or therapy; otherwise the generic name may be recorded. • If a medication is used for multiple indications *[i.e., multiple AEs, and/or Medical History condition(s)]*, list the medication again with each indication as a new line or entry.	In most cases, the verbatim drug names or therapy will be coded to a standard dictionary such as WHO DRUG after the data have been collected on the CRF. For the collection of verbatim drug name or therapy, the recommendation is to ask the sites to provide the full trade or proprietary name since it is more exact than the generic. The full trade name provides the base generic and the appropriate salt for that particular drug. In addition, for coding purposes it helps with ATC selection. For example the medication Tylenol with codeine #1 has a different ATC code from Tylenol with codeine #3.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
4	Active Ingredient(s)	**CMINGRD**	Medication Ingredients.	• Prior to a subject's clinical visit, remind all subjects to bring all medications bottles, packs etc. they are taking with them to their clinical visit. • Record all active ingredient(s) off the medication label and separate each ingredient with a comma for the name of drug medication or therapy taken. For example, the medication Dolmen, if manufactured in Spain, the active ingredients should be reported as noted below: Active Ingredient: Acetylsalicylic Acid, Ascorbic acid, codeine phosphate	This may be collected in addition to the "Medication / Therapy Name". Collecting this provides more detailed information when coding to a medication dictionary like WHO Drug Enhanced format C which now codes to the ingredient level for many trade named medication. For example, the medication Dolmen, depending on the country where it is manufactured, the active ingredients may be different. Spain: Acetylsalicylic Acid, Ascorbic acid, codeine phosphate Italy and Czech Republic: contains Tenoxicam Estonia and Latvia: contains Dexketoprofen trometamol	Optional
5	Indication	CMINDC	The reason for administration of a concomitant (non-study) medication. *(e.g., Nausea, Hypertension)* This is not the pharmacological/ therapeutic classification of an agent *(e.g., antibiotic, analgesic, etc.)*, but the reason for its administration to the subject.	• Record the reason the medication was taken base on clinical investigator's evaluation. • If taken to treat a condition, and a diagnosis was made, the indication should be the diagnosis. • If taken to treat a condition, and no diagnosis was made, the indication should be the signs and 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.	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	AE Line #	**CMAENO**	Identifier for the adverse event that is the indication for this medication.	•Record the AE line number of the Adverse Event for which this medication was taken. The AE line number is located on the Adverse Events CRF. •If the medication is taken for multiple indications (*i.e., multiple AEs, or Medical History condition*), list the medication again with each indication as a new line or entry.	Intent is to establish a link between the adverse event and the medication taken for the adverse event, but there may be other ways to collect this type of information. Utilizing this variable to maintain a link to a sequence number associated with an AE may result in unnecessary data cleaning work. Potential reconciliation issues occur for example, if the AE line number is deleted or a new AE is added due to a query response or a correction by the clinical site or an AE verbatim is split for coding. *Note: CMAENO will not be included in the SDTMIG CM domain in submissions.*	Optional
7	MH Line #	**CMMHNO**	Identifier for the medical history condition that is the indication for this medication.	•Record the MH line number of the medical history event for which this medication was taken. The MH line number is located on the Medical History CRF. •If the medication is taken for multiple indications (*i.e., multiple AEs, or Medical History condition*), list the medication again with each indication as a new line or entry.	Intent is to establish a link between the medical history condition and the medication taken for the medical history condition, but there may be other ways to collect this type of information. Utilizing this variable to maintain a link to a sequence number associated with an MH condition may result in unnecessary data cleaning work. Potential reconciliation issues occur for example, if the MH line number is deleted or a new MH is added due to a query response or a correction by the clinical site or an MH verbatim is split for coding. *Note: CMMHNO will not be included in the SDTMIG CM domain in submissions.*	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
8	Dose	CMDSTXT	The dose of medication taken per administration.	Record the dose of medication taken per administration *(e.g., 200)*. Please do not record a dosing range (*e.g., 200-400*) for dose.	Where this level of dosing information is required by a sponsor, this field may be included. Defining this data collection field as a dose text field allows for flexibility in capturing text dose entries. CMDSTXT is not a direct mapping to the SDTMIG variable CMDOSTXT. The data collected in this dose text-format field need to be separated or mapped to either SDTMIG CMDOSE if numeric or CMDOSTXT if text.	Optional
9	Total Daily Dose	CMDOSTOT	Total daily dose taken.	Record the total dose of medication taken daily.	In some clinical trials (such as Phase I), individual doses are more likely to be collected. In clinical trials when dosing data do not need to be that precise, e.g., in later phase trials (such as Phase IV/post marketing trials), the total daily dose may be all that is collected. For general medication, it is not recommended to use "Total Daily Dose". Instead, this can be calculated or derived from other fields such as Units, Dose, and Frequency to avoid confusion and calculation by the clinical site.	Optional
10	Unit	CMDOSU	This is the unit associated with the dose of medication taken per administration of a total daily dose *(e.g., "mg" in "2mg three times per day)*. {UNIT} (See Section 2.2.)	Record the dose unit of the dose of medication taken *(e.g., mg.)*.	When sponsors collect data for amount of dose taken *(i.e., "Dose", "Total Daily Dose", "Unit")* must be collected as well.	Optional
11	Dose Form	CMDOSFRM	Name of the pharmaceutical dosage form *(e.g., tablets, capsules, syrup)* of delivery for the drug. {FRM} (See Section 2.2.)	Record the pharmaceutical dosage form *(e.g., tablets, capsules, syrup)* of delivery for the medication taken.	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.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
12	Frequency	CMDOSFRQ	How often the medication was taken *(e.g., BID, every other week, PRN).* {FREQ} (See Section 2.2.)	Record how often the medication or therapy was taken. *(e.g., BID, every other week, PRN).*	When collected, the recommendation is to collect dosing information in separate fields for specific and consistent data collection and to enable programmatically utilizing these data for analysis. See below for the rest of the dosing information components (Dose per Administration, and Unit.)	Optional
13	Route	CMROUTE	Identifies the route of administration of the drug. {ROUTE} (See Section 2.2.)	Provide the route of administration for the drug.	This additional information may be important to collect on the CRF when the sponsor would want to capture a medication's route of administration for purposes such as coding and the medication may have more than one route. Some companies may use route in coding medications to be able to choose a precise preferred name and ATC code.	Recommended/ Conditional
14	Start Date	**CMSTDAT**	Date when the medication was first taken.	•Record the date the medication or therapy was first taken using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section. •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 taken during the study are expected to have a complete start date. •Prior medications that are exclusionary should have both a start and end date	The preferred method is to collect a complete Start Date. Partial dates *(i.e., providing year only)* for medications started a considerable amount of time prior to the start of study are acceptable. **For the SDTM-based dataset,** the SDTMIG variable CMSTDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into CMSTDTC using the ISO 8601 format.	Highly Recommended
15	Mark if taken prior to study	**CMPRIOR**	To determine if medications were taken prior to study start.	Indicate if this medication or therapy was started before the study or during the study.	If instead of Start Date, information such as BEFORE or DURING or AFTER is collected, this information is derived in the CMSTRF variable.	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
16	Start Time	**CMSTTIM** *(Note: If collected, will be used to derive* CMSTDTC.*)*	Time the medication was started.	Record the time (as complete as possible) that the medication or therapy was started. For more detail see the Best Practice section.	Recommend collecting the time a medication was started when a protocol or data collection scenarios supports it. Typically, a start time is not collected unless the subject is under the direct care of the site at the time a medication is taken. **For the SDTM-based dataset,** the SDTMIG variable CMSTDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into CMSTDTC using the ISO 8601 format.	Recommended/ Conditional
17	End Date	**CMENDAT**	Date that the subject stopped taking the medication or therapy.	Record the date the subject stopped taking the medication or therapy using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section. If the subject has not stopped taking the medication leave this field blank.	The assumption is that sponsors should either have a complete end date or will indicate that the medication or therapy was ongoing at the end of the study. **For the SDTM-based dataset**, the SDTMIG variable CMENDTC is derived by concatenating CDASH End Date and Time (if time is collected) into CMENDTC using the ISO 8601 format.	Highly Recommended
18	Mark if Ongoing	**CMONGO**	Indicates medication or therapy is ongoing when no End Date is provided. {NY} (See Section 2.2.)	Record the medication or therapy as ongoing if the subject has not stopped taking the medication or therapy at the time of data collection and the end date should be left blank.	This box should be checked to indicate that the medication or therapy has not stopped at the time of data collection. At study completion, it is expected that every reported medication or therapy should have either End Date or be checked as Ongoing, but not both. This is not a direct mapping to CMENRF. The date of data collection in conjunction with end date and the ongoing check box would determine how CMENRF will be populated.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
19	End Time	CMENTIM	Time when the subject stopped taking the medication or therapy.	Record the time (as complete as possible) that the medication was stopped. For more detail see the Best Practice section.	Recommend collecting the time a medication was ended when a protocol or data collection scenarios supports it. Typically, an end time is not collected unless the subject is under the direct care of the site at the time a medication is stopped. **For the SDTM-based dataset**, the SDTMIG variable CMENDTC is derived by concatenating CDASH End Date and Time (if time is collected) into CMENDTC using the ISO 8601 format.	Recommended/ Conditional

5.6. Demographics – DM (Special Purpose)

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

5.6.1. Collection of Age vs. Date of Birth

The DM Domain Team recognizes that sponsors could collect the age or date of birth of the subject, or both. We recognize that knowing the age at a given date leaves the sponsor with a window of uncertainty of, at most, 366 days if the age needs to be recalculated for a date which is different than the date the age was collected. We recognize that knowing the precise date of birth provides the ability to accurately calculate an age for any date. We further recognize that a precise (and complete) date of birth may be seen as too identifying for some privacy oversight boards or governmental regulators. In looking for a solution, we recognize that SDTM allows for the reporting of dates with the amount of precision that was collected (e.g., year only, year + month, year + month + day, year + month + day + time) and that if we treat the components of the date of birth separately we could provide the mechanism to collect data that would leave a smaller window of uncertainty. This solution requires the collection of the year and month of birth, makes the collection of day conditional and the collection of time of birth as optional (such as when needed for infant, neonatal or pediatric studies). This approach would minimally collect sufficient data about the date of birth which would give a window of uncertainty of, at most, 31 days for all age calculations.

The DM Domain Team concluded that, by identifying the component parts of a complete SDTMIG variable BRTHDTC (year + month + day +/- time of birth), we could provide a solution which balances the collection of meaningful analytical source data with meeting privacy requirements.

The DM Domain Team's preference is to collect the date of birth (minimally birth year and birth month) and derive age, rather than collecting age, even when there are privacy concerns with collecting the complete date of birth. This approach does not disallow the collection of age, it merely makes age an optionally collected variable.

The DM Domain Team recommends collecting the components of a full date of birth as follows: Year + Month +/- Day +/- Time of birth. The design of the CRF should place the fields to be collected together, but they may be electronically stored together or separately, however the entry and storage is best managed. If entered or stored separately, the date of birth values collected may be concatenated into a reportable date, with possibly a lesser degree of precision than a complete date. The sponsor should be able use the concatenated data for analysis. This imprecision should also obscure the personal information enough to protect the privacy of the trial participant and should satisfy regulatory or privacy boards that oversee the collection of these data.

When the mandatory "birth year" and "birth month" components are collected but the conditional "birth day" is not collected the sponsor may report the date in ISO 8601 structure (compliant with SDTM) and the BRTHDTC variable would be created by populating the year and month components of ISO 8601, but omitting the day.

5.6.2. Collection of Sex, Ethnicity and Race

The collection of some demographics data are useful to perform simple analyses based upon population stratification. These analyses are based on phenotypic traits of the subjects. The first, and most obvious of these data, is the sex of the subject. This is not to be confused with a genotypic determination of a subjects' chromosomally determined gender, but a less scientifically controlled method of visual determination that HL7 has defined as "administrative sex."

A secondary analysis is often made using the phenotypic race of the subject. The racial determination, as defined by the U.S. Center for Disease Control as "an arbitrary classification based on physical characteristics;...", has historically been seen as a group of peoples based on physical traits such as skin color, cranial or facial features, hair texture, etc. and that these traits were attributed to "...a group of persons related by common descent or heredity" (the second part of the CDC definition). Today most scientists study human genotypic and phenotypic variation using concepts such as "population" and "clinal gradation". Many contend that while racial categorizations may be marked by phenotypic or genotypic traits, the idea of race itself, and actual divisions of persons into races, are social constructs. While genotyping would provide a more scientific approach to categorizing population groups for clinical analysis (safety or efficacy), the demographics domain does not contain these genotyping data, but instead provide a self-reported approach that aligns more closely to the phenotype of the subjects.

The category of ethnicity is similar to race but, as defined by the CDC as an arbitrary classification based on cultural, religious, or linguistic traditions; ethnic traits, background, allegiance, or association. In a fairly heterogeneous country, such as in the U.S., ethnicity data might be useful only to confirm that ethnic groups are not being discriminated against by being unfairly excluded from clinical research. In other more homogenous countries, such as Japan, the ethnicity of subjects might be collected to assure regulators that the results in this ethnic group should be the same as in the rest of the population of the country (or so that data of subjects who were outside of Japan could be used in the same manner as for subjects who are within Japan).

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Date of Birth (and time)	**BRTHDAT**** **or** **BRTHYR** **BRTHMO** **BRTHDY** **BRTHTIM**	A subject's date of birth (with or without the time of birth). The complete Date of Birth is made from the temporal components of Birth Year, Birth Month, Birth Day and Birth Time.	Record the date of birth to the level of precision known *(e.g., day/month/year, year, month/year, etc)*.	The sponsor may choose to database as a single variable BRTHDAT or separate variables for each temporal component of the date/time. If subject has provided written authorization *(i.e., informed consent)* for the reporting of personal information, we consider the reporting of a full and accurate date of birth appropriate. This approach is generally consistent with the privacy laws of most countries. See the Additional Information for Sponsors for each of the temporal components (rows 1a-1d) below. Below are some examples of complete and reduced precision when recording date of birth: • Subjects without birth records might only be able to provide their date of birth to the decade level (reduced precision - imputation may be needed for analyses). • Subjects in countries where privacy rules preclude the collection of personal data containing more detail than the year of birth might only provide date of birth data to the year level (reduced precision - imputation may be needed for analyses). Note: It is recommended that the CRF should be modified for sites in these counties to prevent the clinician from entering the data that would violate the privacy rule *(i.e., gray out the month and day fields on paper or make them inaccessible for entry in an EDC system)*.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
	Date of Birth (and time), ***continued***				• Subjects in most studies would provide date of birth data to the day level of precision. This would provide the expected level of detail to perform age-related analyses (expected precision for analyses requirements). • In studies where the analyses would require more precise knowledge of age, such as pediatric, natal or neo-natal studies, it would be necessary to collect date of birth data to the hour level, even in countries with privacy constraints (expected precision for analyses requirements). Note: Appropriate written authorization from parent or guardian *(i.e., informed consent)* as well as IAB and DPA (Data Protection Authority) approvals may be required in these cases. It is expected that what is collected for BRTHDAT is reported for the SDTM BRTHDTC in the ISO 8601 format. If data are collected In a manner resulting in one of the reduced precision levels noted above, then the reported AGE (SDTM required variable), if not collected on the CRF, should be derived using a documented algorithm that describes how the age was derived and/or imputed for those birth dates collected with reduced precision. (See Section 5.6.1 Collection of Age vs. Date of Birth and also Section 3.4. FAQs on Best Practices for Creating Data Collection Instruments)	
1a	Year of Birth	**BRTHYR**	Year of the subject's birth.	Record the subject's year of birth *(e.g., YYYY, a four digit year).*	Year of Birth is the collected variable used for recording the year component of the "Date of Birth". (See Section 5.6.1 Collection of Age vs. Date of Birth and also Section 3.4. FAQs on Best Practices for Creating Data Collection Instruments)	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1b	Month of Birth	**BRTHMO**	Text value for the month of the subject's birth.	Record the subject's month of birth *[e.g., (in local language short month format) (JAN-DEC) or (ENE-DIE) or (JAN-DEZ), etc.]*.	Month of Birth is the collected variable used for recording the month component of the "Date of Birth". The month of birth should be collected unless an Ethics Committee or local Data Protection Authorities (DPA) disagrees with the collection of the complete date of birth due to privacy concerns. In this case it might be best to omit this component of the "Date of Birth" to assuage those concerns. (See Section 5.6.1 Collection of Age vs. Date of Birth and also Section 3.4. FAQs on Best Practices for Creating Data Collection Instruments)	Recommended/ Conditional
1c	Day of Birth	**BRTHDY**	Numeric day of the month of the subject's birth.	Record the subject's day of birth *(e.g., 01-31)*.	Day of Birth is the collected variable used for recording the day component of the "Date of Birth". The day of birth should be collected unless an Ethics Committee or local Data Protection Authorities (DPA) disagrees with the collection of the complete date of birth due to privacy concerns. In this case it might be best to omit this component of the "Date of Birth" to assuage those concerns. (See Section 5.6.1 Collection of Age vs. Date of Birth and also Section 3.4. FAQs on Best Practices for Creating Data Collection Instruments)	Recommended/ Conditional
1d	Time of Birth	**BRTHTIM**	Time of subject's birth.	Record the time of birth (as completely as possible). For more detail see the Best Practice section.	The level of detail collected by Time of Birth may be necessary for analysis for some pediatric, natal or neonatal studies. (See Section 5.6.1 Collection of Age vs. Date of Birth and also Section 3.4. FAQs on Best Practices for Creating Data Collection Instruments)	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
2	Age	AGE	Numeric age of subject.	Record age of the subject.	If Age is collected, it should be collected as a number and, to be correctly interpreted, the age value needs to be associated to a variable for the Age Unit. It may be necessary to know when the age was collected as an age may need to be recalculated for analysis, such as deriving age at a reference start time (RFSTDTC for SDTM). If AGE is collected, then it is recommended that the date of collection also be recorded, either separately or by association to the date of the visit. (See Section 5.6.1 Collection of Age vs. Date of Birth)	Optional
3	Age Units	AGEU	Those units of time that are routinely used to express the age of a person. (NCI) {AGEU} (See Section 2.2.)	Record the appropriate age unit *(e.g., years, months, weeks, etc.)*.	If Age is captured on the CRF, the age unit must be known to make the "Age" value meaningful. The age unit might be collected on the CRF, in those cases where the protocol allows for any age group, or it may be pre-printed on the CRF (typically with the unit of "years"). (See Section 5.6.1 Collection of Age vs. Date of Birth)	Optional
4a	Today's date	**DMDAT**	Date of collection.	Record the date the demographics data were collected in the CDASH-recommended date format *(e.g., 08-AUG-2008)*.	The date of collection may be derived from the date of visit and if so, a separate date field is not needed. **For the SDTM-based dataset**, the SDTMIG variable DMDTC is derived by formatting the CDASH Date of collection into DMDTC using the ISO 8601 format. (See AGE Additional Information for Sponsors.)	Recommended/ Conditional
5	Sex	SEX	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} (See Section 2.2.)	Record the appropriate sex *(e.g., female, male)*.	Collect the subject's sex or gender, as reported by subject or caretaker. This is the self-reported sex of the individual and/or is the clinician's assignment based on a physical examination. This is a phenotypic assessment and a genotypic assessment (see Section 5.6.2 Collecting Sex, Ethnicity and Race).	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	Ethnicity	ETHNIC	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 (NCI – CDISC Definition). {ETHNIC} (See Section 2.2.)	Study participants should self-report ethnicity, with ethnicity being asked about before race.	If more detailed characterizations of ethnicity are collected to enhance data quality and consistency, it is recommended that they be "collapsible" up to the two categories for reportable ethnicity, as needed for reporting to FDA under its guidance. **Other regulatory bodies may expect the reporting of ethnicity values (different than the US FDA) which more appropriately reflect the population of their areas *(e.g., Japanese ancestry for MHLW reporting to Japan)*. These may be collected as an extension to the suggested NCI-CDISC code list.**	Recommended/ Conditional
7	Race	RACE *Note: If multiple races are collected, an alternate sponsor-defined variable structure would be required.*	An arbitrary classification based on physical characteristics; a group of persons related by common descent or heredity (U.S. Center for Disease Control).	Study participants should self-report race, with race being asked about after ethnicity. (The FDA guidance suggests "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: -American Indian or Alaska Native -Asian -Black or African American* -Native Hawaiian or Other Pacific Islander -White *For studies where data are collected outside the US, the recommended categories are the same except for "Black" instead of "Black or African American". 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 race, as well as the two categories for reportable 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.	Recommended/ Conditional

5.7. Disposition – DS (Events)

The DS Domain Team took as its remit the extensive consideration of only disposition events, but was also requested to consider protocol milestones. We note that the DS domain allows for the documentation (and submission) of the completion of protocol milestones (e.g., informed consent obtained, randomized). The DS Domain Team has not considered the specification of CRF questions (or "mini CRF modules") to capture protocol milestones, but accepts that such questions may be included in appropriate places in the CRF (e.g., the date of informed consent is typically collected on the same CRF page as demography data but is mapped for submission to the DS domain) for those sponsors who desire to formally document the completion of protocol milestones.

