Clinical Data Acquisition Standards Harmonization

Package-4

Lab (LB)

ECG (EG)

Collaborative Group Review

January 2008

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Section 1. Collaborative Group Review Process and Instructions

1. CDASH Package-4

CDASH Package-4 contains basic data collection variables for Lab (LB) and ECG (EG). Both Harmonized Versions (HV) contain the following sections:

- Introduction and Background
- Scenarios
- Table 1: Data Collection Variables
- Table 2: Data Collection Variables Considered Not Necessary to Collect on CRF

1.1 Review Process

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

Do the proposed data variables cover the basic variables common to most clinical research?

Is the document, taking into account the above, appropriate for broader public review?

1.2 Comment Process

A package consisting of 2 HVs and an Excel comments spreadsheet will be sent to each Collaborative Group (CG) member for distribution within their respective organizations.

We request that each organization consolidate all comments from into one Excel spreadsheet. Be sure to provide the identifying information for each comment (see example below).

Example:

Num	*Reviewer*	*Affiliation*	*Domain*	*Page*	*Variable Name*	*Suggested Change*	*Rationale*
1	*John Smith*	*ABC Pharma*	*DA*	*5*	*DATEST*	*Typo*	*editorial*

Please send consolidated comments to scamhi@cdisc.org no later than 22 February 2008.

Comments will be addressed and a "Reviewed Version" will be then achieved.

2. Introduction

This document contains the final Clinical Data Acquisition Standards Harmonization (CDASH) Package to be submitted for Collaborative Group (CG) review. CDASH Package-4 consists of Harmonized Versions (HV) for the Lab (LB) and ECG (EG) domains.

The Clinical Data Interchange Standards Consortium (CDISC) Operating Procedure (CDISC-COP-001 Standards Development) is the basis for the CDASH process. The Initial Consensus Versions or Harmonized Versions (HVs) were developed by the respective work streams. The HVs included with this document have been reviewed internally by the CDISC Technical Leadership Committee (TLC), comments have been addressed to produce these HVs. The next step in the CDISC consensus-based standards development process is the external focused review or in this case the Collaborative Group review.

The comments from this Collaborative Group review will be collated and each will be addressed. Once all of the HVs from each of the 18 domains have been reviewed by the Collaborative Group and comments have been

addressed, the resulting 18 domains will be posted on the CDISC website for public review. After comments have been addressed CDASH Version 1.0 will be released.

3. Best Practice (General Recommendations and Observations Applicable to all Domains)

3.1 Implementation of CDASH Recommendations

The CDASH project seeks to identify the basic data collection fields needed from a clinical, scientific and regulatory data collection perspective, to enable efficient data collection at the investigative sites. Clearly, the more data fields that are collected, the greater the chances of introducing and/or not identifying errors and the greater the resources needed for monitoring, auditing, conduct and management of the project. Hence, while the Study Data Tabulated Model (SDTM) provides a standard for a 'superset' of data that could potentially be collected or derived, CDASH intentionally identifies a basic set of highly recommended and recommended variables or data collection fields that are expected to be present on the majority of case report forms (CRFs). Although it is assumed that additional data fields will be needed to address the study requirements, this approach forces a thought process among sponsors to determine specifically which fields, if any, must be added to these CDASH recommendations based upon the protocol and the business practices of the sponsor. Specifically, until therapeutic area-specific (TA) data fields have been standardized, these variables will need to be added to the CDASH recommended fields to fulfill the protocol-specific requirements.

While SDTM and CDASH are clearly related, there are instances where they do not exactly match due to their varied purposes, (submission vs. data collection). For example, the SDTM standard may contain derived data while CDASH variables should not be derived at the data acquisition stage. Basic data collection fields identified by CDASH project teams (via the CDISC consensus process) are mapped into the SDTM and are compliant with the SDTM IG. As part of this mapping the SDTM core designation (e.g., required, expected, permissible) has also been provided where applicable as an aide to reviewers. All SDTM "required" data collection fields have been addressed in the CDASH recommendations. The CDASH work streams have intentionally not reproduced other sections of the SDTM standard, and reviewers are asked to refer to the CDISC SDTM Implementation.