The DS Domain Team held extensive discussions around the vocabulary to be used in a controlled terminology list for "Reason for discontinuation", basing these discussions on the list already published by the CDISC Terminology group. The DS Domain Team will continue to work to agree upon recommendations to be discussed at a later date with the Terminology group.

	Data Collection Field	**Variable Name (CDASH variable name shaded)**	**Definition**	**Case Report Form Completion Instructions**	**Additional Information for Sponsors**	**CDASH Core**
1	Trial Epoch	EPOCH	Trial epoch *(e.g., trial cycle, phase, end of study, etc.)* for which subject disposition is being collected.	(Typically, the trial epoch will be pre-printed on the CRF as the title of the page; however, for those companies whose standard CRF module includes a "pick-list" of epochs, the following instruction is given). Check the <*epoch, or insert more appropriate wording*> for which disposition is being recorded.	Typically, the trial epoch will be pre-printed on the CRF as the title of the page; however, some companies have a standard CRF module that includes a "pick-list" of epochs. *NOTE: See SDTMIG for further information regarding EPOCH.*	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
2	Subject Status	DSDECOD ***And*** DSTERM	Standardized Disposition Term {NCOMPLT} (See Section 2.2.) ***And*** Reported term for the Disposition Event of the subject at a selected trial epoch *Record the subject's status at <insert text corresponding to the selected trial epoch>. If the subject discontinued prematurely, record the primary reason for discontinuation*	Document the subject's status at *<insert text corresponding to the selected trial epoch>*. If the subject discontinued prematurely, record the primary reason for discontinuation.	Controlled terminology is available for DSDECOD, and we strongly recommend that it be used (the current, approved controlled terminology list is under discussion for completeness, accuracy, and extensibility). The Subject Status data collection field should be presented on the CRF as a check box linked to an item from the approved controlled terminology list (DSDECOD). For those companies that wish to collect sponsor- and/or study-specific reasons for discontinuation (DSTERM), we recommend that these reasons be pre-printed on the CRF, with check boxes for completion wherever possible, as sub-categories of the appropriate DSDECOD item. However, we recommend limiting the use of sponsor- and study-specific reasons in order to promote consistent use of terminology and hence permit the combination of data across multiple sponsors. In some circumstances (e.g. DSDECOD = "Withdrawal by subject" or "Other"), where additional information may be valuable but where it may not be possible to specify sub-categories explicitly, "specify" lines may be inserted next to the appropriate controlled terminology items to permit this information to be collected. The controlled terminology list may be filtered to omit terms that are not applicable for a study or particular milestone.[2]	Highly Recommended

[2] The controlled terminology item "Completed" may be omitted if completion is not possible due to study design; "Completed" should be clearly defined either on the CRF or in CRF Completion Instructions (in the latter case, preferably on the facing page to the CRF (for paper CRFs), or in a pop-up window on the screen (for electronic CRFs)); "Completed" should be defined in the protocol, and the definition provided in the CRF or CRF Completion Instructions must be consistent with the contents of the protocol; "Completed" should be separated from the other terms (reasons for non-completion) in the CRF lay-out in order to re-emphasize its importance

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
3	Date of Completion or Discontinuation	**DSSTDAT**	The date that the subject completed the selected trial epoch, or the date that the subject discontinued from the selected trial epoch, using the CDASH recommended collection date format.	Record the date that the subject completed the *<epoch, or insert more appropriate wording>* as defined in the protocol and/or CRF Completion Instructions using the CDASH recommended collection date format. If the subject did not complete the *<epoch, or insert more appropriate wording>*, record the date as defined in the protocol and/or CRF Completion Instructions using the CDASH-recommended date format *(e.g., 08-AUG-2008)* For more detail see the Best Practice section.	Define in the protocol and/or CRF Completion Instructions the criteria for completion of each trial epoch for which a disposition CRF will be provided. Define also the date of completion or discontinuation. Only collect the date of completion or discontinuation on the disposition CRF module if the same information is not being collected on another CRF module. For example, if the date of the last dose is defined to mark the end of the Treatment Phase epoch, and is collected on the Exposure form, then this field would not be collected on the Disposition CRF module. If not collected elsewhere, this variable should be collected on the Disposition CRF module. **For the SDTM-based dataset,** the SDTMIG variable DSSTDTC is derived by concatenating CDASH Date and Time of Completion or Discontinuation (if time is collected) into DSSTDTC using the ISO 8601 format.	Recommended / Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
4	Time of Completion or Discontinuation	**DSSTTIM**	The time that the subject completed the selected trial epoch, or the time that the subject discontinued from the selected trial epoch.	Record the time (as complete as possible) that the subject completed the selected trial epoch as defined in the protocol and/or CRF Completion Instructions. If the subject did not complete the selected trial epoch, record the time (as complete as possible) as defined in the protocol and/or CRF Completion Instructions. For more detail see the Best Practice section.	Define in the protocol and/or CRF Completion Instructions the criteria for completion of each trial epoch for which a disposition CRF will be provided. Define also the date of completion or discontinuation. Collecting the time of completion or discontinuation 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 time be collected unless the subject is under the direct care of the site at the time of the event. Only collect the time of completion or discontinuation on the disposition CRF module if the same information is not being collected on another CRF module. For example, if the time of the last dose is defined to mark the end of the Treatment Phase epoch, and is collected on the Drug Exposure form, then this field would not be collected on the Disposition CRF module. **For the SDTM-based dataset,** the SDTMIG variable DSSTDTC is derived by concatenating CDASH Date and Time of Completion or Discontinuation (if time is collected) into DSSTDTC using the ISO 8601 format.	Optional
5	Was treatment unblinded by the site?	**DSUNBLND**	Identifies in a blinded trial whether or not the subject's blind was broken by the site. *Was the subject's treatment assignment unblinded by the site?*	Was the subject's treatment assignment unblinded by the site?	None.	Optional
6	Will the subject continue?	**DSCONT**	Plan for subject continuation to the next phase of the trial or another related trial at the time of completion of the CRF.	To the best of your knowledge, record if the subject will be continuing to *<the next phase of this trial or another related trial>* (sponsor to specify as appropriate).	Sponsor should specify what the next phase of the trial or the related trial is.	Optional
7	Next trial epoch or new trial subject will be entering	**DSNEXT**	Identifies the trial epoch or new trial in which the subject will participate.	Record the trial *<epoch or trial identifier>* (sponsor to specify as appropriate) if the subject is continuing.	Sponsor should specify what the next phase of the trial or the related trial is.	Optional

5.8. Drug Accountability – DA (Findings)

The aim of the CDASH Drug Accountability proposal is to define the variables needed to assess drug accountability for clinical trial subjects. The Drug Accountability variables are sometimes used to calculate the subject's compliance with the study treatment, however, in most study designs and depending on the drug under study, this may not provide the most accurate information as medication that is not returned may not necessarily have been consumed by the subject, thereby giving a false estimate of compliance. In addition, the SDTMIG standard separates drug accountability from compliance and treats each differently.

This proposal has pro-actively included the SDTMIG variables that are planned to appear in the SDTMIG 3.1.2. The name of the study treatment (DATEST values) can be pre-specified on the CRF if the data are collected in a horizontal format. SDTMIG states "1 record per drug accountability finding per subject". The combined use of SDTMIG variables provides the ability to uniquely identify findings.

The term "dispensed" refers to when the test article/study product is given to the subject. This is independent of other dosing conditions specified in the protocol.

The inclusion of a Drug Accountability CRF/eCRF is optional. The DA Domain Team recommends that this data collection instrument not be used for single dose studies. The Domain Team discussed various drug accountability scenarios for single dose studies and concluded that this standard would be of limited value for studies with a single dose.

The proposal for Drug Accountability does not include recommendations for devices. However, it is our understanding that the following information is typically collected. This information is provided for reference purposes only:

- Model number
- Serial, Lot or Batch Number
- Receipt date
- Name of person receiving shipment
- Date used
- Subject ID
- Date returned to sponsor
- Reason for return to sponsor
- Date of disposal (if permitted)
- If disposed, method of disposal
- Person returning or method of disposing

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Date Study Treatment Dispensed	**DADDAT**	Date the study treatment was dispensed.	Record the exact date the study treatment was dispensed, using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	The date study treatment dispensed should be recorded for each dispensation for a study with multiple periods or multiple products dispensed. **For the SDTM-based dataset,** the SDTMIG variable DADTC is derived by putting the CDASH Date Study Treatment Dispensed into DADTC using the ISO 8601 format.	Recommended / Conditional
2	Study Treatment Dispensed or Returned	DATEST	Verbatim name, corresponding to the topic variable, of the test or examination used to obtain the drug accountability assessment *(e.g., dispensed, returned).* {DATEST and DATESTCD} (See Section 2.2.)	Not applicable.	*Note: DATEST must be used in concert with DAORRES and DAORRESU to describe these distinct pieces of data.*	Highly Recommended
3	Results of Study Treatment Dispensed or Returned	DAORRES	Result of the Drug Accountability assessment as originally dispensed *(i.e., actual amount).*	Record the actual amount of study treatment dispensed.	For a study with multiple periods or multiple products dispensed, drug accountability should be assessed for each dispensation. In this case, a sequence number or a group ID should be used to tie together a block of related records and to link dispensed product to returned product.	Highly Recommended
4	Units of Study Treatment Dispensed or Returned	DAORRESU	Unit for DAORRES *(i.e., tablets).* {UNIT} (See Section 2.2.)	Record the units in which the study treatment was dispensed.	Unit of product dispensed *(i.e., tablets).* The unit will need to be pre-printed on the CRF or a field provided on the CRF to capture it.	Highly Recommended
5	Date Study Treatment Returned	**DARDAT**	Date that the study treatment was returned.	Record the exact date the study treatment was returned, using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	The date study treatment returned should be recorded for each dispensation for a study with multiple periods or multiple products dispensed. If there is only one dose dispensed at a single time the collection of this data are not applicable. **For the SDTM-based dataset,** the SDTMIG variable DADTC is derived by putting the CDASH Date Study Treatment Returned into DADTC using the ISO 8601 format.	Recommended / Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	Study Treatment Category	DACAT	Used to define a categorization level for a group of related records.	Record the type of study treatment dispensed/returned *(i.e., Study Medication, Comparator, Placebo).*	Not applicable.	Optional
7	Study Treatment Sub-category	DASCAT	Used to define a further categorization level for a group of related records.	Record the name of the study treatment dispensed/returned *(i.e., Drug A, Drug B, Placebo).*	Not applicable.	Optional

5.9. ECG Test Results – EG (Findings)

The EG Domain Team opted to not specify which ECG measurements should be collected as this is a medical and scientific decision that should be based on the needs of the protocol.

The tables below are provided for three different scenarios.

Scenario 1: **Central reading:** In this scenario, results are captured directly by an electronic device and transmitted separately, or read by a central vendor – not recorded on the CRF. The CRF is used to aid in reconciliation of the electronic data.

Scenario 2: **Local reading:** In this scenario, subject ECGs are performed and analyzed, and then the results are reported directly on the CRF.

Scenario 3: **Central reading with Clinical Significance Assessment and/or Overall Interpretation:** In this scenario results are captured directly by an electronic device and provided directly to the sponsor and also to the investigator for assessment of clinical significance of abnormal values or an overall interpretation of the results to be recorded on the CRF. The specific results used to make this assessment are not recorded on the CRF but instead are captured in the electronic data.

5.9.1. Scenario 1: Central reading: ECG results are captured directly by an electronic device and transmitted separately or read centrally – not recorded on the CRF.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Indicate if ECG was performed	EGPERF	Status of whether or not ECG was done. {NY} (See Section 2.2.)	Indicate whether or not ECG was done.	This may be implemented for an entire ECG or on a test-by-test basis This is intended to be used as a data management tool to verify that results missing from the electronic transfer were intentional. **For the SDTM-based dataset,** the SDTMIG variable EGSTAT can be derived from EGPERF.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
2	ECG Reference ID	EGREFID	Internal or external identifier.	Record the identifier number assigned.	This can be used to confirm that the appropriate data record is present in the electronic transfer if this reference ID happens to be available to the site at the time of collection *(*e.g., *UUID for external waveform file, session number automatically generated by electronic equipment).*	Optional
3	Method of ECG	EGMETHOD	Method used to measure ECG. *What was the position of the subject during the ECG?* {EGMETHOD} (See Section 2.2.)	Record the method used to measure ECG.	Results may be affected by whether conditions for ECG as specified in the protocol were properly met. One possible condition is the method used to collect the ECG data *(e.g., 12-Lead or 1-Lead).* If the protocol requires this type of information, then this question may be included to confirm that the method used matches the protocol. The following are examples of when it is not necessary to collect these data on the CRF: •Method of ECG is provided as part of the electronic data, or •Method of ECG is not pertinent to the protocol, or •The protocol specifies only one possible method for collecting ECG measurements and the sponsor does not feel there is significant risk of the sites performing the ECG using the incorrect method	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
4	Position of the Subject	EGPOS	Position of the subject during the ECG measurement. *What was the position of the subject during the ECG?* {POSITION} (See Section 2.2.)	Record the position of the subject during the ECG.	Results may be affected by whether conditions for ECG as specified in the protocol were properly met. One common condition is the subject's position *(e.g., Supine, Standing)*. If the protocol requires this type of information, then this question may be included to confirm that the subject's position matches the protocol. The following are examples of when it is not necessary to collect these data on the CRF: •Position of the subject is provided as part of the electronic data, or •Position of the subject is not pertinent to the protocol, or •The protocol specifies only one possible position and the sponsor does not feel there is significant risk of the sites performing the ECG with the subject in the wrong position	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
5	Date of ECG	**EGDAT**	Date of ECG.	Record the date ECG was done using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	A complete date is expected. The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required. Intended for reconciliation purposes. If electronic data are being supplied continuously and in real time to the sites, then collecting the date on the CRF for reconciliation may not be needed. Likewise, if a sponsor's process considers the date electronically created by the ECG equipment as the source data then collecting this field is not necessary. If Date of ECG is not collected, it is still recommended to confirm that the electronic data contain measurements for each visit where an ECG was done. **For the SDTM-based dataset,** the SDTMIG variable EGDTC is derived by concatenating CDASH Date and Time of ECG (if time is collected) into EGDTC using the ISO 8601 format.	Recommended / Conditional
6	Planned Time Point	EGTPT	Text description of planned time point when measurements should be taken for use when multiple sequential assessments are done.	Record the time point labels for when the ECG test should be taken, if not pre-printed on the CRF.	Planned time point would be needed to differentiate for multiple sequential assessments. It is recommended that time points should be pre-printed on the CRF rather than collected in a field that requires the site to enter text. If ECG is not being done at multiple time points within a visit, do not include this item on the CRF.	Recommended / Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
7	Time of ECG	EGTIM	Time of ECG.	Record the time the ECG was done (as complete as possible). For more detail see the Best Practice section.	Especially important when multiple assessments are done on one day. Intended for reconciliation purposes. If electronic data are being supplied continuously and in real time to the sites, then collecting the time on the CRF for reconciliation may not be needed. Likewise, if a sponsor's process considers the time electronically created by the ECG equipment as the source data then collecting this field is not necessary. If Time of ECG is not collected, it is still recommended to confirm that the electronic data contain measurements for each time point where an ECG was done. **For the SDTM-based dataset,** the SDTMIG variable EGDTC is derived by concatenating CDASH Date and Time of ECG (if time is collected) into EGDTC using the ISO 8601 format.	Recommended / Conditional

5.9.2. Scenario 2: Local reading: ECGs are performed and analyzed and results are reported directly on the CRF

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Indicate if ECG was performed	**EGPERF**	Status of whether or not ECG was done. {NY} (See Section 2.2.)	Indicate whether or not ECG was done.	This may be implemented for an entire ECG, or on a test-by-test basis. This is intended to be used as a data management tool to verify that results missing from the CRF are intentionally missing. **For the SDTM-based dataset,** the SDTMIG variable EGSTAT can be derived from EGPERF.	Highly Recommended
2	Method of ECG	EGMETHOD	Method used to measure ECG. {EGMETHOD} (See Section 2.2.)	Record the method used to measure ECG.	Results may be affected by whether conditions for ECG as specified in the protocol were properly met. One possible condition is the method used to collect the ECG data *(e.g., 12-Lead or 1-Lead)*. If the protocol requires this type of information, then this question may be included to confirm that the method used matches the protocol. The following are examples of when it is not necessary to collect these data on the CRF: •Method of ECG is provided as part of the electronic data, or •Method of ECG is not pertinent to the protocol, or •The protocol specifies only one possible method for collecting ECG measurements and the sponsor does not feel there is significant risk of the sites performing the ECG using the incorrect method	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
3	Position of the Subject	EGPOS	Position of the subject during the ECG measurement. *What was the position of the subject during the ECG?* {POSITION} (See Section 2.2.)	Record the position of the subject during the ECG.	Results may be affected by whether conditions for ECG as specified in the protocol were properly met. One common condition is the subject's position *(e.g., Supine, Standing)*. If the protocol requires this type of information, then this question may be included to confirm that the subject's position matches the protocol. The following are examples of when it is not necessary to collect these data on the CRF: •Position of the Subject is provided as part of the electronic data, or •Position of the Subject is not pertinent to the protocol, or •The protocol specifies only one possible position and the sponsor does not feel there is significant risk of the sites performing the ECG with the subject in the wrong position	Optional
4	Date of ECG	**EGDAT**	Date of ECG.	Record the date ECG was done using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	A complete date is expected for ECGs that occur during the study. The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required. **For the SDTM-based dataset,** the SDTMIG variable EGDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into EGDTC using the ISO 8601 format.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
5	Planned Time Point	EGTPT	Text description of planned time point when measurements should be taken for use when multiple sequential assessments are done.	Record the time point labels for when the ECG test should be taken, if not pre-printed on the CRF.	Planned time point would be needed to differentiate for multiple sequential assessments. It is recommended that time points should be pre-printed on the CRF rather than collected in a field that requires the site to enter text. If ECG is not being done at multiple time points within a visit, do not include this item on the CRF.	Recommended / Conditional
6	Time of ECG	**EGTIM**	Time of ECG.	Record the time the ECG was done (as complete as possible). For more detail see the Best Practice section.	Especially important when multiple assessments are done on one day. **For the SDTM-based dataset,** the SDTMIG variable EGDTC is derived by concatenating CDASH Date and Time of ECG (if time is collected) into EGDTC using the ISO 8601 format.	Recommended / Conditional
7	Test Name	EGTEST	Descriptive name of the measurement or finding. {EGTEST} (See Section 2.2.)	Record the name of the ECG measurement or finding, if not pre-printed on the CRF.	Required to identify which ECG test the result is for. If specific tests are required, these should be pre-printed on the CRF rather than collected in a field that requires the site to enter text.	Highly Recommended
8	Test Result	EGORRES	Result of the measurement or finding as originally received or collected.	Record test results, interpretations or findings.	Both quantitative results and interpretive findings or summaries may be recorded here.	Highly Recommended
9	Units	EGORRESU	Original units in which the data were collected. {UNIT} (See Section 2.2.)	Record the original units in which these data were collected, if not pre-printed on CRF.	May be included if quantitative results are recorded. Because units for quantitative ECG results are typically limited *(e.g., seconds, milliseconds or beats per minute)*, units should be pre-printed on the CRF rather than having the sites record the units. This item is not necessary for qualitative results.	Recommended / Conditional
10	Clinical Significance	**EGCLSIG**	Whether ECG results were clinically significant. *Is the result clinically significant?* {NY} (See Section 2.2.)	Record whether ECG results were clinically significant.	May be included if required by the protocol. Could apply to specific measurements or to overall interpretation.	Optional