The CDASH project deliverables will ultimately provide essentially an Implementation Guide for the SDTM on the data collection end of a project. Highly Recommended data collection variables should always be present on the CRF and should be completed, however, it is assumed that Sponsors will add data collection variables as needed to meet protocol specific and other data collection requirements (e.g. therapeutic area (TA) specific data variables and others as required per protocol, business practice and operating procedures).

It is strongly recommended that standards are defined at the sponsor level taking into consideration the requirements of the stage of clinical development, the individual therapeutic area requirements and NOT on a trial-by-trial basis within the sponsor organization.

3.2 Terminology

Terminology used by the CDASH project is developed through the CDISC Terminology Team and is published by the National Cancer Institute's Enterprise Vocabulary Services (NCI EVS). The CDASH final document, will only list the name of the code list stored in NCI's EVS. *(http://cdebrowser.nci.nih.gov/CDEBrowser/)*

Terminology proposed by the CDASH project will be forwarded to the CDISC Terminology team for consideration and vetting via the consensus-based development process.

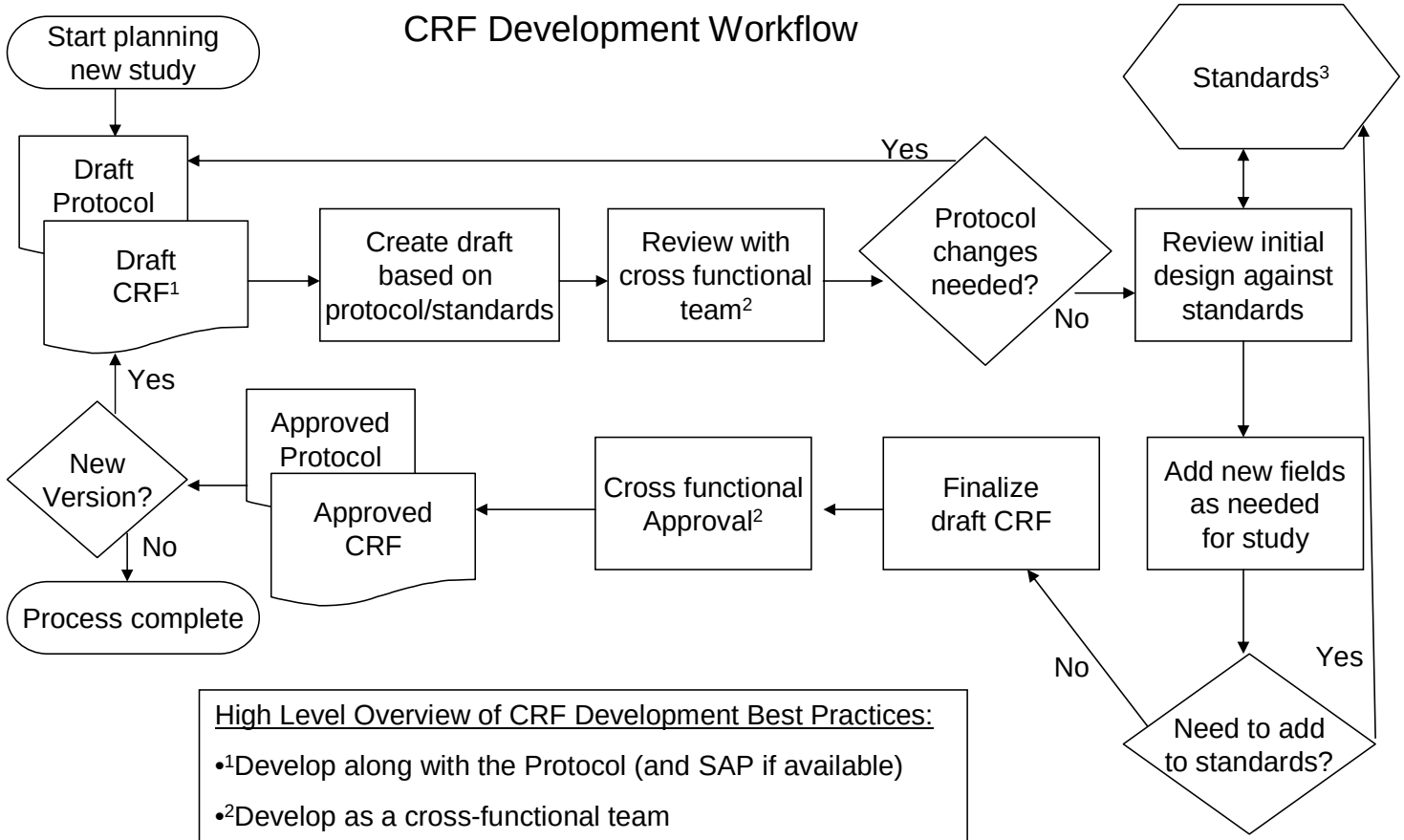
3.3 Recommended Methodologies for Creating Data Collection Instruments