5.9.3. Scenario 3: Central processing but CRF includes site assessment of clinical significance and/or overall interpretation. In this scenario, data are sent for central processing. Results are returned to the sites, and the sites complete a CRF page of clinical significance for any abnormal / unexpected values and/or record an overall interpretation of the results. The actual testing results are transmitted electronically, as in scenario 1, but the CRF includes the data necessary to identify and rate the clinical significance of the abnormal results.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Indicate if ECG was performed	**EGPERF**	Status of whether or not ECG was done. {NY} (See Section 2.2.)	Indicate whether or not ECG was done.	This may be implemented for an entire ECG, or on a test-by-test basis. This is intended to be used as a data management tool to verify results provided. **For the SDTM-based dataset,** the SDTMIG variable EGSTAT can be derived from EGPERF.	Highly Recommended
2	ECG Reference ID	EGREFID	Internal or external identifier.	Record the identifier number assigned.	This can be used to confirm that the appropriate data record is present in the electronic transfer if this reference ID happens to be available to the site at the time of collection. It can also be used to link the clinical significance assessment to the proper record in the electronic data. *(e.g., UUID for external waveform file, session number automatically generated by electronic equipment).*	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
3	Method of ECG	EGMETHOD	Method used to measure ECG. {EGMETHOD} (See Section 2.2.)	Record the method used to measure ECG.	Results may be affected by whether conditions for ECG as specified in the protocol were properly met. One possible condition is the method used to collect the ECG data *(e.g., 12-Lead or 1-Lead)*. If the protocol requires this type of information, then this question may be included to confirm that the method used matches the protocol. The following are examples of when it is not necessary to collect these data on the CRF: •Method of ECG is provided as part of the electronic data, or •Method of ECG is not pertinent to the protocol, or •The protocol specifies only one possible method for collecting ECG measurements and the sponsor does not feel there is significant risk of the sites performing the ECG using the incorrect method	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
4	Position of the Subject	EGPOS	Position of the subject during the ECG measurement. *What was the position of the subject during the ECG?* {POSITION} (See Section 2.2.)	Record the position of the subject during the ECG.	Results may be affected by whether conditions for ECG as specified in the protocol were properly met. One common condition is the subject's position *(e.g., Supine, Standing)*. If the protocol requires this type of information, then this question may be included to confirm that the subject's position matches the protocol. The following are examples of when it is not necessary to collect these data on the CRF: •Position of the Subject is provided as part of the electronic data, or •Position of the Subject is not pertinent to the protocol, or •The protocol specifies only one possible position and the sponsor does not feel there is significant risk of the sites performing the ECG with the subject in the wrong position	Optional
5	Date of ECG	**EGDAT**	Date of ECG.	Record the date ECG occurred using the CDASH-recommended date format *(i.e., DD-MMM-YYYY)*. For more detail see the Best Practice section.	A complete date is expected It can be used to link the clinical significance assessment to the proper record in the electronic data. The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required. **For the SDTM-based dataset,** the SDTMIG variable EGDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into EGDTC using the ISO 8601 format.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	Planned Time Point	EGTPT	Text description of planned time point when measurements should be taken - for use when multiple sequential assessments are done.	Record the time point labels for when the ECG test should be taken, if not pre-printed on the CRF.	Planned time point would be needed to differentiate for multiple sequential assessments. It is recommended that time points should be pre-printed on the CRF rather than collected in a field that requires the site to enter text. The planned time point can be used to link the clinical significance assessment to the corresponding record in the electronic data. If ECG is not being done at multiple time points within a visit, do not include this item on the CRF.	Recommended / Conditional
7	Time of ECG	**EGTIM**	Time of ECG.	Record the time the ECG was done (as complete as possible). For more detail see the Best Practice section.	Especially important when multiple assessments are done on one day. **For the SDTM-based dataset,** the SDTMIG variable EGDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into EGDTC using the ISO 8601 format.	Recommended / Conditional
8	Test Name	EGTEST	Descriptive name of the measurement or finding. (EGTEST} (See Section 2.2.)	Record the name of the ECG measurement or finding, if not pre-printed on the CRF.	Required to identify which ECG test the result is for. If specific tests are required, these should be pre-printed on the CRF.	Highly Recommended
9	Test Result	EGORRES	Result of the measurement or finding as originally received or collected.	Record test results, interpretations or findings.	Both quantitative results and interpretive findings or summaries may be recorded here. Not required if results are already provided from central vendor. If the investigator is providing an overall interpretation, this interpretation should be collected in this field.	Recommended / Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
10	Units	EGORRESU	Original units in which the data were collected. (UNIT) (See Section 2.2.)	(*If units are not pre-printed on the CRFs)* Record the original units in which these data were collected.	Not required if units are already provided from central vendor. May be included if quantitative results are recorded by the investigator. Because units for quantitative ECG results are typically limited *(e.g., beats per minute, seconds or milliseconds)*, units may be pre-printed on the CRF rather than having the sites record the units. CDISC controlled terminology is available for this field. See the Commonly Used CDISC Controlled Terminology appendix for the most commonly used terms and as well as a link to the full EVS code lists.	Optional
11	Clinical Significance	**EGCLSIG**	Whether ECG results were clinically significant. *Is the result clinically significant?* {NY} (See Section 2.2.)	Record whether ECG results were clinically significant.	Key data collected in this scenario.	Highly Recommended

5.10. Exposure – EX (Interventions)

This proposal includes the SDTMIG-based variables that appear in the SDTMIG 3.1.1. The SDTMIG defines the EX domain model as follows:

"The Exposure domain model records the details of a subject's exposure to protocol-specified study treatment. Study treatment may be any intervention that is prospectively defined as a test material within a study, and is typically but not always supplied to the subject. Examples include but are not limited to placebo, active comparator, and study treatment. Treatments that are not protocol-specified should be recorded in the Concomitant Medications (CM) domain."

The dose variables in this proposal refer to the collection of the "actual dose" rather than the "planned dose".

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Start Date	**EXSTDAT**	Start date of treatment.	Record the exact date of the study treatment administration using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	Date when constant dosing interval of the study treatment started or single administration occurred. **For the SDTM-based dataset,** the SDTMIG variable EXSTDTC is derived by concatenating CDASH Start Date and Time of treatment (if time is collected) into EXSTDTC using the ISO 8601 format.	Highly Recommended
2	Start Time	**EXSTTIM** *(Note: If collected, will be used to derive* EXSTDTC.*)*	Start time of treatment.	Record the time (as complete as possible) when administration of study treatment started. For more detail see the Best Practice section.	Time when study treatment period started. **For the SDTM-based dataset,** the SDTMIG variable EXSTDTC is derived by concatenating CDASH Start Date and Time of treatment (if time is collected) into EXSTDTC using the ISO 8601 format.	Recommended / Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
3	End Date	**EXENDAT**	End date of treatment.	Record the end date or last date of administration of study treatment using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	Date when study treatment period stopped. If start date and end date are not expected to be on the same date, the end date is required. If the trial design indicates that the start and end date are on the same day, the end date is not required since it can be assigned to be equal to the start date. **For the SDTM-based dataset,** the SDTMIG variable EXENDTC is derived by concatenating CDASH End Date and Time of treatment (if time is collected) into EXENDTC using the ISO 8601 format.	Recommended / Conditional
4	End Time	**EXENTIM** *(Note: If collected, will be used to derive* EXENDTC.*)*	End time of treatment.	Record the time, (as complete as possible) when study treatment administration stopped *(e.g., for infusions this is the time when the infusion ended).* For more detail see the Best Practice section.	Time when study treatment "constant dosing interval" ended. **For the SDTM-based dataset,** the SDTMIG variable EXENDTC is derived by concatenating CDASH End Date and Time of treatment (if time is collected) into EXENDTC using the ISO 8601 format.	Recommended / Conditional
5	Dose Amount	EXDOSE	Dose per administration.	Record the dose or amount of study treatment that was administered to/taken by the subject in the period recorded; from the start date/time to the end date/time inclusive.	Dose or amount taken for single administration of study treatment or per constant dosing interval recorded. Dose must be collected if it cannot be derived via other methods *(e.g., derived from randomization data).*	Recommended / Conditional
6	Dose Unit	EXDOSU	Units for EXDOSE. {UNIT} (See Section 2.2.)	Record the unit of dose or amount taken per period recorded *(e.g., ng, mg, or mg/kg).*	Unit of dose or amount taken per "constant dosing interval" recorded. Dose must be collected if it cannot be derived via other methods *(e.g., derived from randomization data).* The unit will need to be pre-printed on the CRF or a field provided on the CRF to capture it.	Recommended / Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
7	Study Treatment Identification Number	EXLOT	EXLOT = Lot Number of the EXTRT product.	Record the reference number that appears on the container holding the study treatment *(e.g., Lot Number).*	Reference number that appears on the container holding the study treatment. Study Treatment Identification Number is a unique number, which provides mapping to Lot Number and possibly the randomization schema. In open label studies, the reference number on the study treatment container could represent an actual Lot Number and should be stored using EXLOT.	Optional
8	Study Treatment Name	EXTRT	Name of the intervention treatment - usually the verbatim name of the study treatment given per single administration or during the "constant dosing interval" for the observation.	Record the name of study treatment.	Name of study treatment that was administered to the subject. This must be collected if it cannot be derived. Variable must always be present in the underlying database, however, it may not be populated until after unblinding.	Recommended / Conditional
9	Dose Adjusted?	**EXDOSADJ**	Confirmation of dose adjustment.	Select either "Yes" or "No" to indicate whether there was a change in dosing.	Will provide a definitive response regarding dose changes.	Optional
10	Reason for Dose Adjustment	EXADJ	Describes reason or explanation of why a dose is adjusted – used only when an adjustment is represented in EXPOSURE dataset. May be used for variations from protocol-specified doses, or changes from expected doses.	If there was a change in dosing, record the reason for change.	Captures reason dose was changed / modified. The reason may be chosen from a select list or entered as free text. The list could include the values: escalated, decrease, delay or interrupted.	Optional
11	Frequency	EXDOSFRQ	Usually expressed as the number of dosings given per a specific interval. {FREQ} (See Section 2.2.)	Record the frequency the study treatment was administered for a defined period of time *(e.g., BID, QID, TID).*	Number of doses given per a specific interval.	Optional
12	Route	EXROUTE	Route of administration for EXTRT. {ROUTE} (See Section 2.2.)	Record the route of administration *(e.g., IV, oral or transdermal)* or enter the appropriate code from the code list.	Route of study treatment administration. This will often be pre-printed on the CRF. This must be collected if it can not be pre-printed or derived from the protocol.	Recommended / Conditional
13	Formulation	EXDOSFRM	Dose form for EXTRT. {FRM} (See Section 2.2.)	Record the formulation *(e.g., solution, tablet, lotion)* or enter the appropriate code from the code list.	Formulation of study treatment. This must be collected if it can not be derived. Variable must always be present in the underlying database.	Recommended / Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
14	Duration of Interruption (including units)	**EXINTP**	Duration of the treatment interruption.	Record the duration of treatment interruption.	Duration of treatment interruption. In some situations, the duration of the interruption may be calculated from the administration start and end times recorded elsewhere in the CRF.	Optional
		EXINTPU	Unit for the duration of treatment interruption. {UNIT} (See Section 2.2.)	Record the unit *(e.g., minutes, hours, days)* for the duration of treatment interruption.	The unit *(e.g., minutes, hours, days)* needs to be collected as a qualifier to the number for duration.	Optional
15	Body Location	EXLOC	Specifies anatomical location of administration. {LOC} (See Section 2.2.)	Record the body location where the study treatment was administered *(e.g., shoulder, hip, arm).*	Location where the study treatment was administered. This may be pre-printed or collected.	Optional
16	Total Volume Administered	**EXVOLT**	Exposure volume amount.	Record the total volume that was administered/given to the subject.	Administration volume that was given to the subject.	Optional
17	Total Volume Administered Unit	**EXVOLTU**	The unit of measure for the exposure volume amount. {UNIT} (See Section 2.2.)	Record the unit of total volume administered/ given to the subject *(e.g., mL).*	Unit of the administration volume *(e.g., mL).*	Optional
18	Flow Rate	**EXFLRT**	Rate of infusion.	Record the Rate of Infusion *(e.g., 10 mL/min. Record "10"as the infusion rate).*	Infusion rate can be used to derive dose.	Optional
19	Flow Rate Unit	**EXFLRTU**	The unit of measure for the rate of infusion. {UNIT} (See Section 2.2.)	Record the unit for the infusion rate *(e.g., mL/min).*	Unit of the infusion rate *(e.g., mL/min).*	Optional
20	Planned Time Point	EXTPT	Planned time point name.	Record the planned time point of study treatment administration *(e.g., 5 minutes post dose).*	Indicates the planned time point of study treatment administration *(e.g., 5 minutes post dose).* This may be pre-printed or collected.	Optional
21	Did subject complete full course of study med?	**EXMEDCMP**	Confirmation point for exposure.	Select either "Yes" or "No" to indicate whether subject has completed the full course of treatment.	Depending on how the study treatment details are collected via the CRF/ eCRF, it may be possible to derive those data.	Optional
22	Planned Dose	EXPDOSE	Planned dose per administration.	Record the dose the subject was scheduled to receive.	Important note: This field must be used in conjunction with "actual dose" EXDOSE since this field captures the planned dose rather than the dose the subject actually received.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
23	Planned Dose Units	EXPDOSEU	Units for EXPDOSE. {UNIT} (See Section 2.2.)	Record the unit of dose or amount planned per period *(e.g., ng, mg, or mg/kg).*	Important note: This field must be used in conjunction with "actual dose" EXDOSE and "actual dose units" EXDOSEU since this field captures the unit of the planned dose rather than the dose the subject actually received.	Optional

5.11. Inclusion / Exclusion Criteria Not Met – IE (Findings)

5.11.1. Collecting IE Data and Mapping to the SDTMIG

The IE Domain Team noted that some of the CRF variables collected may have either a one-to-one mapping to SDTMIG variables, or a many-to-one mapping depending on a particular sponsor company's data collection method. The IE CRF standard recommended in this document is flexible enough to allow a variety of data collection methods that will all map to a single SDTMIG standard.

Since the SDTMIG variables served as the target for collected data, the IE Domain Team referred to CDISC SDTMIG Version 3.1.1, and incorporated the assumptions regarding the IE domain from that Guide into the development of this data collection standard.

The first SDTMIG assumption is that the intent of the IE domain model is to only submit those criteria that cause the subject to be in violation of the Inclusion/Exclusion criteria, not to submit a response to each criterion for each subject. The IE Domain Team recommends that the site be given an entry criteria worksheet to be used for each subject during screening. This worksheet should be considered a source document, used in monitoring activities, and maintained with the subject's site files. The worksheet should identify each entry criterion using a unique identifier which can be easily recorded on the CRF if a subject does not meet that criterion.

The second assumption is that the IE domain is intended to collect only eligibility information for the inclusion and exclusion criteria for entry into a study; not protocol deviations or protocol violations incurred during the course of the study. Any of the CRF fields that were reviewed by the IE Domain Team and determined to be related to protocol deviations or protocol violations were deferred to the DV Domain Team for consideration.

The last assumption that was used in the development of this standard was that enough data need to be collected to satisfy safety concerns and regulatory requirements and to populate or derive the required SDTM-based submission variables. Thus, all SDTMIG variables that are required for submission are either explicitly collected in the CRF or may be derived (e.g., IEORRES, IESTRESC) from the data collected using the Highly Recommended, Recommended/Conditional CDASH variables presented in the table. Specific recommendations for the collection and derivation of data are described in the "Additional Information for Sponsors" column.

5.11.2. Adaptive Trial Design

The IE Domain Team considered the potential for entry criteria to change over the life of a study or project, e.g., when adaptive trial design is used and the recommended approach is designed to more efficiently accommodate changing criteria as the study progresses. CDASH recommends the use of uniquely numbered entry criteria within a study to effectively manage protocol changes and to facilitate both the collection and submission of IE data.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Met All Eligibility Criteria?	IEYN	Response for whether the subject met all the eligibility requirements for this study at the time the subject was enrolled. *Did subject meet all eligibility criteria?* {NY} (See Section 2.2.)	Record "Yes" if all eligibility criteria were met for the study. Record "No" if subject did not meet all criteria at the time the subject was enrolled.	This is a Yes/No question that is intended to be used primarily as a **monitoring and/or data management tool** to verify that the investigator/site reported any entry criteria that were not met. May be used to derive data into IEORRES. **Must be recorded on the CRF.**	Highly Recommended
2	Criterion Identifier[3]	IETESTCD	The identifier associated with the criterion that the subject did not meet. This must be a unique identifier that corresponds to a specific entry criterion[4].	If "No", enter the identifying code for each criterion not met. Record this *only* for the criterion / criteria that this subject did not meet[5]. **Paper**: Record the criterion identifier from the list of inclusion/ exclusion criteria provided by the sponsor. **EDC**: Select the criterion from the pick-list.	This field is required to appear on the CRF, but may be null if all criteria are met. Multiple responses should be allowed on CRF. CDASH recommends that the sponsor determine how many lines are needed on the CRF based on their experience and maximum allowed. This would probably be only 2 or 3 for most studies.	Highly Recommended
3	Criterion	IETEST	The wording of an inclusion or exclusion criterion.	**EDC:** Verify the wording of this criterion.	**EDC:** The primary use of this field would be on an eCRF in an EDC system. This field could be automatically populated when the Criterion Identifier is populated, and then be verified by the PI to ensure the right Identifier was selected. **Paper:** The monitoring process should include a cross-verification of entry criteria against the medical records for each subject to ensure that any criteria not met were recorded on the CRF.	Optional

[3] This variable is only populated in SDTM for those criteria that are not met, and it will only be recorded on the CRF for those criteria that are not met. *Note: The IE Team considered the possibility of some organizations using criteria lists without unique identifiers (i.e. bulleted lists). After the Collaborative Group review of the IE standards, and on the recommendation of the FDA reviewers, the Team decided to remove the alternative approach that was in the Harmonized Version of this document and present a single standard for IE data collection. FDA reviewers recommended that organizations that currently use bulleted lists should move toward using unique identifiers for entry criteria.*

[4] If inclusion and exclusion criteria lists are independently numbered (e.g., inclusion 001-100, exclusion 001-100), then this identifier must include a means of identifying the TYPE of criterion (e.g., I001-I100, E001-E100). The examples provided are only examples; your organization's numbering scheme may be different.

[5] This identifier may be used to derive values into IETEST and IECAT from a protocol definition or other source external to the clinical database, and into IEORRES.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
4	Inclusion or Exclusion?	IECAT	Specifies whether the criterion is inclusion or exclusion.	Record whether the criterion that this subject did not meet was "Inclusion" or "Exclusion". **Checkbox:** Check "Inclusion" or "Exclusion".	Only records for criteria that are not met appear in the IE SDTMIG domain and for those records IECAT must also be populated. This criterion category may be collected on the CRF in a checkbox format, or, it may be included as part of the Criterion Identifier *(e.g., I01, E01)*, or derived from the inclusion / exclusion criteria in the Trial Inclusion (TI) trial dataset, or other protocol definitions external to the clinical database when a unique criterion identifier is recorded in the IETESTCD field.	Optional

5.12. Laboratory Test Results – LB (Findings)

The LB Domain Team opted to not specify which lab parameters should be collected as this is a medical and scientific decision that should be based on the needs of the protocol.

The tables below are provided for three different scenarios.

Scenario 1: **Central processing:** In this scenario, subject samples are taken at site, sent out for processing and results are provided directly to the sponsor. This scenario also applies when results are captured directly via an electronic device – not recorded on the CRF.

Scenario 2: **Local processing:** In this scenario, subject samples are taken and analyzed, and then the results are reported directly on the CRF.

Scenario 3: **Central processing with Clinical Significance Assessment for abnormal values:** In this scenario, subject samples are taken at site, sent out for processing and results are provided directly to the sponsor and also to the investigator for assessment of clinical significance for any abnormal values to be recorded on CRF. This scenario also applies when results are captured directly via an electronic device – not recorded on the CRF.

5.12.1. Scenario 1: Central processing: Where samples are taken at site, but sent out and results are provided separately or where results are captured directly by an electronic device and transmitted separately – not recorded on the CRF. CRF data are captured at the site for tracking/ header reconciliation. The fields for test results are not defined here, as these data are not part of the CRF.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Lab Status	LBPERF	Status of whether or not lab sample was collected or measurement performed.	Indicate whether or not lab sample was collected or measurement performed.	This may be implemented for an entire panel, or on a test-by-test basis. This is intended to be used as a data management tool to verify that missing results are confirmed missing.	Highly Recommended
2	Date of Collection	LBDAT	Date of sample collection.	Record the date when sample collection occurred using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more details see Best Practice Recommendations.	A complete date is expected. The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required. **For the SDTM-based dataset,** the SDTMIG variable LBDTC is derived by concatenating CDASH Date and Time of collection (if time is collected) into LBDTC using the ISO 8601 format.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
3	Time of Collection	**LBTIM** *(Note: If collected, will be used to derive* LBDTC.*)*	Time of sample collection.	Record time of collection (as complete as possible). For more details see Best Practice Recommendations.	Especially important when multiple assessments are done on one day. **For the SDTM-based dataset,** the SDTMIG variable LBDTC is derived by concatenating CDASH Date and Time of collection (if time is collected) into LBDTC using the ISO 8601 format.	Recommended/ Conditional
4	Panel Name	LBCAT LBSCAT	Type of draw / category / panel name. Used to define a category of related records.	Record the lab test category, if not pre-printed on the CRF.	To be included if lab status is collected for each panel *(e.g., HEMATOLOGY, URINALYSIS, CHEMISTRY).* If specific panels are required, these should be pre-printed on the CRF rather than collected in a field that requires the site to enter text.	Recommended/ Conditional
5	Planned Time Point	LBTPT	Text description of planned time point when measurements should be taken for use when multiple sequential assessments are done.	Record the planned time point labels for the lab test, if not pre-printed on the CRF.	Planned time point would be needed to differentiate for multiple sequential assessments. It is recommended that time points should be pre-printed on the CRF rather than collected in a field that requires the site to enter text.	Recommended/ Conditional
6	Protocol-defined testing conditions met	**LBCOND**	Condition imposed on the subject for testing defined in the protocol *(e.g., fasting)*.	Record whether protocol defined testing conditions were met.	The specific testing conditions required should be pre-printed on the CRF, such as "Did subject meet fasting requirements?". Results may be affected by whether conditions for testing were properly met *(e.g., fasting).* This may not be relevant for all tests. **For the SDTM-based dataset,** the SDTMIG variable LBFAST could be derived from LBCOND.	Recommended/ Conditional
7	Accession Number	LBREFID	Internal or external specimen identifier.	Record the sample or accession number assigned.	This can be used to confirm that the appropriate data record is present in the electronic transfer *(e.g., Specimen ID)*	Recommended/ Conditional

5.12.2. Scenario 2: Local processing: When results of sample analysis are reported directly on the CRF.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Lab Status	**LBPERF**	Status of whether or not lab sample was collected or measurement performed.	Indicate whether or not lab sample was collected or measurement performed.	This may be implemented for an entire panel, or on a test-by-test basis. This is intended to be used as a data management tool to verify that missing results are confirmed missing.	Highly Recommended
2	Date of Collection	**LBDAT**	Date of sample collection.	Record the date when sample collection occurred using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more details see Best Practice Recommendations.	A complete date is expected. The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required. **For the SDTM-based dataset,** the SDTMIG variable LBDTC is derived by concatenating CDASH Date and Time of collection (if time is collected) into LBDTC using the ISO 8601 format.	Highly Recommended
3	Time of Collection	**LBTIM** *(Note: If collected, will be used to derive* LBDTC.*)*	Time of sample collection.	Record time of collection (as complete as possible). For more details see Best Practice Recommendations.	Especially important when multiple assessments are done on one day. **For the SDTM-based dataset,** the SDTMIG variable LBDTC is derived by concatenating CDASH Date and Time of collection (if time is collected) into LBDTC using the ISO 8601 format.	Recommended/ Conditional
4	Panel Name	LBCAT LBSCAT	Type of draw / category / panel name. Used to define a category of related records.	Record the lab test category, if not pre-printed on the CRF.	Included as needed for clarity *(e.g., HEMATOLOGY, URINALYSIS, CHEMISTRY).*	Recommended/ Conditional
5	Planned Time Point	LBTPT	Text description of planned time point when measurements should be taken for use when multiple sequential assessments are done.	Record the planned time point labels for the lab test, if not pre-printed on the CRF.	Planned time point would be needed to differentiate for multiple sequential assessments. It is recommended that time points should be pre-printed on the CRF rather than collected in a field that requires the site to enter text.	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	Protocol-defined testing conditions met	**LBCOND**	Condition imposed on the subject for testing defined in the protocol *(e.g., fasting)*.	Record whether protocol defined testing conditions were met.	The specific testing conditions required should be pre-printed on the CRF, such as "Did subject meet fasting requirements?". Results may be affected by whether conditions for testing were properly met *(e.g., fasting)*. This may not be relevant for all tests. **For the SDTM-based dataset,** the SDTMIG variable LBFAST could be derived from LBCOND.	Recommended/ Conditional
7	Sample Status	LBSPCCND	Free or standardized text describing the condition of the specimen.	Record condition of sample.	Results may be affected by whether conditions for sample were properly met *(e.g., HEMOLYZED, ICTERIC, LIPEMIC)*	Recommended/ Conditional
8	Test Name	LBTEST	Verbatim name of the test or examination used to obtain the measurement or finding. Note any test normally performed by a clinical laboratory is considered a lab test. {LBTEST} (See Section 2.2.)	Record the type or name of the lab test, if not pre-printed on the CRF.	Required to identify the test. It is recommended that the test names be pre-printed on the CRF.	Highly Recommended
9	Test Result	LBORRES	Result of the measurement or finding as originally received or collected.	Record test results.	Key data collected.	Highly Recommended
10	Units	LBORRESU	Original units in which the data were collected.	Record the units of the lab test, if not pre-printed on the CRF or captured in an external "lab normal" file.	May be included if not standardized.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
11	Reference Range Lower Limit Numeric Value	LBORNRLO	The lowest continuous numeric value of a given lab result expected in the population of interest. See SDTMIG for additional information.	Record the lower limit of the reference range of the lab test.	LBORNRLO and LBORNRHI should be populated only for continuous results; LBSTNRC should be populated only for non-continuous results. These data may be obtained from the lab or the electronic equipment. These data could be derived from a site or lab specific set of normal ranges stored in a look up table. *NOTE: See SDTMIG for details on mapping on selecting the proper variable name.*	Recommended/ Conditional
12	Reference Range Upper Limit Numeric Value	LBORNRHI	The highest continuous numeric value of a given lab result expected in the population of interest. See SDTMIG for additional information.	Record the upper limit of the reference range of the lab test.		Recommended/ Conditional
13	Reference Range for Character Results in Standard Units	LBSTNRC	The set of categorical lab values expected in the population of interest. See SDTMIG for additional information.	Record the boundaries of reference ranges of the lab test.		Recommended/ Conditional
14	Abnormal Flag	LBNRIND	Reference Range Indicator Indicates where value falls with respect to reference range defined by high and low ranges.	Record whether sample was outside range.	Abnormal flags may be included if not derived or determined programmatically after data collection.	Recommended/ Conditional
15	Clinical Significance	**LBCLSIG**	Whether lab test results were clinically significant.	Record whether lab results were clinically significant.	May be included if required by the protocol.	Recommended/ Conditional
16	Lab Name	LBNAM	Name of lab analyzing sample.	Record the laboratory name.	May be included on CRF if multiple labs are used by a site. If collecting lab names as free text, sponsors might consider developing a LAB ID so that different ways of writing the names of certain labs will not appear in datasets as different labs.	Recommended/ Conditional
17	Accession Number	LBREFID	Internal or external specimen identifier.	Record the sample or accession number assigned.	This can be used to confirm that the appropriate data record is present in the electronic transfer May be included for linking back to samples *(e.g., Specimen ID).*	Recommended/ Conditional

5.12.3. Scenario 3: Central processing but CRF includes site assessment of clinical significance. In this scenario, data are sent for central processing. Results are returned to the sites, and the sites complete a CRF page of clinical significance for any abnormal / unexpected values. The actual testing results are transmitted electronically, as in Scenario 1, but the CRF includes the data necessary to identify and rate the clinical significance of the abnormal results.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Lab Status	**LBPERF**	Status of whether or not lab sample was collected or measurement performed.	Indicate whether or not lab sample was collected or measurement performed.	This may be implemented for an entire panel, or on a test-by-test basis. This is intended to be used as a data management tool to verify that missing results are confirmed missing.	Highly Recommended
2	Date of Collection	**LBDAT**	Date of sample collection.	Record the date when sample collection occurred using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more details see Best Practice Recommendations.	A complete date is expected. The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required. **For the SDTM-based dataset,** the SDTMIG variable LBDTC is derived by concatenating CDASH Date and Time of collection (if time is collected) into LBDTC using the ISO 8601 format.	Highly Recommended
3	Time of Collection	**LBTIM** *(Note: If collected, will be used to derive* LBDTC.*)*	Time of sample collection.	Record time of collection (as complete as possible).	Especially important when multiple assessments are done on one day. **For the SDTM-based dataset,** the SDTMIG variable LBDTC is derived by concatenating CDASH Date and Time of collection (if time is collected) into LBDTC using the ISO 8601 format.	Recommended/ Conditional
4	Panel Name	LBCAT LBSCAT	Type of draw / category / panel name. Used to define a category of related records.	Record the lab test category, if not pre-printed on the CRF.	Optional if already provided from central lab *(e.g., HEMATOLOGY, URINALYSIS, CHEMISTRY)*.	Recommended/ Conditional
5	Planned Time Point	LBTPT	Text description of planned time point when measurements should be taken for use when multiple sequential assessments are done.	Record the planned time point labels for the lab test, if not pre-printed on the CRF.	Planned time point would be needed to differentiate for multiple sequential assessments. It is recommended that time points should be pre-printed on the CRF rather than collected in a field that requires the site to enter text.	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	Protocol-defined testing conditions met	**LBCOND**	Condition imposed on the subject for testing defined in the protocol *(e.g., fasting)*.	Record whether protocol defined testing conditions were met.	The specific testing conditions required should be pre-printed on the CRF, such as "Did subject meet fasting requirements?". Results may be affected by whether conditions for testing were properly met *(e.g., fasting)*. This may not be relevant for all tests. **For the SDTM-based dataset,** the SDTMIG variable LBFAST could be derived from LBCOND.	Recommended/ Conditional
7	Test Name	LBTEST	Verbatim name of the test or examination used to obtain the measurement or finding. Note: any test normally performed by a clinical laboratory is considered a lab test. {LBTEST} (See Section 2.2.)	Record the wording of the lab test if not pre-printed on the CRF.	Required to identify the test. It is recommended that the test names be pre-printed on the CRF.	Highly Recommended
8	Test Result	LBORRES	Result of the measurement or finding as originally received or collected.	Record test results.	Optional if already provided from central lab.	Recommended/ Conditional
9	Clinical Significance	**LBCLSIG**	Whether lab test results were clinically significant.	Record whether lab results were clinically significant.	Key data collected in this scenario.	Highly Recommended
10	Accession Number	LBREFID	Internal or external specimen identifier.	Record the sample or accession number assigned.	This can be used to confirm that the appropriate data record is present in the electronic transfer May be included for linking back to samples *(e.g., Specimen ID)*.	Recommended/ Conditional

5.13. Medical History – MH (Events)

For the purposes of this effort, only General Medical History was considered. Indication-specific History such as Oncology, though not expressly addressed, was considered in the definitions of such variables as MHCAT. The rationale for addressing only General Medical History was that a higher degree of detail may be required for the indication specific histories. It may well be possible to record indication specific history on these forms if the protocol does not require more information than are addressed by the optional variables. Sponsors should define the appropriate collection period for Medical History.

Example CRFs and Regulatory requirements for the recording and coding of Medical History were reviewed. Though varied, it was determined that not only relevant Medical History, but additionally the disease under study may be recorded as General Medical History. Dependent upon protocol requirements, an exhaustive list of conditions is not required, but rather focus should be on particular diseases or conditions of concern.

The Regulatory requirements were reviewed for the coding of Medical History, none were identified. Coding using MedDRA, though not required by the FDA, is recommended. Coding of Medical History is recommended because it provides methodology to match Medical History to specific adverse events, makes it easier to mine data for potential relationship to past treatments and to the safety profile, as well as a providing a means to help identify unexpected safety concerns. If coding is performed it is recommended that it be done during the performance of a study rather than after it is completed as this facilitates efficient resolution of coding queries. A strategy for classifying/organizing uncoded Medical History utilizing conditional variables is being recommended. For un-coded Medical History, a sponsor-defined categorization of Medical History Events will be required. This categorization will be achieved using the MHSCAT variable. Sponsors who code Medical History will use the dictionary variables for the coded terms.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Has the subject experienced any past and / or concomitant diseases or past surgeries?	**MHYN**	General prompt question to aid in monitoring and data cleaning. *Has the subject experienced any past and / or concomitant diseases or past surgeries?* {NY} (See Section 2.2.)	If the subject has experienced any past and / or concomitant diseases or has had any type of surgery, select "Yes" and provide the requested information. Otherwise, select "No" and leave the page blank.	Note that MHYN is **not** defined in the SDTMIG MH domain. Some sponsors may find this data point useful from an administrative perspective. ***It should not be included in the submission.*** Also note that the sponsor may choose to collect surgical history elsewhere in the CRF.	Optional
2	Pre-printed row number *(e.g., 1, 2, 3)*	MHSPID	Optional sponsor-defined reference number *(e.g., pre-printed line number)*.	Not applicable.	Some sponsors may pre-number the rows used to capture the data. If these identifiers are submitted, MHSPID should be used.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
3	Type of Medical History being collected	MHCAT	Used to define a category of related records *(e.g., CARDIAC or GENERAL)*.	Not applicable.	The sponsor may or may not pre-print on the CRF the type of medical history being captured. If specific medical history *(e.g., disease diagnosis)* is captured in addition to the general medical history, it may be helpful to pre-print the history type on the CRF. Regardless, MHCAT may be populated in the database as derived field. Note: *MHCAT must be in the database if MHSCAT is used.*	Recommended/ Conditional
4	Category of Medical History being collected	MHSCAT	A categorization of the condition or event pre-printed on the CRF or instructions.	Note: The CRF instructions will depend upon the format of the CRF. Some sponsors ask the sites to use a numeric code *(e.g., "123")* to designate a particular category *(e.g., "cardiovascular")* while other sponsors will simply pre-print the categories on the CRF and provide space for the site to record the ailment, disease or surgery. Instruction examples: Use the *(sponsor-defined)* code list to group the past and / or concomitant medical conditions or surgeries. For example, if the subject has a history of high blood pressure, use code "123" for "cardiovascular". ***OR*** Record the concomitant medical conditions or past surgeries under the appropriate category. For example, "high blood pressure" should be recorded under "cardiovascular".	The pre-printed groupings should be used if the sponsor will not code medical history. The categories should be sponsor-defined as sponsors may have different needs. *(Code "123" used in the instructions is simply an example.)* The MedDRA SOCs should not be used as categories on the CRF for several reasons. Sites are probably not familiar with the SOCs. It would be cumbersome to include the 26 organ classes on the CRF, entry screen or completion instructions. The reviewers expect this information to be stored in MHBODSYS. Finally, the sponsor may only wish to inquire about particular groupings or specific diseases; not actual *body systems.* Note that "123" would not be stored in MHSCAT. In this example, "cardiovascular" is the MHSCAT. Numeric codes used on the CRF as an operational tactic to facilitate data entry must be removed prior to submission as they provide no meaning to the reviewer. Also Note that MHCAT must be in the database if MHSCAT is used.	Recommended/ Conditional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
5	Reported Term	MHTERM	Verbatim or preprinted CRF term for the medical condition or event.	Record all relevant past and / or concomitant medical conditions and past surgeries, as defined in the protocol. Record only one condition or surgery per line. When recording a condition and surgery related to that condition, use one line for the condition and one line for the surgery. Ensure that any of the conditions listed on the Medical History page do not meet any of the exclusion criteria.	Note that if sponsors need to capture more detailed surgery information *(e.g., VNS implantation for Epilepsy trials)*, an additional CRF module should be used, modeled as an Interventions domain.	Highly Recommended
6	Ongoing?	**MHONGO**	Identifies the end of the event as being ONGOING.	Select the most appropriate response.	Note that MHONGO is **not** defined in the SDTMIG MH domain. If collected, it should be used to derive MHENRTPT. The Visit Date, captured in the header, or MHDAT, should be used as the reference time point (MHENTPT).	Optional
7	Disease controlled?	**MHCTRL**	Identifies the end of the event as being ONGOING.	Select the most appropriate response.	Note that MHONGO is **not** defined in the SDTMIG MH domain. If collected, it should be used to derive MHENRTPT. The Visit Date, captured in the header, or MHDAT, should be used as the reference time point (MHENTPT).	Optional
8	Pre-printed prompt for a specific condition/surgery *(e.g., Does the subject have high blood pressure?)*	MHOCCUR	A pre-printed prompt used to indicate whether or not a medical condition has occurred.	Please indicate if *"xyz"* has occurred by checking "Yes" or "No".	MHOCCUR should only be used if the condition pre-printed on the CRF elicits a "Yes" or "No" response. MHOCCUR should not be used if the conditions are collected on the CRF in a manner that requires a free-flow text response.	Optional
9	Onset Date	**MHSTDAT**	Start date of Medical History event.	Record the onset date using the CDASH-recommended date format *(e.g., 22-AUG-2008)*. For more details see Best Practice Recommendations.	The sponsor may choose to capture a complete date or any variation thereof *(e.g., month & year or year, etc.)*. **For the SDTM-based dataset,** the SDTMIG variable MHSTDTC is derived from the CDASH Onset Date using the ISO 8601 format.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
10	End Date	**MHENDAT**	End date of Medical History event.	Record the end date using the CDASH-recommended date format *(e.g., 22-AUG-2008)*. For more details see Best Practice Recommendations.	The sponsor may choose to capture a complete date or any variation thereof (month & year or year, etc.). **For the SDTM-based dataset,** the SDTMIG variable MHENDTC is derived from the CDASH End Date using the ISO 8601 format.	Optional
11	Completion Date	**MHDAT**	Completion date of the Medical History data collection form.	Record the date on which the Medical History was taken using the CDASH-recommended date format *(e.g., 22-AUG-2008)*. For more details see Best Practice Recommendations.	This should be a complete date.	Optional

5.14. Physical Examination – PE (Findings)

The scope of the PE domain tables is limited to general physical examinations as part of overall safety data collection. The data collection fields defined in the following tables may not fit the needs of targeted body system evaluations as part of therapeutic area specific assessments. After reviewing the different PE forms, the PE Domain Team organized them into 3 usage categories:

A. Use of a PE form at baseline and post baseline visits.

B. Use of a PE form at baseline, but not at post baseline visits. Sites are instructed to record any post-baseline abnormalities or baseline conditions that worsened post baseline on the AE form.

C. Use of a PE form only to record whether or not the exam was performed, and if so, the date of the examination. Sites are instructed to record baseline abnormalities on medical history form, targeted medical history form (e.g., study specific form requesting assessment of a pre-defined set of medical and/or surgical history events) or baseline conditions form. Sites are instructed to record any post baseline abnormalities or baseline conditions that worsened post baseline on the AE form or other sponsor defined form.

In Options A and B, similar fields were captured; date of exam, body system/code, normal/abnormal, and description of abnormality. As the PE Domain Team discussed the options, factors supporting Option C began to outweigh the traditional methods incorporated in Options A and B. The primary factors leading to recommending Option C as the best practice include:

- Eliminates collection and reconciliation of duplicate data by capturing abnormal data in one central location. Abnormalities identified during a physical examination must also be recorded on an AE form, a medical history form, or other similar form.
- Reduces number of queries, thus reducing workload for data managers and site personnel.
- Supports consistency/standardization for data reporting purposes. Domain Team members polled their medical writing and biostatistics departments and it was found that physical examination data are rarely summarized, only tabulated in listing format. Any trend analysis or summarization of abnormalities is performed on AE data, and medical history data are available for reference.
- Reduces coding needs (if PE abnormalities are coded).

As Option C represents a radical change from the more traditional approach for collection of physical examination data, two sets of PE domain tables are being presented. The table/approach outlined in Section 5.14.1 (Option C) is being proposed by the PE Domain Team as an alternative to the traditional approach and recommended as best practice. All fields in the best practice table/approach are defined as optional as these fields are for monitoring and data cleaning purposes. Since the fields are not required for safety or efficacy evaluations, a sponsor may decide not to collect them on the CRF. The table presented in Section 15.14.2 (Options A/B) reflects the traditional approach to physical examination data collection.

5.14.1. Best Practice Approach

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Was the Physical Examination Performed?	**PEYN**	Used to indicate if the overall physical examination was performed as scheduled. *Was the physical examination performed?* {NY} (See Section 2.2.)	If physical examination was performed as planned then select "Yes", otherwise, select "No"	BASELINE: If examination is performed, CRF and CRF Instructions will direct site to report all abnormal findings/conditions on appropriate CRF *(e.g., Medical History, Baseline Findings, Adverse Events)* POST-BASELINE: If examination is performed *and* abnormality is new or worsened, CRF and CRF Instructions will direct site to capture all changes on appropriate CRF *(e.g., Post-baseline Assessment, Adverse Events).* This field is used to assist in data monitoring and cleaning	Optional
2	Date of Examination	**PEDAT**	Date of examination.	Record complete date of examination, day, month and year using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	The date of examination may be derived from the date of visit and therefore a separate assessment date field is not required. **For the SDTM-based dataset,** the SDTMIG variable PEDTC is derived by concatenating CDASH Date and Time of Examination (if time is collected) into PEDTC using the ISO 8601 format.	Optional
3	Time of Examination	**PETIM** *(Note: If collected, will be used to derive* PEDTC.)	Time of examination.	Record the time of examination (as complete as possible). For more detail see the Best Practice section.	**For the SDTM-based dataset,** the SDTMIG variable PEDTC is derived by concatenating CDASH Date and Time of Examination (if time is collected) into PEDTC using the ISO 8601 format.	Optional

As specified via each study's protocol, physical examinations will be performed based on protocol schedule. At the time of the examination, use the PE CRF page to collect only the status of whether or not the exam was performed and, if the response is "Yes", the date (and time, if collected) of the exam. Sites should be prompted to record any abnormalities identified during the exam on appropriate CRF pages. For baseline visits, sites will be directed to report abnormal findings/conditions on a CRF such as Baseline Assessment, Medical History or Adverse Event. For post-baseline visits, sites may be directed to use a CRF such as Post-Baseline Assessment or Adverse Event.