Ref	Methodology	Rationale
1	NECESSARY DATA ONLY: CRF Designers need to avoid collecting too much data or collecting redundant data and focus on collecting the right data. Collect only what is needed to answer the research question and to provide adequate safety data.	• It is very costly and time-consuming to collect data that will not be used in the product submission. Usually, only data that will be used for analysis should be collected on the CRF. Data that is collected must be reviewed and cleaned. • When available, the Statistical Analysis Plan needs to be reviewed to ensure that the parameters needed for analysis are collected and can be easily analyzed.
2	CONTROL: Control the process of designing, printing, distributing and accounting for unused CRFs.	• 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.
3	ADEQUATE REVIEW: The team that designs the data collection instruments for a study needs to be involved in the development of the protocol, with appropriate expertise represented on the CRF design team (statistics, SAS programmers, data management, clinical operations, science, regulatory, pharmacovigilance). Ideally, the CRF should be developed in conjunction with the Protocol and SAP. All essential data on the CRF should be addressed in the protocol to specify how and when it will be collected.	• 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. • Scientific experts should provide input on the efficacy and/or safety data collection fields, and educate the 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.
4	SITE WORKFLOW: The team developing the data collection instruments needs to consider the workflow at site and the standard of care.	• The CRF needs to be quick and easy for site personnel to complete. • The CRF should be designed so that it mirrors the order of assessments performed by the site personnel. Clinical Operations staff should review the CRF for compatibility with site workflow. • Although Clinical Data Management should make the final decisions about CRF design, those decisions should be informed by study and user requirements.

Ref	Methodology	Rationale

5	STANDARDS: Data collection standards should be employed to collect consistent data across compounds and therapeutic areas.	• Using data collection standards across compounds and therapeutic areas saves time and money at every step of drug development.
		• Develop in-house standards wherever possible
		• 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, 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.
		  • reduces global library maintenance in the database.
		  • addresses FDA Critical Path Opportunities (#44 and 45).

6	CLARITY: CRF Questions and completion instructions should not "lead" the site.	Questions should be clear and unambiguous, but designed in such a way as not to introduce bias or errors into the study data. This includes making sure that the options for answering the question are complete (e.g., "Other", "None"). Data also needs to be collected in a way that does not bias answers which can also jeopardize the analysis.
7	TRANSLATIONS: Translations of CRFs into other languages should be a parallel process with separate reviews and approvals by the appropriate experts.	Cultural and language issues should be addressed appropriately during the process of translating CRFs to make sure the CRF questions have consistent meaning in all language versions.
8	CRF COMPLETION GUIDELINES: CRF questions should be as self-explanatory as possible, thereby reducing the need for instructions. Prompts and short instructions may be placed on the CRF page. More detailed instructions may be presented in CRF Completion Guideline for paper CRFs, or in a context-sensitive help file for eCRFs. All instructions need to be concise. For studies which require extensive, detailed instructions explaining conditional actions, use a brief prompt on the CRF page to reference the appropriate location for the detailed instructions. Instructions should be standardized along with the CRF as much as possible.	Putting short instructions and prompts on the CRF increases the probability that they will be read and followed, and enhances flow of the CRF. More detailed instructions break up the flow of the CRF. 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 CRO costs (e.g., processing may be calculated per page). • Decreased Data Management costs (e.g., decreased Data Entry costs).