5.14.2. Traditional Approach

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Was the Physical Examination Performed?	**PEYN**	Used to indicate if the overall physical examination was performed as scheduled. *Was the physical examination performed?* {NY} (See Section 2.2.)	If physical examination was performed as planned then select "Yes", otherwise, select "No"	A subject/page level question can be used asking the site if the physical exam was performed at the specified time point. If this field is used then the result should only be mapped to PESTAT in SDTMIG if the overall examination, at the subject level, was not performed. If the overall examination was performed then the value of PESTAT would be null for the examined body systems and Not Done for any body systems not examined (see PERES). This field is used to assist in data monitoring and cleaning	Optional
2	Date of Examination	**PEDAT**	Date of examination.	Record complete date of examination, day, month and year using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section.	The date of examination may be derived from the date of visit and therefore a separate assessment date field is not required. **For the SDTM-based dataset,** the SDTMIG variable PEDTC is derived by concatenating CDASH Date and Time of Examination (if time is collected) into PEDTC using the ISO 8601 format.	Recommended/ Conditional
3	Time of Examination	**PETIM** *(Note: If collected, will be used to derive* PEDTC.)	Time of examination.	Record the time of examination (as complete as possible). For more detail see the Best Practice section.	**For the SDTM-based dataset,** the SDTMIG variable PEDTC is derived by concatenating CDASH Date and Time of Examination (if time is collected) into PEDTC using the ISO 8601 format.	Optional
4	Sponsor-Defined Identifier	PESPID	Sponsor-defined reference number.	Not applicable.	May be pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
5	Body System Examined	PETEST	Name of the body system.	Per protocol, perform physical examinations of specified body systems.	Sponsor should pre-populate CRF with all body systems to be examined. The use of a complete list of body systems eliminates the need for an other/specify category as any abnormalities identified should fall under one of the pre-specified categories. Even if the sponsor does not require all body systems to be examined at a given time point, the complete list should still be used. Instructions should be given to the site to record "Not Done" in Exam Result field for any systems not examined.	Highly Recommended
6	Examination Result	**PERES**	Overall assessment of examined body system.	For each body system listed, record the result of the examination (Normal or Abnormal). If the examination is not performed or not required select Not Done.	For each body system listed on the CRF, provide the following options for results: Normal, Abnormal and Not Done. Sites should be directed to complete overall assessment for each exam category/body system listed. In SDTMIG, if the examined body system is normal then the value in PEORRES should be NORMAL. If the body system is not examined, then the value in PEORRES should be Null and the value in PESTAT should be Not Done. If the examined body system is abnormal, then the value of PEORRES should contain the text of the abnormal findings. If the sponsor's data collection system allows for up front recording of the abnormality and status using one variable then the SDTMIG variable name PEORRES should be used in place of CDASH variable names PERES and PEDESC	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
7	Abnormal Findings	**PEDESC**	Text description of any abnormal findings.	Record all abnormal findings for the given body system in the space provided.	Text entered under abnormal findings (PEDESC) should be mapped to PEORRES. If the sponsor's data collection system allows for up front recording of the abnormality and status using one variable then the SDTMIG variable name PEORRES should be used in place of CDASH variable names PERES and PEDESC	Highly Recommended
8	Clinical Significance	**PECLSIG**	Whether physical examination abnormality is clinically significant	Record whether abnormality is clinically significant.	If this level of information is needed for reconciliation with adverse events, this field may be added to the CRF.	Optional
9	Evaluator	PEEVAL	Role of the person who provided the evaluation.	Enter the role of the person who provided the evaluation *(e.g., investigator, adjudication committee, vendor).*	Used only for results that are subjective. Should be null for records that contain collected or derived data.	Optional

5.15. Protocol Deviations – DV (Events)

5.15.1. Considerations Regarding Usage of a Protocol Deviations CRF

The DV Domain Team recommends avoiding the creation of a Protocol Deviations CRF (individual sponsors can determine whether it is needed for their particular company). During DV Domain Team deliberations, most participants emphasized that their companies did not utilize specific CRFs for collection of protocol deviations. This information was derived from other CRF domains or system functionalities. The DV Domain Team did, however, develop a CDASH data collection standard for Protocol Deviations, which maps to the SDTMIG DV domain. Although one data collection field in the table below is categorized as highly recommended this is only the case when a DV CRF is created. The DV table was developed as a guide that clinical teams could use for designing a Protocol Deviations CRF and study database should they choose to do so. *(Note: Definitions of Protocol Deviation and Protocol Violation are available in the List of Abbreviations and Glossary appendix.)*

5.15.2. Rationale

If a sponsor decides to use a Protocol Deviations CRF, the DV Domain Team felt the sponsor should not rely on this CRF as the only source of protocol deviation information for a study. Rather, they should also utilize monitoring, data review and programming tools to assess whether there were protocol deviations in the study that may affect the usefulness of the datasets for analysis of efficacy and safety. By utilizing this information a sponsor can then decide which method is best for their company.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Were there any protocol deviations?	**DVYN**	Indication of whether or not there was a protocol deviation. {NY} (See Section 2.2.)	Enter "Yes" if a protocol deviation occurred and "No" if none occurred. Ensure that any adverse event, concomitant medication use, newly discovered medical history, etc. which triggers a protocol deviation is noted in the respective CRF.	May be derived in the analysis (submission) dataset if not collected on a CRF.	Optional
2	Protocol Deviation Term (text) and or Protocol Deviation Coded Term	DVTERM *And/or* DVDECOD	Verbatim text of the variation from processes or procedures defined in a protocol and/or controlled terminology for the name of the protocol deviation.	Record protocol deviation identified and/or select the appropriate code from the list of protocol deviation terms.	This may be derived. Only "Highly Recommended" if collecting protocol deviations on a CRF.	Highly Recommended
3	Start Date	**DVSTDAT**	Start date of Deviation.	Record complete date that the protocol deviation began using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail instructions see the Best Practice section. This should be the start or occurrence of the protocol deviation and not the date it was discovered or reported.	This may be derived if not collected on a CRF. **For the SDTM-based dataset,** the SDTMIG variable DVSTDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into DVSTDTC using the ISO 8601 format.	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
4	Start Time	**DVSTTIM** *(Note: If collected, will be derived into* DVSTDTC.)	Start time of Deviation.	If appropriate, record the time (as complete as possible) the protocol deviation began. For more detail instructions see the Best Practice section. This should be the start or occurrence of the protocol deviation and not the time it was discovered or reported.	**For the SDTM-based dataset,** the SDTMIG variable DVSTDTC is derived by concatenating CDASH Start Date and Time (if time is collected) into DVSTDTC using the ISO 8601 format.	Optional
5	End Date	**DVENDAT**	End date of Deviation.	Record the date that the Protocol deviation ended using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail see the Best Practice section. This should be the date the protocol deviation stopped and not the date it was discovered or reported.	**For the SDTM-based dataset,** the SDTMIG variable DVENDTC is derived by concatenating CDASH End Date and Time (if time is collected) into DVENDTC using the ISO 8601 format.	Optional
6	End Time	**DVENTIM** *(Note: If collected, will be derived into* DVENDTC.)	End time of Deviation.	Optionally, if appropriate, record the time (as complete as possible) the protocol deviation ended. This should be the time the protocol deviation stopped and not the time it was discovered or reported.	**For the SDTM-based dataset,** the SDTMIG variable DVENDTC is derived by concatenating CDASH End Date and Time (if time is collected) into DVENDTC using the ISO 8601 format.	Optional
7	Sponsor-Defined Identifier	DVSPID	Sponsor-defined reference number.	Not applicable.	Can be pre-printed on the CRF as an explicit line identifier or defined in sponsor's operational database *(e.g., Line number on a CRF page).*	Optional

5.16. Subject Characteristics – SC (Findings)

As mentioned earlier, the CDASH process began by using the SDTMIG as a model to identify data domains or categories of data for CDASH Standard Version 1.0 and example CRFs to identify regularly used variables, aligned to these SDTMIG domains. The Subject Characteristics domain was identified as a necessary domain to include in CDASH Standard Version 1.0 as it has been included as one of the SDTMIG domains since Version 3.0. The SDTM model (Version 1.1) states that “the demographics domain describes the essential characteristics of the study subjects and is used by reviewers for selecting populations for analysis." (p. 13). Neither the SDTM nor the SDTMIG explicitly define what data are in the Subject Characteristics domain, but the SDTMIG does say that:

1) "...data in this domain is collected only once per subject" (p. 29)
2) "Subject Characteristics is for data not collected in other domains that is subject-related." (p. 83) and
3) "The structure for demographic data is fixed and includes date of birth, age, sex, race, ethnicity and country. The structure of subject characteristics is based on the Findings SDTM Observation Class and is an extension of the demographics data, allowing the reporting of "non-essential" subject characteristics which might be useful as additional population selection criteria for analysis. Subject Characteristics consists of data that are collected once per subject (per test) and that is not expected to change during the trial. The SDTMIG states that "Subject characteristics contains data such as additional information about race, subject initials, economic information, and eye color." (p. 83)

The example CRFs that the SC Domain Team reviewed indicated a wide variety of data collected as Subject Characteristics. Some examples of these questions include: Marital status, Economic status, Education level achieved. These data might be useful for risk-benefits analyses or for quality of life analyses. Another example that the team identified is "Gestational age at birth".

The SDTM VS domain utilizes a normalized data structure, i.e., one variable, SCTEST, is used to capture the test name and another variable, SCORRES, is used to capture the result. The SC Domain Team considered providing two options for the SC domain table; a normalized structure similar to that of SDTM and the other suggesting unique variables for each test. The normalized structure is recommended and is consistent with other Findings domains. If Subject Characteristics are collected then the table below describes what variables should be collected.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Subject Characteristic Question	SCTEST	Name of the subject characteristic being queried. {SCCD} (See Section 2.2.)	Not applicable.	It is recommended that the questions be pre-printed on the CRF	Highly Recommended
2	Subject Characteristic Answer/Result	SCORRES	Answer/result of the subject characteristic question as originally received or collected.	Record the answer to the question.	Not applicable.	Highly Recommended

Examples of Subject Characteristics Questions

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors
1	Gestational Age at Birth	SCTEST	The age (in weeks) of the newborn infant, counted from the woman's last menstrual period (LMP) or health status indicators / Clinical Estimate (CE).	Not applicable.	A constant that may be useful for analysis in pediatric or neonatal study analyses.
2	Childbearing Potential	SCTEST	Subject's childbearing potential.	Check the correct box to indicate the subject's childbearing potential, or postmenopausal or sterilized as required for the form.	Not applicable.
3	Education	SCTEST	Education level achieved at start of study (Reference date).	Not applicable.	Not applicable.
4	Sub-study Participation	SCTEST	Sub-study participation information.	Not applicable.	For some studies sub-study information is captured, such as "subject is on fasting sub-study" or "subject is on PK sub-study".

5.17. Substance Use – SU (Interventions)

The primary recommendation was to not limit by category the initial response to a "Yes/No" flag question, but rather use a more descriptive response for substance use. The prompt variable, stored as SUPPSU QNAM SUNCF, would require a response to "Never, Current, or Former". Again, based on the wide variability of protocol definitions of use, the specific definitions and timeframes for this response would be sponsor/protocol-defined. By using these categories for usage, a number of questions about use and frequency can be collapsed, in turn decreasing the number of data points required in the SU Domain. More detailed information about duration, amount, start and end dates are optionally captured.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Type of substance used?	SUTRT	The type of substance *(e.g., TOBACCO, ALCOHOL, CAFFEINE, etc.* **Or** *CIGARETTES, CIGARS, COFFEE, etc.).*	Not applicable.	Note that sponsors may require different types of substance use data *(e.g., illicit drug use, cigarettes, etc.)*; the value for category may be pre-printed on the CRF as a label for the prompt for Substance Use. If a more detailed type of substance appears on the CRF *(e.g., cigarettes, cigars, rather than tobacco)*, SUCAT should be "tobacco" and SUTRT should be "cigarettes". If the sponsor does not specify a type of tobacco on the CRF, SUTRT should be "tobacco".	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
2	Substance use?	SUNCF	Substance Use Occurrence	Check the appropriate box to indicate if the subject has ever used/consumed *tobacco / alcohol / caffeine*, currently consumes *tobacco / alcohol / caffeine*, or formerly used/consumed *tobacco / alcohol / caffeine*.	The Domain Team recommends the use of "NEVER", "CURRENT" and "FORMER" as responses. The three options, "NEVER", "CURRENT" and "FORMER" should be sponsor-defined. If the sponsor has specific definitions for the three, these definitions should be detailed in the instructions to the site. As this type of response does not easily correspond to an SDTMIG variable. The Domain Team recommends using SUNCF as the variable name in the clinical database. Note that SUNCF is **not** defined in the SDTM and, generally, should be dropped prior to submission. If submitted, it should be stored in SUPPSU. Note that "NEVER" maps to SUOCCUR as "N". "CURRENT" and "FORMER" map to SUOCCUR as "Y".	Highly Recommended
3	Category of substance used	SUCAT	Used to define a category of related records *(e.g., TOBACCO, ALCOHOL, CAFFEINE, etc.)*.	Not applicable.	Note that sponsors may require different types of substance use data *(e.g., illicit drug use, cigarettes, etc.)*; the value for category may be pre-printed on the CRF as a label for the Prompt for Substance Use. If a more detailed type of substance appears on the CRF *(e.g., cigarettes, cigars, rather than tobacco)*, SUCAT should be "tobacco" and SUTRT should be "cigarettes". If the sponsor does not specify a type of tobacco on the CRF, SUTRT should be "tobacco".	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
4	Amount	SUDOSTXT	Substance use consumption amounts or a range of consumption information collected in text form *[e.g., 1-2 (packs), 8 (ounces), etc]*.	Check the appropriate box to indicate the amount of *tobacco / alcohol / caffeine* the subject consumes on a regular basis.	Where possible, the options for dose/amount should be pre-printed on the CRF. Note that in the example given in the Definition, "(packs)" and "(ounces)" have been included as a point of reference. They would, of course, be stored as SUDOSU. If the dose is part of a planned analysis, then the use of SUDOSE, a numeric field, should be considered.	Optional
5	Unit	SUDOSU	Units for SUDOSTXT *(e.g., PACKS, OUNCES, etc.).*	Not applicable.	Where possible, the options for dose/amount units should be pre-printed on the CRF.	Optional
6	Frequency	SUDOSFRQ	Usually expressed as the number of uses consumed per a specific interval *(e.g., PER DAY, PER WEEK, OCCASIONAL).*	Not applicable.	Where possible, the options for dose/amount frequency should be pre-printed on the CRF.	Optional
7	Start Date	**SUSTDAT**	Date substance use started.	Record the start date using the CDASH-recommended date format *(e.g., 22-AUG-2008)*. For more details see Best Practice Recommendations.	The sponsor may choose to capture a complete date or any variation thereof *(e.g., month & year or year, etc.).*	Optional
8	End Date	**SUENDAT**	Date substance use ended.	Record the end date using the CDASH-recommended date format *(e.g., 22-AUG-2008)*. For more details see Best Practice Recommendations.	The sponsor may choose to capture a complete date or any variation thereof *(e.g., month & year or year, etc.).*	Optional

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
9	Duration	**SUCDUR**	The duration of the substance use.	Provide the duration of the Substance Abuse *(e.g., Record how long the subject has smoked).*	This should only be collected on the CRF if this level of detail is needed and if SUSTDTC & SUENDTC are **not** collected on the CRF. The sponsor-defined options *(e.g., weeks, months, years, etc.)* should be pre-printed on the CRF to avoid making this a free text field. This will allow the response to be translated into ISO 8601 format. **For the SDTM-based dataset,** the SDTMIG variable SUDUR can be derived by concatenating the CDASH duration and duration units variables.	Optional
10	Unit for Duration	**SUCDURU**	Units for SUCDUR *(e.g., weeks, months, years, etc.).*	Not applicable.		Optional

5.18. Vital Signs – VS (Findings)

The review of vital signs data elements was fairly straightforward as all sponsor reviewed CRFs captured similar data and the items were consistent with the SDTM VS domain. The key topic for discussion and consideration was how to link the collected elements to the SDTM-defined variables. For example, many VS CRFs collect each unique result in its own field (e.g., height, weight, blood pressure, etc.) and the resulting values are stored as separate variables in the clinical data management system. The SDTM VS domain utilizes a normalized data structure, i.e., one variable, VSTEST, is used to capture the test name and another variable, VSORRES, is used to capture the result. The VS Domain Team considered providing two options for the VS domain table; a normalized structure similar to that of SDTM and the other suggesting unique variables for each test. The normalized structure is recommended and is consistent with other Findings domains.

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
1	Date of Measurements	**VSDAT**	Date of measurements	Record date of measurements using the CDASH-recommended date format *(e.g., 08-AUG-2008)*. For more detail instructions see the Best Practice section.	The date of measurement can usually be derived from the date of visit and in such cases a separate measurement date field is not required. **For the SDTM-based dataset,** the SDTMIG variable VSDTC is derived by concatenating CDASH Date and Time of Vital Sign Measurements (if time is collected) into VSDTC using the ISO 8601 format.	Recommended/ Conditional
2	Time of Vital Sign Measurements	**VSTIM** *(Note: If collected, will be used to derive* VSDTC.)	Time of measurements.	Record time of measurement (as complete as possible). For more detail instructions see the Best Practice section.	**For the SDTM-based dataset,** the SDTMIG variable VSDTC is derived by concatenating CDASH Date and Time of Vital Sign Measurements (if time is collected) into VSDTC using the ISO 8601 format.	Recommended/ Conditional
3	Sponsor-Defined Identifier	VSSPID	Sponsor-defined reference number	Not applicable.	Pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database.	Optional
4	Planned Time Point	VSTPT	Text description of time when measurement should be taken	Not applicable.	If applicable, this will be pre-printed on CRF when measurements are required at multiple time points within a visit day.	Recommended/ Conditional
5	Vital Sign Test Name	VSTEST	Verbatim name of the test or examination used to obtain the measurement or finding. {VSTEST} (See Section 2.2.)	Record the name of the vital sign test if not pre-printed on the CRF.	It is recommended that the test names be pre-printed on the CRF.	Highly Recommended

	Data Collection Field	Variable Name (CDASH variable name shaded)	Definition	Case Report Form Completion Instructions	Additional Information for Sponsors	CDASH Core
6	Vitals Status	VSSTAT	Used to indicate that a vital signs measurement was not done.	If measurement not taken please indicate on CRF by selecting Not Done.	If CRF design provides for individual status check boxes where site can indicate Not Done for the given parameter, information would be stored as Not Done in VSSTAT. If value exists in VSORRES then the result in VSSTAT is Null. If CRF guidelines direct site to enter Not Done (or similar text) in the result field, then value of VSSTAT is Not Done, otherwise if numeric value exists in result variable (VSORRES) then value of VSSTAT is Null. This field is used to assist in data monitoring and cleaning	Recommended/ Conditional
7	Vital Sign Test Result or Finding	VSORRES	Result of the vital signs measurement as originally received or collected.	Record vital sign results.	Key data collected.	Highly Recommended
8	Original Units	VSORRESU	Original units in which the data were collected.	Record or select the unit of measure associated with the test, if not pre-printed on the CRF.	It is recommended that the units be sponsor-defined and pre-printed on the CRF when possible.	Highly Recommended
9	Clinical Significance	VSCLSIG	Whether vital sign result was clinically significant.	Record whether vital sign result was clinically significant.	If this level of information is needed, it may be added to the CRF.	Optional
10	Location of Vital Signs Measurement	VSLOC	Location relevant to the collection of Vital Signs measurement. Example: LEFT ARM for blood pressure.	Record or select location on body where measurement was performed, if not pre-printed on CRF.	Location may be pre-defined as part of CRF label.	Optional
11	Position of Subject	VSPOS	Position of the subject during a measurement or examination. {POSITION} (See Section 2.2.)	Record the position of subject at time of test.	Position may be pre-defined as part of CRF label or site may be given one or more options to select from.	Recommended/ Conditional

6. Change Control and the Process for Creating New CDASH Domains

We recognize that additional feedback on CDASH Standard Version 1.0 will be acquired once organizations begin to implement the standard in real clinical studies. To capture this information, we will put out an open call for feedback from "Early Implementers". Once this feedback is received, it will be consolidated and considered by the CDASH Core Team and suitable changes will be made. In addition, new CDASH domains will be developed when a need is identified, e.g., the SDTM develops a new domain that requires collection fields. All changes to the published version of CDASH Standard Version 1.0 will be handled according to the CDISC operating procedure COP-001, Section 2.4 Stage IV: Standards Update and Maintenance. See http://www.cdisc.org/about/about_bylaws.html for further information.

7. Appendices

7.1. Commonly Used CDISC Controlled Terminology

Although outside the original scope of the CDASH project, the CDASH Core Team recognized that providing commonly used terms would encourage consistent implementation and optimal use of the CDASH standard as well as streamlining the collection of data at clinical sites. The purpose of the Commonly Used CDISC Controlled Terminology appendix is to include frequently used terms from the CDISC controlled terminology code lists for a number of data collection fields where there a numerous possibilities. Commonly used terms are available for the following domains contain: CM, DA, EG, EX, VS.

The CDASH abbreviations column contains standard medical abbreviations that are commonly used in medical records (source documents) and on paper CRFs. When commonly used medical abbreviations are not available, this is indicated by dashes ("---") in the CDASH abbreviations column. Mapping to the CDISC Controlled Terminology is provided to assist implementers. The full EVS code lists can be accessed via the following link: http://www.cancer.gov/cancertopics/terminologyresources/CDISC.

CDASH Data Collection Field	CDASH Definition	CDISC Approved Terminology Codelist	Commonly Used Terms from the CDISC Terminology Codelists *See codelist for full list of values*			
			Description	**CDASH Abbreviation**	**CDISC Submission Value**	**NCI EVS CUI (Concept Unique Identifier)**
CMDOSU	Dose Units	Unit Codelist C71620 *Extensible*	milligram	mg	mg	C28253
			microgram	ug	ug	C48152
			milliliter	mL	mL	C28254
			gram	g	g	C48155
			International Unit	IU	IU	C48579
			tablet	tab	TABLET	C48542
			capsule	cap	CAPSULE	C48480
			puff	- - -	PUFF	C65060
CMDOSFRM	Dose Form	Pharmaceutical Dosage Form Codelist C66726 *Extensible*	tablet	tab	TABLET	C42998
			capsule	cap	CAPSULE	C25158
			ointment	oint	OINTMENT	C42966
			suppository	supp	SUPPOSITORY	C42993
			aerosol	aer	AEROSOL	C42887
			spray	- - -	SPRAY	C42989
			suspension	susp	SUSPENSION	C42994
			patch	- - -	PATCH	C42968
			gas	- - -	GAS	C42933
			gel	- - -	GEL	C42934
			cream	- - -	CREAM	C28944
			powder	- - -	POWDER	C42972

CDASH Data Collection Field	CDASH Definition	CDISC Approved Terminology Codelist	Commonly Used Terms from the CDISC Terminology Codelists *See codelist for full list of values*			
			Description	**CDASH Abbreviation**	**CDISC Submission Value**	**NCI EVS CUI (Concept Unique Identifier)**
CMDOSFRQ	Dosing Frequency Per Interval	Frequency Codelist C71113 *Extensible*	twice daily	BID, BD	BID	C64496
			three times a day	TID	TID	C64527
			four times daily	QID	QID	C64530
			every other day	QOD	QOD	C64525
			every month	QM	QM	C64498
			as needed	PRN	PRN	C64499
			unknown	U	UNKNOWN	C17998
CMROUTE	Route of Administration	Route Codelist C66729 *Extensible*	oral	PO	ORAL	C38288
			topical	TOP	TOPICAL	C38304
			subcutaneous	SC	SUBCUTANEOUS	C38299
			transdermal	- - -	TRANSDERMAL	C38305
			intraocular	- - -	INTRAOCULAR	C38255
			intramuscular	- - -	INTRAMUSCULAR	C28161
			inhalation	- - -	RESPIRATORY (INHALATION)	C38216
			intralesion	- - -	INTRALESION	C38250
			intraperiteoneal	- - -	INTRAPERITEONEAL	C38258
			nasal	- - -	NASAL	C38284
			vaginal	- - -	VAGINAL	C38313
			rectal	- - -	RECTAL	C38295

CDASH Data Collection Field	CDASH Definition	CDISC Approved Terminology Codelist	Commonly Used Terms from the CDISC Terminology Codelists *See codelist for full list of values*			
			Description	**CDASH Abbreviation**	**CDISC Submission Value**	**NCI EVS CUI (Concept Unique Identifier)**
DAORRESU	Unit of Drug Dispensed or Returned	Unit Codelist C71620 *Extensible*	bag	- - -	BAG	C48474
			bottle	- - -	BOTTLE	C48477
			box	- - -	BOX	C48478
			capsule	cap	CAPSULE	C48480
			container	- - -	CONTAINER	C48484
			disk	- - -	DISK	C48490
			package	- - -	PACKAGE	C48520
			packet	- - -	PACKET	C48521
			patch	- - -	PATCH	C48524
			tablet	tab	TABLET	C48542
			tube	- - -	TUBE	C48549
			vial	- - -	VIAL	C48551
EGORRESU	ECG Original Units	Units Codelist C71620 *Extensible*	millisecond	msec	msec	C41140
			second	sec	sec	C42535
			beats per minute	- - -	BEATS/MIN	C49673
EXDOSU	Units for Exposure	Unit Codelist C71620 *Extensible*	tablet	tab	TABLET	C48542
			capsule	cap	CAPSULE	C48480
			puff	- - -	PUFF	C65060
			milliliter	mL	mL	C28254
			microgram	ug	ug	C48152
			milligram	mg	mg	C28253
			gram	g	g	C48155

CDASH Data Collection Field	CDASH Definition	CDISC Approved Terminology Codelist	Commonly Used Terms from the CDISC Terminology Codelists *See codelist for full list of values*			
			Description	**CDASH Abbreviation**	**CDISC Submission Value**	**NCI EVS CUI (Concept Unique Identifier)**
EXDOSFRQ	Dosing Frequency Per Interval	Frequency Codelist C71113 *Extensible*	twice daily	BID, BD	BID	C64496
			three times daily	TID	TID	C64527
			four times daily	QID	QID	C64530
			every other day	QOD	QOD	C64525
			every month	QM	QM	C64498
			as needed	PRN	PRN	C64499
			unknown	U	UNKNOWN	C17998
EXROUTE	Route of Administration	Route Codelist C66729 *Extensible*	oral	PO	ORAL	C38288
			topical	TOP	TOPICAL	C38304
			subcutaneous	SC	SUBCUTANEOUS	C38299
			transdermal	- - -	TRANSDERMAL	C38305
			intraocular	- - -	INTRAOCULAR	C38255
			intramuscular	- - -	INTRAMUSCULAR	C28161
			inhalation	- - -	RESPIRATORY (INHALATION)	C38216
			intralesion	- - -	INTRALESION	C38250
			intraperiteoneal	- - -	INTRAPERITEONEAL	C38258
			nasal	- - -	NASAL	C38284
			vaginal	- - -	VAGINAL	C38313
			rectal	- - -	RECTAL	C38295

CDASH Data Collection Field	CDASH Definition	CDISC Approved Terminology Codelist	Commonly Used Terms from the CDISC Terminology Codelists *See codelist for full list of values*			
			Description	**CDASH Abbreviation**	**CDISC Submission Value**	**NCI EVS CUI (Concept Unique Identifier)**
EXDOSFRM	Dose Form	Pharmaceutical Dosage Form Codelist C66726 *Extensible*	tablet	tab	TABLET	C42998
			capsule	cap	CAPSULE	C25158
			ointment	oint	OINTMENT	C42966
			suppository	supp	SUPPOSITORY	C42993
			aerosol	aer	AEROSOL	C42887
			spray	- - -	SPRAY	C42989
			suspension	susp	SUSPENSION	C42994
			patch	- - -	PATCH	C42968
			gas	- - -	GAS	C42933
			gel	- - -	GEL	C42934
			cream	- - -	CREAM	C28944
			powder	- - -	POWDER	C42972
EXINTPU	Unit for the Duration of Treatment Interruption	Unit Codelist C71620 *Extensible*	second	sec	sec	C42535
			minute	min	min	C48154
			hour	hr	HOURS	C25529
EXVOLTU	Total Volume Administration Unit	Unit Codelist C71620 *Extensible*	milliliter	mL	mL	C28254
			microgram	ug	ug	C48152
			milligram	mg	mg	C28253
EXFLRTU	The Unit of Measure for the Flow Rate	Unit Codelist C71620 *Extensible*	micrograms per minute	Ug/min	ug/min	C71211
			microgram per day	Ug/day	ug/day	C71205
			milliliter per minute	mL/min	mL/min	C64777
			millimole per 24 hours	mmol/day	mmol/day	C67420
			micromoles per day	umol/day	umol/day	C67420

CDASH Data Collection Field	CDASH Definition	CDISC Approved Terminology Codelist	Commonly Used Terms from the CDISC Terminology Codelists *See codelist for full list of values*			
			Description	**CDASH Abbreviation**	**CDISC Submission Value**	**NCI EVS CUI (Concept Unique Identifier)**
EXPDOSEU	Units for *Planned* Exposure	Unit Codelist C71620 *Extensible*	tablet	tab	TABLET	C48542
			capsule	cap	CAPSULE	C48480
			puff	- - -	PUFF	C65060
			milliliter	mL	mL	C28254
			microgram	ug	ug	C48152
			milligram	mg	mg	C28253
			gram	g	g	C48155
VSPOS	Vital Signs Position of Subject	Position Codelist C71148 *Extensible*	sitting	- - -	SITTING	C62122
			standing	- - -	STANDING	C62166
			supine	- - -	SUPINE	C62167

7.2. Regulatory References

Introduction
Data capture is part of the regulated activities in clinical trials but very little in the regulations specifically references data capture and management requirements. Regulatory references for unsolicited Subject Characteristics (SC) are not included. The Comments Domain Team reviewed ICH E3 and E6 and did not find any requirements that indicated unsolicited comments should be in submission data. When the CDASH domains were developed, each Domain Team consulted the relevant guidances and regulations to determine the best way to fulfill the apparent requirements and incorporate data capture and management best practices.

The Regulatory References appendix is organized by domain and lists the regulations and guidances that were referenced in developing the CDASH domains. There are brief explanations and/or interpretations of the wording. Note that there are often several ways of interpreting guidances and regulations, and therefore this information should not be taken as an official or FDA/ICH-approved interpretation.

Scope

- Includes information on the collection, analysis and reporting of safety data
- Includes information commonly found in clinical trials databases, and not the extended information required for expedited adverse event reporting.
- Includes descriptions of the kinds of information present in the regulations, but does not list all the individual data fields.
- Excludes references to appropriate protocol designs for enabling safety assessments

Key
Source: defines the regulatory body that issued the regulation or guidelines.

Regulation/Guideline: the reference number and title of the regulation or guidelines.

Description/Wording: provides an interpretation of the intent of the regulations/guidelines as it applies to the collection, analysis and reporting of clinical data, as well as specific wording from the guidelines where useful. Generally the reader should reference the original document for details. Wording in italics contains some suggestions for the implications of the regulation on data capture practices. It is not exhaustive, and users should take these insights and apply them broadly.

Source

- Code of Federal Regulations (CFR)
- European Commission directives including Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use, ENTR/CT3 April 2006.
- ICH Harmonized Efficacy Guidelines finalized as of 14 March 2008 (www.ich.org)
- FDA Guidances finalized as of 14 March 2008 (http://www.fda.gov/opacom/morechoices/industry/guidedc.htm)
- FDA Manual of Policies and Procedures and Compliance Program Guidance Manual (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm)
- NCI Code lists

7.2.1. Common Identifiers and Timing Variables

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E3, Structure of the Clinical Study Report	The purpose of clinical research is to permit comparisons between groups of subjects that display different characteristics, receive different treatments or in some other way demonstrate the relative effects of the characteristic or intervention being studied. Most of the guidelines and regulations about clinical research address some aspect of the process of defining, capturing, displaying and/or analyzing observations in a study, and implicit in the ability to make the comparisons or statements about the study is the ability to link the subjects to the appropriate observations. The ICH E3 guideline is a particularly good example. The entire guideline describes the need to display and analyze subject data. In order to be able to analyze differences in procedures and observations between subjects, each observation must be uniquely attributable to an individual subject. This requires a method of uniquely identifying each observation and of associating it with a unique subject. This is achieved through a combination of data fields, including subject identifiers (e.g., study ID, site ID, subject ID) and timing variables (visit ID, visit date, time of procedure). Sometimes additional fields are necessary to identify observations uniquely, and these are handled within the relevant domain.

7.2.2. Adverse Events (AE)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
CFR	21 CFR Part 312 Investigational New Drug Application	• 312.32: Safety reports following IND submissions: defines "serious" and the terms that are used in the definition. Describes what the reports should contain; defines "associated", "expected" and "unexpected" adverse drug reactions • 312.33.3b Section 1 through 4: Annual reports to INDs related to safety information. May require the production of interim safety summaries and reports which may affect the way the data capture tools are structured. • 312.64: refers to investigator's responsibility to report events that are probably or possibly related to the treatment. While it doesn't specify exactly what should be collected, it implies that there should be an assessment of causality by the investigator, which relates to AEREL
CFR	21 CFR Part 314 Applications for FDA Approval to Market a New Drug	314.80: Definition of SAE.
CFR	21 CFR Part 803 Medical Device Reporting	803.32: provides a list of variables to be collected and reported by user facilities for individual adverse event reports related to medical devices 803.42: provides a list of adverse event-related variables that must be reported for individual safety reports by importers of medical devices 803.52: provides a list of variables to be collected and reported by device manufacturers for individual adverse event reports related to medical devices
EC	European Commission: Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use, ENTR/CT3 April 2006.	Presents extensive information on expedited reporting of serious AEs. It is very similar to ICH E2A and E2B, although it provides somewhat more specificity in places. It doesn't define requirements for any additional data, but rather clarifies roles and responsibilities, and timelines for reporting.
FDA	Guidance for Industry: Premarketing Risk Assessment	Provides guidance on approaches to evaluating a drug's risk profile. While much of it focuses on pooled data and guidelines for pooling data, there are implications for individual studies, particularly in terms of coding, and the analysis of temporal relationships of drugs and AEs. • Section VI.A.1., Accuracy of Coding: provides recommendations around coding AEs, and ensuring appropriate coding. • Section VI.B, Analyzing Temporal or Other Associations: discusses the importance of being able to determine the timing of AEs both relative to treatment dates as well as to length of exposure to treatment. *This emphasizes the need to capture complete and accurate event dates.* • Section VI.G, Long-term Follow-up: discusses the need to determine what an appropriate follow-up period is for AE collection, and suggests that this should be discussed with regulatory authorities, potentially during end-of-Phase-2 meetings. *This should drive the cut-off point for collecting AEs for a study, and how long the database needs to remain open for adding AEs after the study is completed.* • Section VI.H, Important Aspects of Data Presentation: this is a supplement to the ICH E3 guidelines, and it covers additional analyses to be considered. Particularly, it states that for subjects who died during the study, the official CRF should contain copies of hospital records, autopsy reports, biopsy results, and any other pertinent information. This doesn't necessarily mean this information must be specifically collected on sponsor-generated CRFs, but that copies of this information should be stored with the rest of the subject data, and be appropriately indexed and referenced.

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting	Section II: Definitions and Terminology Associated With Clinical Safety Experience • Provides definitions for terms commonly used in safety data reporting, such as adverse event, serious adverse event and expectedness. • By referencing the information to be submitted, it suggests a minimal set of variables to capture the key information. • Defines processes for expedited reporting, including what must be reported and how to determine reporting timeframe • Outlines assessing safety during blinded treatment, associated with placebo treatment, and post-study events • Does not go into any detail around individual data points required, although it contains some inferences about SAE narrative content - The description of the information required for expedited reporting of serious adverse events outlines further information that may be required to characterize deaths, including items such as allergy, drug or alcohol abuse; family history; findings from special investigations. An autopsy or other post mortem findings must be included when available. This may have implications for data to be collected in every study.
ICH	E2B (M) Maintenance Of The ICH Guideline On Clinical Safety Data Management: Data Elements For Transmission Of Individual Case Safety Reports	This document lists data points that must be transmitted when sending expedited AE reports, including in some cases suggested code lists (e.g., action taken with respect to study drug). *While these are often handled by the Regulatory departments in companies, there should be discussions with CDM to determine the relationship of this information to the clinical database.* NB: as of Mar 2006 there is a new version of this document out for review (E2B (R3)). It contains clarifications and improvements. Its expected finalization date is unknown.
ICH	E2C Clinical Safety Data Management: Periodic Safety Update Reports For Marketed Drugs	This covers the requirements for periodic reporting of safety information after product launch. It doesn't list variables in the manner of E2B, but instead focuses on the frequency and timing of safety updates, how to structure the reports, the information the reports should contain (e.g., subject exposure), and some considerations around the need to track and report events internationally. It is rather more applicable to the processes around managing AE data than the data structure and variables themselves.

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E3 Structure and Content of Clinical Study Reports	References to AE analysis and reporting appear in several sections of E3. Section 12.2 addresses the requirements most specifically. • Section 9: discusses rating AEs in terms of severity or relationship to drug. It also states that the report should define how consistency in applying the ratings was achieved between sites. *Be clear in defining the severity and relationship categories, and include the definitions in CRF completion guidelines.* • Section 12.2: provides a fairly detailed description of the kinds of safety summaries that must be conducted for AEs. These include summarization of AEs by body system, by intensity if used, by relationship to treatment if collected, and by treatment emergence. Summaries should include lab findings and vital signs changes identified as AEs. Even if AEs are categorized by relationship and/or treatment emergence, all AEs should be included in the summaries. *Although E3 does not require that relationship to study drug be captured, the EU Directive on AEs (April 2006) does require it. There must be a way to determine treatment emergence (both for increases in severity and in frequency). Labs and vital signs must be mergeable with AEs data, or somehow accessible.* • Section 12.2.3: describes the general analysis approach for AEs, including examination of relationship to dosage level if that seems appropriate. *This implies that the data must include dosage dates and levels, and AE dates and severities.* • Section 12.2.4: provides a list of variables that must be included in AE listings (i.e., that need to be collected). These include typical AE variables, as well as study drug treatment data and concomitant treatment data and assessment of seriousness. Note that while the FDA does not require listings of AE data if AE data have been provided electronically, ICH guidelines do still request these. • Section 12.3: Discusses the display of Deaths & other Serious Adverse Events (SAEs); they should be split out and discussed separately in the report but essentially the same data are required for display. Deaths occurring both during the study as well as during the post treatment follow-up period are to be included. The guideline includes a description of what the subject narrative must discuss, including a list of data points. In the list of appendices, the guidelines indicate that CRFs for subjects who died must be submitted. *This implies that death data must be either collected for all studies on CRFs or on the serious AE collection instruments.* Additionally, it requires that "significant" AEs be split out, i.e., AEs that were not serious, but required some significant concomitant therapy or intervention. *This implies that AEs requiring significant concomitant treatment (either pharmacological or non-pharmacological) be specifically identifiable.*
ICH	E6 (R1) Guideline for Good Clinical Practice	• 1.2, Glossary, Adverse Event: Defines "Adverse Event" • 4.11, Investigator, Safety Reporting: Investigator responsibilities for reporting safety issues to sponsors, specifically deaths, other SAEs, Lab AEs and AEs of special interest in a particular protocol • 5.16, Safety Information: Sponsor responsibilities for ongoing review of safety information; notification of investigators. • 5.17 Adverse Drug Reaction Reporting: - Spells out the sponsor's regulatory responsibility to report all serious and unexpected AEs to IRBs, investigators and regulatory authorities in accordance with ICH E2A - Sponsor responsibilities of periodic safety updates to regulatory authorities. • Most of the rest of GCPs have more to do with actions around data, rather than the data themselves
ICH	E9 Statistical Principles for Clinical Trials	This guideline is fairly general in its observations, but provides some insight into regulatory expectations. • Section VI: Evaluation of Safety and Tolerability: Contains considerable discussion about appropriate approaches to the analysis and reporting of safety data, including summarizing by severity, onset and duration of AE, as well as potential subpopulation analyses (e.g., sex, age). Also provides definition for Treatment Emergence. • Section VII: Reporting – provides a supplement to the info contained in E3.

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
NCI	CTEP Guidelines, Adverse Event Reporting Requirements	A document produced by the National Cancer Institute's Cancer Therapy Evaluation Program. It provides definitions for terms used in reporting AEs, lists the information that should be included when reporting different kinds of AEs resulting from different kinds of treatments for cancer (e.g., marketed, pre-registration). These requirements are somewhat different from those for other types of diseases, due in part to the severity of the disease and the toxicity of the treatments. Among other information, it includes the definitions for AE Grades that are used in oncology in place of severity assessments.

7.2.3. *Prior and* Concomitant Medications (CM)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
FDA	Guideline For The Format And Content Of The Clinical And Statistical Sections Of An Application	There are a number of references to concomitant drugs and other therapies in this guideline. Below are the ones that most clearly impact decisions on the data to collect for a trial. • Section G.2.e, Integrated Efficacy, Subset analyses: concomitant medications are included in the list of parameters to be used for subset efficacy analyses • H.4.i.3.b., Drug/Drug Interactions in the ISS: Specifically states that the concomitant therapies used in all studies should be listed, along with the numbers of subjects using each concomitant drug
ICH	E3 Structure and Content of Clinical Study Reports	• Section 9.4.7, Prior and Concomitant Therapy: This part of the guideline states that allowed prior and concomitant drugs or procedures should be discussed in the report, and an assessment of their potential impact on study endpoints should be addressed. • Section 10.1, Disposition of Subjects: States that it may be useful for the listings of subjects who discontinued the study early to include additional information, including concomitant medications • Section 10.2, Protocol Violations: Subjects who had protocol violations should be summarized in the report text by the type of violation. One type specifically mentioned is subjects who received excluded concomitant treatment. • Section 11.2, Demographic and Other Baseline Characteristics and 11.4.3, Tabulation of Individual Response Data: Concomitant medications should be presented for all subjects in by-subject tabular listings. There are some specific recommendations for presentations in these sections. • Section 12, Safety Evaluation: In the introduction to this section, the guideline states that "Significant Adverse Events" (as distinct from SAEs) should be identified. This is defined as AEs that resulted in an intervention such as dose withdrawal or reduction, or significant additional concomitant therapy, which is understood to include both non-pharmacological interventions and non-study medications. • Section 12.2.4., Listing of Adverse Events by Subject: In the section that describes the information that should be presented in by-subject adverse events listings, variables listed include "concomitant treatment during study" and the list of example answers for "Action Taken" includes "specific treatment instituted." • Section 12.3.1.3, Other Significant Adverse Events: States that significant AEs, other than those listed as SAEs, should be listed as well. One of the ways of identifying "significant AEs" is those that required concomitant therapy. • Section 12.6, Safety Conclusions: Overall safety discussion should pay particular attention to events requiring interventions, especially administration of concomitant medications

7.2.4. Demographics (DM)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
FDA	Guidance for Industry Collection of Race and Ethnicity Data in Clinical Trials	• Outlines the FDA's approach to collecting and categorizing race and ethnicity data • Strong recommendation to collect self-reported race, with selections of "White" "Black" "Native American & Alaska native" "Hawaiian or Pacific Islander" "Other" "Other specify". • 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. Ethnicity is optional, and when collected should be a separate field from race. As outlined, it is primarily for identifying Hispanic vs. non-Hispanic *This regulation remains extremely US-centric, and studies conducted elsewhere may need to adapt codes as necessary. For studies where race and/or ethnicity are expected to be a focus of analysis, a more specific approach should be developed.*
FDA	Guideline For The Format And Content Of The Clinical And Statistical Sections Of An Application	The Format and Content of the Full Integrated Clinical and Statistical Report of a Controlled Clinical Study, Pg 74: The need to display sex, date of birth and race is referenced in numerous sections of this guidance, including listing safety information for each subject.
ICH	E.2.B Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports	Part B.1: Defines demography information to be included with SAE reports
ICH	E3 Structure and Content of Clinical Study Reports	• Section 11.2:- Demographic & other baseline characteristics, States that demography variables are usually expected. • Sections 8, 12 & 14: various sections state requirement that key efficacy and safety data be presented broken down by various demographic variables
ICH	E5 Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data	Guidance discusses what kinds of factors may affect drug efficacy and sensitivity, and defines ethnicity vs. race. It does not include any specifics about race, but provides a good summary of what characterizes ethnicity, how to consider it in evaluating a drug, and what it is most likely to affect.

7.2.5. Disposition (DS)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E3 Structure and Content of Clinical Study Reports	Section 10.1 Disposition of Subjects: Specifically states the need to account for each subject randomized, and to summarize and discuss early withdrawals. An appendix provides an example of a flowchart showing the numbers of subjects who progressed through each phase of the study. *This implies that there must be a way of assessing how many screen failures there were (could bring screen fail CRFs in-house and enter), as well as specifically tracking the number of subjects completing each phase. Easiest way to do this is usually to require that there be a CRF completed specifying the status of the subject at the termination of the phase.*

7.2.6. Drug Accountability (DA)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
CFR	21 CFR 312.57 & 59 Investigational New Drug Application	• Recordkeeping and record retention: discussed the requirements around investigators maintaining adequate records showing the receipt, shipment, or other disposition of the investigational drug. These records are required to include, as appropriate, the name of the investigator to whom the drug is shipped, and the date, quantity, and batch or code mark of each such shipment. • Disposition of unused test article: the sponsor is responsible for ensuring that all test articles is accounted for, and shall maintain written records to that effect.
FDA	Compliance Program Guidance Manual for FDA Staff	• 14.1.1 Compliance Program 7348.811, Bioresearch Monitoring: Clinical Investigators: Extensive instructions on how inspectors should verify who has access to the test article and that proper and controlled storage conditions were in place, associated shipping records, control and documentation of test article dispensed to and retrieved from the subjects and returned to the sponsor or destroyed, whether the amount of test article at the site roughly corresponds to the amount expected given the number of subjects and the dosing schedule,
FDA	Guidance for Industry: Guideline for the Monitoring of Clinical Investigations	• Monitors are required to inspect clinical sites prior to initiating the study to ensure that the investigator understands the obligations they have with respect to controlled handling of the test article
ICH	E3 Structure and Content of Clinical Study Reports	• Section 9.4.8 Treatment Compliance: states that the means of assessing compliance should be presented, including if it involved drug accountability
ICH	E4 Dose-response Information to Support Drug Registration	Discusses various trial designs and various ways of assessing exposure and its relationship to efficacy and to safety issues. The implication of this guidance to study design is that the right data should be collected to allow for fairly specific and detailed analyses of exposure, dose, duration and concentration. • *It is important to note that compliance is not the same as drug accountability. Compliance speaks to whether the subject took the study medication as required by the protocol. Drug accountability means the ability to account for all the study medication, regardless of whether or not the subject took it. Generally, drug accountability records are a poor way of assessing compliance or exposure.*
ICH	E6 Guideline for Good Clinical Practice	• Section 4.6 Investigational Products: outlines the many responsibilities the investigator has for ensuring investigational substances are securely stored and handled, access is restricted to authorized individuals, and appropriate records are maintained that track the location and disposition of all test article from the time it is received by the site to the time it is dispensed to the subject (with any remaining test article returned), returned to the sponsor or destroyed. All test articles must be accounted for. • Section 6.4.7 Protocol Design: methods for ensuring accountability for all test article must be defined in the protocol • Section 8 Essential Documentation: includes shipping records, dispensing and retrieval records, documentation that the test article has been used in accordance with the study protocol, and "To document the final accounting of investigational product(s) received at the site, dispensed to subjects, returned by the subjects, and returned to sponsor"

7.2.7. ECG Test Results (EG)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E14. The Clinical Evaluation Of QT/QTc Interval *Also referred to as the EMEA QT/QTc guidance.*	*These quotes are taken directly from the guidance, and define the requirement for ECG data for general clinical trials* 2.2 The "Thorough QT Study": The "thorough QT/QTc study' would typically be conducted early in clinical development to provide maximum guidance for later trials, although the precise timing will depend on the specifics of the drug under development. It would usually not be the first study, as it is important to have basic clinical data for its design and conduct, including tolerability and pharmacokinetics. Some drugs might not be suitable for study in healthy volunteers because of issues related to tolerability (e.g., neuroleptic agents, chemotherapeutics). The results of the "thorough QT/QTc study" will influence the amount of information collected in later stages of development: • A negative "thorough QT/QTc study" will almost always allow the collection of on-therapy ECGs in accordance with the current practices in each therapeutic area to constitute sufficient evaluation during subsequent stages of drug development (see section 2.3); • A positive "thorough QT/QTc study" will almost always call for an expanded ECG safety evaluation during later stages of drug development (see section 2.3). There could be very unusual cases in which the "thorough QT/QTc study" is negative but the available nonclinical data are strongly positive (e.g., hERG positive at low concentrations and *in vivo* animal model results that are strongly positive). 3. ANALYSIS OF ECG DATA FROM CLINICAL TRIALS Evaluation of the effects of a drug on the standard ECG intervals and waveforms is considered a fundamental component of the safety database of any new drug application. Regardless of the outcome of the "thorough QT/QTc study", ECG changes recorded as adverse events should be pooled from all studies for analysis. ECG interval data from the "thorough QT/QTc study" should only be pooled with subsequent trials of similar rigor with regard to ECG data collection and analysis, but should not be pooled with trials using less rigorous ECG collection. Standardization of ECG collection for similar studies within a clinical trial program will facilitate pooled analyses. The guidance also provides an outline of what the agencies expect with respect to the collection, presentation and analysis of ECGs.

7.2.8. Exposure (EX)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E3 Structure and Content of Clinical Study Reports	Section 12.1, Extent of Exposure: specifies that the CSR should characterize each subject population with respect to the duration of exposure, the dose, and, if available, the drug concentration (i.e., C_{max}). This applies to exposure to placebo and active control as well as study medication. This verbiage is virtually identical to E1, Extent of Population Exposure to Assess Clinical Safety. In order to assess Exposure appropriately, compliance must be gauged.
ICH	E4 Dose-response Information to Support Drug Registration	Discusses various trial designs and various ways of assessing exposure and its relationship to efficacy and to safety issues. The implication of this guidance to study design is that the right data should be collected to allow for fairly specific and detailed analyses of exposure, dose, duration and concentration. *It is important to note that compliance is not the same as drug accountability. Compliance speaks to whether the subject took the study medication as required by the protocol. Drug accountability means the ability to account for all the study medication, whether or not the subject took it. Generally, drug accountability records are a poor way of assessing compliance or exposure.*

7.2.9. Inclusion / Exclusion Criteria Not Met (IE)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
CFR	21 CFR 312.42 Investigational New Drug Application	Discusses some eligibility issues that may incur "clinical holds" for studies that are planned or already in progress. These primarily involve studies where the selection of subjects may inappropriately exclude certain groups, such as people of reproductive potential.
ICH	E3 Structure and Content of Clinical Study Reports	Section 9.3 Selection of Study Population - States that the criteria that subjects had to satisfy in order to enter the trial must be described (e.g., diagnostic criteria, demographic criteria), and any safety or other factors used to exclude subjects must be laid out and discussed. If there is reason to believe that there might have been systematic bias on the part of the investigator (e.g., not entering the sickest subjects), this must be described and its potential effects discussed.
ICH	E6 Guideline for Good Clinical Practice	Section 6.5.1 and 6.5.2: Subject inclusion and exclusion criteria must be specified in the protocol

7.2.10. Laboratory Test Results (LB)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E3 Structure of the Clinical Study Report	• Section 12, Safety Evaluation: Laboratory results are expected to be presented along with AEs, concomitant medications and other data that assess the basic safety profile of the drug • Section 12: laboratory results are one of the criteria for identifying significant non-serious AEs • Section 12.1, Extent of Exposure: CSR is expected to present analyses of drug concentration in relationship to abnormal lab parameters, if seen • Section 12.2.2.2, Adverse Events: significant lab abnormalities are expected to be presented along with other AEs
ICH	E9 Statistical Principles for Clinical Trials	• Section 6.2: states that lab values, along with vital signs and AEs, are expected to form the main body of evidence as to the safety of the drug

7.2.11. Medical History (MH)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E2B Data Elements for Transmission of Individual Safety Case Reports	Section B.1.7., Relevant Medical History: Medical history is listed as one of the elements that must be included in the evaluation and communication of expedited safety event reports. The User Guidance suggests that medical judgment must be used in determining what to record – focus on the findings that are at all likely to have a bearing on the event, rather than an exhaustive list of all observations. *This suggests that if there are specific medical history conditions of interest they might be best captured by asking specific questions, rather than relying on a general list.*
ICH	E3 Structure & Content of Clinical Study Reports	• Section 11.2, Demographic and Other Baseline Characteristics: Describes the information that must be included as part of the general characterization of comparative groups. It includes "relevant previous illness", which refers to diseases other than that under study. This is another term for "Medical History." • Section 11.4.5, Drug-Drug and Drug-Disease Interactions: states that relationships between subject response and prior illness must be described. This does not necessarily imply that medical history must capture an exhaustive list of prior conditions; it may be appropriate to focus on particular conditions or classes of condition. • Section 12.3.2. Narrative of Deaths, Serious AEs: "previous illness" is an element that must be addressed in characterizing serious adverse events.
ICH	E6 Guideline for Good Clinical Practice	Section 8.3.13 Source documents - To document the existence of the subject and substantiate integrity of trial data collected. To include original documents related to the trial, to medical treatment, and history of subject.

7.2.12. Physical Examination (PE)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
FDA	Guidance for Industry: Premarketing Risk Assessment	Section VI H, Important Aspects of Data Presentation - States that physical exam findings are a useful part of the subject narratives associated with serious adverse events
ICH	E3 Structure and Content of Clinical Study Reports	Section 12.5, Vital Signs, Physical Findings and Other Observations Related to Safety - Physical findings must be analyzed and displayed in the same manner as lab values. If any apparent relationship to dose effect or other response was observed, this must be discussed.

The ICH E3 guideline states that physical examination data should be analyzed and presented in the same manner as laboratory data. The best practice recommends that physical findings, e.g., abnormalities, be reported as adverse events or medical history findings. The approach recommended by CDASH as the best practice still accomplishes the ultimate goal of assessing the impact of physical exam findings on the treatment's safety profile. Adverse events are extensively analyzed and medical history data are available for reference and as a result there is no loss of safety information.

There are several reasons for the CDASH recommendation.

- When capturing physical exam findings, sites are instructed to record any clinically significant findings on the Medical History or AE CRF. Collecting these findings as part of the Physical Exam domain as well amounts to double collection of data, which runs counter to the CDASH best practices.
- AE data are already extensively analyzed, and Medical History data are available for reference. Analyzing physical exam findings as well would add little to this information.
- There are currently no dictionaries that are fully suitable for coding physical exam findings, and by extension Medical History findings, such that they are comparable to AEs coding. This can result in conflicting analysis results, which may be difficult to resolve and not add to the clarity of the safety profile. AE data are very comprehensively analyzed, resulting in a more complete safety profile.
- If the intent in summarizing physical findings like lab findings is to produce shift tables, this implies a comparison to baseline. This can be accomplished if baseline data are coded, which, as is noted above, is challenging whether they are captured as physical exam or medical history findings. AE data capture this as part of the definition of an AE is a condition that worsens after treatment begins.
- If there is a desire to assess if particular baseline conditions affect study outcomes or safety profiles, neither physical exam data nor medical history data as generally collected are suitable, as they are both open ended structures. To be useful, the specific conditions should be listed and assessed so that the study can designed appropriately and proper analyses can be conducted.

7.2.13. Protocol Deviations (DV)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
CFR	21 CFR Part 812 – Investigational Device Exemptions	812.140 Records – requires a participating investigator to maintain documentation of the dates of, and reasons for, deviating from the protocol.
ICH	E3 Structure and Content of Clinical Study Reports	Section 10.2, Protocol Deviations - requires the reporting of protocol deviation information "related to study inclusion or exclusion criteria, conduct of the trial, patient managements or patient assessment' within the body of the text and patient data listings.

7.2.14. Substance Use (SU)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
ICH	E2A Clinical Safety Data Management: Definitions And Standards For Expedited Reporting	Attachment 1, Section 4, Details of suspected adverse drug reaction: includes history of drug or alcohol abuse as information that may help in characterizing potential AEs.
ICH	E3 Structure and Content of Clinical Study Reports	Section 9.5.4, Drug Concentration Measurements: mentions that assessments of study drug concentrations should take into account characteristics that may affect it, such as concomitant medication/alcohol/caffeine/nicotine, among others.
ICH	E5 Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data	Refers to alcohol and tobacco usage as “extrinsic” ethnic factors that may be relevant when studying a drug in a different population.
ICH	E11 Clinical Investigation of Medicinal Products in the Pediatric Population	Section 2.5.5 Adolescents (12 to 16-18 years (dependent on region)): encourages the examination of recreational use of drugs, alcohol and tobacco when doing studies in this population.

7.2.15. Vital Signs (VS)

SOURCE	REGULATION/GUIDELINE	DESCRIPTION/WORDING
FDA	Guidance for Industry: Premarketing Risk Assessment	• Section VI F, Rigorous Ascertainment of Reasons for Withdrawals from Studies: a detailed analysis of all withdrawals should be conducted, especially for those that withdrew due to changes that may not be captured as adverse events, such as ECGs or vital signs. • Section VI H, Important Aspects of Data Presentation: States that adverse events important to a drug class should be comprehensively analyzed in the integrated summary of safety, along with relevant ancillary information such as vital signs.
FDA	MAPP (Manual of Policies and Procedures) for the Evaluation of NDAs	• Section 7.2.5, Adequacy of Routine Clinical Testing: Vital Signs monitoring is considered to be one of the key indicators of whether good quality clinical care was provided to subjects in trials in an NDA.
ICH	E3 Structure and Content of Clinical Study Reports	• Section 12.2.2., Display of Adverse Events: states that changes in vital signs considered relevant to adverse events should be displayed with the AEs. • Section 12.5, Vital Signs, Physical Findings and Other Observations Related to Safety: Vital Signs should be analyzed and displayed in the same manner as lab values. If any apparent relationship to dose effect or other response was observed, this should be discussed.
ICH	E9 Statistical Principles for Clinical Trials	Section 6.2, Choice of Variables and Data Collection: Vital Signs are listed as one of the items that generally contribute to the body of evidence characterizing safety.

7.3. CDASH Project Development Process

7.3.1. Project Background

The CDASH project sought to address FDA's Critical Path Opportunity (#45), the purpose of which was to facilitate standardized collection of clinical research data at investigative sites.

> ***#45 Consensus on Standards for Case Report Forms.*** *Clinical trial data collection, analysis, and submission can be inefficient and unnecessarily expensive. A wide array of different forms and formats are used to collect clinical trial information, and most data are submitted to the FDA on paper. Differences in case report forms across sponsors and trials creates opportunities for confusion and error. Standardization of the look and feel of case report forms could reduce these inefficiencies and also help accelerate progress toward electronic data capture and submission.*[6]

Standards can substantially reduce time and resource needs for clinical research studies, particularly when they are implemented in the start-up stage. In addition, they have been reported to improve project team communication and resulting data quality.[7]

Although the CDASH project did not address "look and feel" (referenced above in C-Path opportunity #45), through standardization of basic data collection variables efficiencies can be achieved that will result in less confusion across sponsors, investigators and research sites and will require less data cleaning and facilitate more efficient monitoring, audit, submission and review procedures.

The CDASH project continued the CRF standardization work initiated by the Association of Clinical Research Organizations (ACRO). It was recommended that CDISC take the leadership role during the January 2006 - DIA Open Forum "Creating Clinical Trial Efficiencies through Standard Data Collection" organized by CDISC, FDA and ACRO. CDISC has expertise in standards development demonstrated by former CDISC work, such as in the development of the SDTM for reporting results in regulatory submissions to FDA that can be leveraged in the CDASH project.

In June 2006 the initial Collaborative Group was announced by Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, at the Annual DIA Meeting in Philadelphia in the session titled "Human Subject Protection/Bioresearch Monitoring Initiative and Critical Path Update".

Developing the CDASH project strategy and providing volunteer resources were the responsibilities of the Collaborative Group, which is comprised of the following organizations:

- American Medical Informatics Association (AMIA)
- Association of Clinical Research Organizations (ACRO)
- Association of Clinical Research Professionals (ACRP)
- Baylor College of Medicine
- Biotechnology Industry Organization (BIO)
- Clinical Data Interchange Standards Consortium (CDISC)
- Clinical Research Forum
- Critical Path Institute

[6] Critical Path Opportunities List (Innovation / Stagnation) link: http://www.fda.gov/oc/initiatives/criticalpath/reports/opp_list.pdf

[7] *Applied Clinical Trials, June 2007, Saving Time and Money, Carol Rozwell (Gartner), Rebecca Kush (CDISC), Ed Helton (SAS).*

- Duke Clinical Research Institute (DCRI)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH)
  - Clinical Research Policy Analysis and Coordination Program
  - National Center for Research Resources (NCRR)
  - National Cancer Institute (NCI); caBIG
  - National Institute of Child Health and Human Development (NICHD)
  - National Library of Medicine (NLM)
- Pharmaceutical Research and Manufacturers Association (PhRMA)
- Society for Clinical Data Management (SCDM)

A CDASH project kick-off meeting was held in October 2006 during which 3 Domain Teams were formed and work was commenced on the Adverse Events, Concomitant Medication, Demographics and Subject Characteristics domains.

The primary goal of the CDASH project is the development of "content standards" for a basic set of global data collection variables that will support clinical research studies. These "content standards" consist of data collection variables, definitions, completion instructions for the clinical site, and additional information and rationale for sponsors.

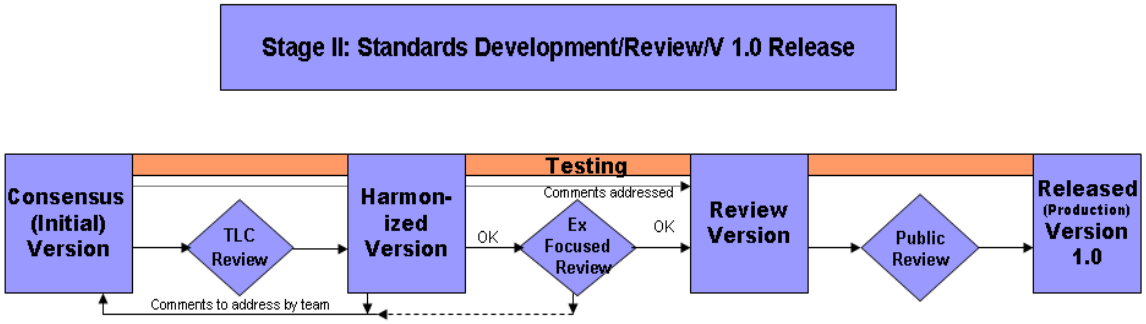
Basic data collection variables identified by CDASH Domain Teams were mapped into the SDTM and are compliant with the SDTMIG. See Section 2.1 for more information on CDASH and the SDTM.

The initial scope of the project was the development of CRF content for 16 core domains. These domains are common to all therapeutic areas. As mentioned above, the initial scope was limited to CRF content, not the physical layout of CRFs.

Domains	
Adverse Events (AE)	Inclusion and Exclusion Criteria (IE)
Comments (CO)	Laboratory Test Results (LB)
Concomitant Medications (CM)	Medical History (MH)
Demographics (DM)	Physical Examination (PE)
Disposition (DS)	Protocol Deviations (DV)
Drug Accountability (DA)	Subject Characteristics (SC)
ECG Test Results (EG)	Substance Use (SU)
Exposure (EX)	Vital Signs (VS)

7.3.2. Process and Deliverables

The CDASH project followed the CDISC Operating Procedure (COP-001) for Standards Development (http://www.cdisc.org/about/bylaws_pdfs/CDISC-COP-001-StandardsDevelopment-Feb2006.pdf). Following is flow diagram that describes Stage II: Standards Development/Revision/Release of Version 1.0.



The CDISC Standards Development Process calls for a minimum of three reviews to build consensus towards the Version 1.0 standard. The CDASH domain-specific recommendations were first reviewed by an internal CDISC Technical Leadership Committee (TLC) to ensure that they did not diverge from the other relevant CDISC standards. They were then combined into "review packages" for external review by the Collaborative Group, which acted as an external focus group in the case of the CDASH project. The entire set of domains was reviewed together in a final open public review process prior to the release of Version 1.0.

The project deliverables included in the original CDASH charter were to agree on basic data collection fields, map these fields to the SDTM, write definitions and CRF instructions for clinical sites, as well as write implementation instructions for sponsors.

During the initial CDASH kick-off meeting in October 2006, ACRO presented the following ***guiding principles***. These guiding principles were reviewed at the initiation of each Domain Team and were used to set the tone for the work. Data collection fields identified should:

- Be "standard" yet flexible to allow customizing within defined limits
- Be limited to required and necessary variables
- Comply with regulatory requirements
- Reduce redundancies and do not duplicate information found elsewhere in CRFs
- Increase collection of meaningful data
- Facilitate use of standards by all users
- Be appropriate for use in both pre- and post-approval studies
- Allow consistent and efficient collection, transmission, analysis and archival of data

The Domain Teams began by reviewing CRF samples supplied by ACRO (where available), as well as other CRF samples that are currently used by industry. Domain Teams were asked to document the data collection variables reviewed along with a justification for including or excluding them in the CDASH recommendations.

For each data collection field, the question text was refined; the SDTMIG variable name or CDASH data collection variable name assigned; definitions, CRF completion instructions and instructions for the clinical sites were written; and a CDASH "core designation" was assigned (Highly Recommended, Recommended/ Conditional or Optional). The SDTM submission variables served as a target for deliverable data. Data collection variables were mapped to the SDTMIG variables as applicable.

Each Domain Team reviewed CRF samples, compiled a list of data collection fields and established the administrative procedures to be used. Domain Team members were also encouraged to collect feedback from relevant functions within their respective companies, both nationally and internationally (i.e., Regulatory Affairs, Drug Safety, etc.). Weekly or biweekly teleconferences were held to review and establish basic data collection fields for each domain. Once CRF samples were collected and a frequency analysis completed, each data collection field was reviewed and the most appropriate core designation (i.e., Highly Recommended, Recommended/Conditional, Optional) was agreed and assigned by the Stream. Definitions were then review and agreed and CRF and sponsor completion instructions written. In the rare instance when there was a disagreement within a Domain Team, a majority vote determined the approach taken. The resulting Initial Consensus Version (ICV) and later the Harmonized Version (HV) were submitted for review by the TLC and later in the process by the Collaborative Group (see first paragraph in the Process and Deliverables appendix above).

7.3.3. Volunteers

The CDASH project work was performed primarily by volunteers representing pharmaceutical and biopharmaceutical companies (~50%), contract research organizations (42%), academia and government (~8%).

Volunteers were recruited via open invitation. Effort was made to ensure that representation on each Domain Team comprised representatives from different companies representing functional areas required in the drug development process (i.e., data management, biostatistics, drug safety, etc.).

The majority of volunteers were from US-based organizations, however, international representation and participation was encouraged and sought whenever possible. The number of volunteers on the Domain Teams varied from 10 - 40 members. See Participating Companies appendix for a list of participating companies, agencies and institutions.

The CDASH Core Team (or Management Team) was comprised of a qualified, multidisciplinary team of 16 members. The Core Team was responsible for executing the project plan by holding regular conference calls and face-to-face meetings, as appropriate, to achieve the strategic objectives. Each Core Team member either led a safety Domain Team or was responsible for some aspect of the CDASH Standard, Version 1.0. See the CDASH Core Team Members appendix for a list of CDASH Core Team members and their affiliations.

7.4. CDASH Core Team Members and Participating Companies

7.4.1. CDASH Core Team Members

Following is a list of the CDASH Core Team members:

Team Leader	Affiliation	Email Address	Team / Responsibility
Rhonda Facile	CDISC	rfacile@cdisc.org	Project Director
Paul Bukowiec	Millennium Pharmaceuticals	Paul.Bukowiec@mpi.com	Physical Exam & Vital Signs
Dorothy Dorotheo	InterMune, Inc. and SCDM	DDorotheo@intermune.com	Prior & Concomitant Medications, CDASH & ODM
Lorna Griffin	Merck & Company	lorna_griffin1@merck.com	Appendices, Editing
Kit Howard	Kestrel Consulting	kit@kestrelconsultants.com	References, Editing
Shannon Labout	Astellas EU and SCDM	shannon.labout@eu.astellas.com	Inclusion/Exclusion, Best Practice
Jay Leeka	AstraZeneca	Jay.Leeka@astrazeneca.com	Comments & Protocol Deviations
Liz Nulton-Bodiford	GlaxoSmithKline	liz.m.nulton-bodiford@gsk.com	Drug Accountability & Exposure, Best Practice, Terminology
Holly Peterson	Forest Laboratories	Holly.peterson@frx.com	Adverse Events
Cathy Schleuning	Schwarz BioSciences/UCB	cathy.schleuning@ucb-group.com	Editor, Appendices
Lauren Shinaberry	PRA International	ShinaberryLauren@PRAIntl.com	ECG, CDASH & ODM
Trisha D. Simpson	Schwarz BioSciences/UCB	Trisha.Simpson@ucb-group.com	Medical History & Substance Use
David Tatum	Eli Lilly & Co./Consultant	tatum4@comcast.net	Adverse Events
Kim Truett	KCT Data, Inc.	Kim.Truett@kctdm.com	Lab
Alec Vardy	CV Therapeutics/Exelixis	avardy@exelixis.com	Disposition, End of Study, Terminology
Gary Walker	Quintiles	gary.walker@quintiles.com	Demographics & Subject Characteristics, CDASH & ODM

7.4.2. Participating Companies

Due to the nature of being a volunteer effort, there have been changes in both the membership of the Domain Teams and the degree of participation over the course of this project. As a result we have listed only the company affiliation. Participating companies appear in alphabetical order.

Participating Companies, Agencies and Institutions

1. Abbott
2. Accenture
3. Accovion GmbH
4. AdvaMed
5. American Medical Informatics Association (AMIA)
6. Amgen
7. ArisGlobal, LLC
8. Association of Clinical Research Organizations (ACRO)
9. Association of Clinical Research Professionals (ACRP)
10. Astellas
11. AstraZeneca
12. Bausch & Lomb
13. Baxter
14. Baylor College of Medicine
15. Biogen Idec
16. Biopharma Data Services
17. Biotechnology Industry Organization (BIO)
18. Boehringer Ingelheim
19. Boston Scientific Corporation
20. Bristol-Myers Squibb
21. Brown University
22. Building Points of View
23. Cambridge Cognition
24. CEDRA
25. Cephalon
26. Cleveland Clinic (CCF)
27. Clinical Data Interchange Standards Consortium (CDISC)
28. Clinical Research Forum
29. CliniPharma Consulting
30. Cognizant Technology Solutions
31. Commitum AB
32. Covidien (formerly Tyco Healthcare/Mallinckrodt)
33. Critical Path Institute
34. CSS Informatics
35. CV Therapeutics
36. Daedalus Software, Inc
37. DataLabs
38. DataScene
39. Duke Clinical Research Institute (DCRI)
40. Eisai Global Clinical Development
41. Eli Lilly and Company
42. Enzon Pharmaceuticals, Inc.
43. Ethicon (Johnson & Johnson)
44. Exelixis
45. Fast Track Systems
46. Food and Drug Administration (FDA)
47. Formedix Inc.
48. Forest Laboratories, Inc.
49. Genentech, Inc.
50. Genzyme Corp.
51. Gilead Colorado, Inc.
52. GlaxoSmithKline
53. Global Research Services, LLC
54. Harvard Clinical Research Institute
55. Health Decisions
56. HealthRoad Co. Ltd,
57. ICON Clinical Research
58. ImClone Systems Incorporated
59. Insmed Incorporated
60. InterMune, Inc.
61. Johnson & Johnson
62. Kai Research
63. KCT Data, Inc.
64. Kestrel Consultants
65. Kos Pharmaceuticals, Inc.
66. Lab Connect LLC
67. Medidata
68. Medifacts
69. Merck & Company
70. Millennium Pharmaceuticals, Inc.
71. National Institutes of Health (NIH)
    - Clinical Research Policy Analysis and Coordination Program
    - National Cancer Institute (NCI); caBIG
    - National Cancer Institute - Center for Bioinformatics
    - National Center for Research Resources (NCRR)
    - National Institute of Child Health and Human Development (NICHD)
    - National Library of Medicine (NLM)
    - NCI Cancer Therapy Evaluation Program
    - NCI Enterprise Vocabulary Service
    - NIH Office of Biotechnology Activities (OBA)
72. Nextrials, Inc.
73. Nounsware Company
74. Novartis Pharmaceuticals Corporation

Participating Companies, Agencies and Institutions, continued

75. Octagon Research Solutions
76. Ofni Systems Inc.
77. Omnicare
78. Oracle Health Sciences
79. Organon
80. Othera Pharmaceuticals, Inc
81. PAREXEL International
82. Percipenz
83. Pfizer, Inc.
84. Pharmaceutical Research and Manufacturers Association (PhRMA)
85. PharmaNet, Inc
86. Phoenix Data Systems
87. PHT Corp
88. PPD, Inc.
89. PRA International
90. Procter & Gamble
91. PTC Therapeutics
92. QIMR
93. Quintiles Transnational
94. Regeneron
95. Rho Inc.
96. RTI International
97. Schering-Plough Corporation
98. Schwarz BioSciences
99. Society for Clinical Data Management (SCDM)
100. SpaceLabs Healthcare
101. Statistics & Data Corporation
102. Stellar Systems
103. Synteract, Inc
104. TAKE Solutions Inc.
105. Takeda Global Research & Development Centre (Europe) Ltd.
106. Teva Neuroscience
107. The University of Texas Health Science Center at Houston
108. Tyco Healthcare Mallinckrodt
109. UCB Pharma SA
110. University of California, Irvine
111. University of Pennsylvania School of Medicine
112. University of Utah Health Science Center
113. Wake Forest University Baptist Medical Center
114. Westat Inc.
115. Wyeth Inc.
116. ZymoGenetics

7.5. List of Abbreviations and Glossary

The following abbreviations and terms are used in this document. Additional definitions can be found in the CDISC Glossary available at http://www.cdisc.org/glossary/index.html.

Abbreviation / Acronym / Term	Definition
21 CFR	Title 21 of the Code of Federal Regulations (CFR). Title 21 of the CFR is reserved for rules of the Food and Drug Administration.
AE	Adverse event, also refers to the Adverse Events domain
ATC code	Anatomic Therapeutic Chemical code from WHO Drug
AMIA	American Medical Informatics Association, a Collaborative Group Member
ACRO	Association of Clinical Research Organizations, a Collaborative Group Member
ACRP	Association of Clinical Research Professionals, a Collaborative Group Member
BID	Twice a Day (Latin: *bis in die*)
BIO	Biotechnology Industry Organization, a Collaborative Group Member
BRIDG	Biomedical Research Integrated Domain Group
caBIG	**c**ancer **B**iomedical **I**nformatics **G**rid™. An information network enabling all constituencies in the cancer community – researchers, physicians, and patients – to share data and knowledge.
CDASH	Clinical Data Acquisition Standards Harmonization Project. The name for the project that delivers basic data collection fields (this document)
CDISC	Clinical Data Interchange Standards Consortium, a Collaborative Group Member
CDM	Clinical Data Management
Collaborative Group	Group of organizations that support the CDASH project
CM	Concomitant Medications domain; the CDASH Standard Version 1.0 also includes recommendations on *Prior* Medications
C_{MAX}	Concentration maximum; used in pharmacokinetics and bioequivalence testing to indicate maximum plasma concentration for a drug.
CO	Comments domain
Collected	Within this document collected refers to information that is recorded and/or transmitted to the sponsor. This includes data entered by the site on CRFs/eCRFs as well as vendor data such as core lab data. This term is a synonym for "captured".
CRF	Case report form (sometime case record form) A printed, optical, or electronic document designed to record all required information to be reported to the sponsor for each trial subject.
CTCAE	Common Terminology Criteria for Adverse Events
DA	Drug Accountability domain
Databased	To put (data) into a database.
Dataset	A collection of structured data in a single file
Derived	Within this document derived refers to information that is not directly entered into the specific data field by the investigator site or by a core lab. This category includes autoencoded data, calculated data and similar electronically generated data, but not prepopulated fields.
DM	Demographics domain
Domain	A collection of observations with a topic-specific commonality about a subject
DS	Disposition domain
DV	Protocol Deviations domain
eCRF	Electronic case report form
EC	The European Commission (formally the Commission of the European Communities) is the executive branch of the European Union.
EDC	Electronic data capture
EG	ECG Test Results domain
EMEA	The European Medicines Agency. A decentralized body of the European Union, main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use.
Epoch	Interval of time in the planned conduct of a study. An epoch is associated with a purpose (e.g., screening, randomization, treatment, follow-up), which applies across all arms of a study.

EVS	Enterprise Vocabulary Services
EX	Exposure domain
FAQs	Frequently Asked Questions
FDA	Food and Drug Administration Part of the US Department of Health and Human Services Agency. The regulatory authority for all pharmaceuticals (including biologics and vaccines) and medical devices in the US.
GCDMP	Good Clinical Data Management Practices (GCDMP). SCDM publication on clinical data management processes
GCP	Good Clinical Practice
hERG	human Ether-a-go-go Related Gene
HITSP	Health Information Technology Standards Panel
HL7	Health Level 7
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICH E2A	ICH guidelines on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting
ICH E2B	ICH guidelines on Clinical Safety Data Management: Data Elements For Transmission Of Individual Case Safety Reports
ICH E2C	ICH guidelines on Clinical Safety Data Management: Periodic Safety Update Reports For Marketed Drugs
ICH E3	ICH guidelines on Structure and Content of Clinical Study Reports
ICH E4	ICH guidelines on Dose-response Information to Support Drug Registration
ICH E5	ICH guidelines on Ethnic Factors in the Acceptability of Foreign Clinical Data
ICH E6 (R1)	ICH guideline for Good Clinical Practice
ICH E9	ICH guidelines on Statistical Principles for Clinical Trials
ICH E11	ICH guidelines on Clinical Investigation of Medicinal Products in the Pediatric Population
ICH E14	ICH guidelines on the Clinical Evaluation Of QT/QTc Interval
IE	Inclusion/Exclusion Criteria Not Met domain
IND	Investigational New Drug. IND application required by the US FDA before clinical trials of a new drug or new biological agent may be initiated.
IRB	Institutional Review Board. Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects
ISO 8601	International Organization for Standardization document of character representation of dates, date/times, intervals, and durations of time
JIC	Joint Initiative Council
LB	Laboratory Test Results domain
MedDRA	Medical Dictionary for Regulatory Activities (new global standard medical terminology designed to supersede other terminologies (such as COSTART and ICD9) used in the medical product development process
MH	Medical History domain
NA	Not applicable
NCI	National Cancer Institute (NIH)
NCI EVS	National Cancer Institute (NIH) Enterprise Vocabulary Services
NCRR	The National Clinical Research Resources, a Collaborative Group Member
NDA	New Drug Application
NICHD	The National Institute of Child Health and Human Development, a Collaborative Group Member
NIH	National Institutes of Health
NLM	National Library of Medicine
ODM	Operational Data Model. Format for representing the study metadata, study data and administrative data associated with a clinical trial
OTC	Over The Counter.
PE	Physical Examination domain
PK	Pharmacokinetics. The study of the absorption, distribution, metabolism and excretion of a drug.
PhRMA	Pharmaceutical Research and Manufacturers Association
PRBC	Packed Red Blood Cells
Preprinted (pre-printed)	Items that are part of the original printing on a paper CRF. For example the unit required for a response, such as "years" for an age question. These data may or may not be stored in the database.

Prepopulated (pre-populated)	Items that are part of the eCRF (or data collection device) that are not enterable/modifiable. (also see preprinted). These data are stored in the study database.
PRN	As Needed (Latin: *pro re nata*)
Protocol Deviation	A variation from processes or procedures defined in a protocol. Deviations usually do not preclude the overall evaluability of subject data for either efficacy or safety, and are often acknowledged and accepted in advance by the sponsor. NOTE: Good clinical practice recommends that deviations be summarized by site and by category as part of the report of study results so that the possible importance of the deviations to the findings of the study can be assessed. *Compare to protocol violation*. [See ICH E3]
Protocol Violation	A significant departure from processes or procedures that were required by the protocol. Violations often result in data that are not deemed evaluable for a per-protocol analysis, and may require that the subject(s) who violate the protocol be discontinued from the study. *Compare to protocol deviation.*
QD	Every Day (Latin: *quaque die*)
QID	Four Times Daily (Latin: *quater in die*)
RCRIM	Regulated Clinical Research Information Management
RIM	Reference Information Model
SAP	Statistical Analysis Plan
SC	Subject Characteristics domain
SCDM	Society for Clinical Data Management, a Collaborative Group Member
SDS	Submission Data Standards. Also the name of the Team that created the SDTM and SDTMIG
SDOs	Standards developing organizations
SDTM	Study Data Tabulation Model
SDTMIG	Submission Data Standards SDTM Implementation Guide for Human Clinical Trials
SOCs	System Organ Classes (from MedDRA)
Study Treatment	The drug, device, therapy, or process under investigation in a clinical trial which has an effect on outcome of interest in a study: e.g., health-related quality of life, efficacy, safety, pharmacoeconomics. *Synonyms: intervention, therapeutic intervention, medical product.*
SU	Substance Use domain
TA	Therapeutic area
TID	Three Times Daily (Latin: *ter in die*)
Uncoded	Not coded. Not having or showing a code.
UUID	Universally Unique Identifier
VS	Vital Signs domain
vs.	Versus. Against. In contrast to or as the alternative of.
WHO	World Health Organization
WHO ART	World Health Organization Adverse Reaction Terminology (WHO-ART) has been developed over more than 30 years to serve as a basis for rational coding of adverse reaction terms.
WHO DRUG (WHO Drug)	World Health Organization Drug Dictionary

7.6. Acknowledgements

CDISC thanks the Collaborative Group and all the companies that have generously donated their resources in staff, time and other forms of support to the CDASH project.

The CDASH Core Team thanks all CDISC standards teams for their cooperation and collaboration in reviewing the CDASH drafts in accordance with the CDISC COP-001.

The CDASH Core Team also thanks the ~190 team volunteers who have participated in the development of the CDASH Standard Version 1.0.

7.7. Representation and Warranties, Limitations of Liability, and Disclaimers

7.7.1. CDISC Patent Disclaimers

It is possible that implementation of and compliance with this standard may require use of subject matter covered by patent rights. By publication of this standard, no position is taken with respect to the existence or validity of any claim or of any patent rights in connection therewith. CDISC, including the CDISC Board of Directors, shall not be responsible for identifying patent claims for which a license may be required in order to implement this standard or for conducting inquiries into the legal validity or scope of those patents or patent claims that are brought to its attention.

7.7.2. Representations and Warranties

Each Participant shall be deemed to represent, warrant, and covenant, at the time of a Contribution by such Participant (or by its Representative), that to the best of its knowledge and ability: (a) it holds or has the right to grant all relevant licenses to any of its Contributions in all jurisdictions or territories in which it holds relevant intellectual property rights; (b) there are no limits to the Participant's ability to make the grants, acknowledgments, and agreements herein; and (c) the Contribution does not subject any Contribution, Draft Standard, Final Standard, or implementations thereof, in whole or in part, to licensing obligations with additional restrictions or requirements inconsistent with those set forth in this Policy, or that would require any such Contribution, Final Standard, or implementation, in whole or in part, to be either: (i) disclosed or distributed in source code form; (ii) licensed for the purpose of making derivative works (other than as set forth in Section 4.2); or (iii) distributed at no charge, except as set forth in Sections 3, 5.1, and 4.2. If a Participant has knowledge that a Contribution made by any Participant or any other party may subject any Contribution, Draft Standard, Final Standard, or implementation, in whole or in part, to one or more of the licensing obligations listed in Section 9.3, such Participant shall give prompt notice of the same to the CDISC President who shall promptly notify all Participants.

7.7.3. No Other Warranties/Disclaimers

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