High Level Overview of CRF Development Best Practices:

- [1]Develop along with the Protocol (and SAP if available)
- [2]Develop as a cross-functional team
  - All data for analysis collected?
  - Possible to collect this way at the site?
  - Sufficient data to address safety?
- [3]Develop and/or enforce standards

3.4 FAQs on Best Practices for Creating CRF Content and Structure

Ref	Question	CRF Type	Best Practice Recommendation	Rationale
1	Should “Yes/No” questions be preferred over “Tick 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 'Tick all that apply' questions. • Exceptions to this recommendation might include 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.	• Yes/No questions provide a definite answer. The absence of a response is ambiguous as it can mean “no” or that the response is missing. • 'Tick all that apply' questions are occasionally needed where the number of options is high.
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 facilitates the use of the CRF • Presenting Yes/No responses in a standard order could reduce bias. Add some wording to say it 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 is recommending an unambiguous date format. • For paper CRFs, or electronic studies in which the date is manually entered, CDASH recommends the format of DD-MON-YYYY for all date collection fields (whether the components are collected as a group or as separate components of day, month and year). • For non-English study data, use a character-based month abbreviation that is recognized in that language. • For electronic data capture, the user may be able to select a date from a calendar, and this would also meet the requirement for an unambiguous date.	• Using the international date format (DD-MON-YYYY) will provide unambiguous dates that will be as the same date by anyone who reads them. For example, the date 06/08/02, can be interpreted as June 8, 2002 or August 6, 2002. • Note: If subject-completed CRF pages are translated into a local language, the international date may make it easier to translate the documents. • Dates are collected in a user-friendly format and then converted to the ISO 8601 format for submission.

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 and start the new 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 system. • Times are collected in a user-friendly format and then converted to the ISO 8601 format for submission.
5	Should calculated data items be recorded on the CRF?	Paper and electronic	• 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 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 record 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 that 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. (examples would be an entry criteria worksheet, or a dose titration worksheet.) • Some data points are collected to facilitate data cleaning, and are not used for reporting or analysis. • Some fields, such as Investigator's Signature, can be verified by the data entry staff, but cannot actually be databased.	• Although the data recorded on worksheets are supporting documentation for key information collected elsewhere in the CRF, these data do not add value to the key information collected and are deemed redundant. • All such worksheets should be considered source documents or monitoring tools, and should be maintained at the site with the study files.

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 "check if not done" box; in others it might be a blank flag or list of values to indicate why data are missing.	• This will provide a definitive indicator to both clinical and statistical programmers of why a data field has missing data. • 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, or solicited comments 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 Data Management 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	• Pre-printing or pre-populating any data in the CRF is discouraged.	• The CRF should be used as a tool to collect unknown study data. • In general, data should be collected and recorded by the site, not pre-populated.
10	Should location of measurement (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, sitting or standing)..	• Location options are only used when the protocol specifies.
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 that training be provided to the sites so they provide the required information in a reported term to enable meaningful coding. • 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 and/or result in inconsistent coding.	• Providing guidance to the site on how the coding dictionaries will be used, and on the importance of clearly associating related terms (e.g., concomitant medications that are given for an adverse event) will facilitate the data verification process, reduce bias and facilitate coding.

3.5 Common Identifier Variables

The following variables apply across all of the data collection domains.

	CDASH CRF Label/Question	Clinical Database Variable Name ***CDASH variables shaded***	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Protocol/Study Identifier	STUDYID (*required*)	Unique Identifier for a study within a submission.		This is typically pre-printed in the header of each CRF page. In an EDC study, this would be hard-coded into the study design. For data received from electronic data providers (i.e., central lab) this information should be provided to the e-data provider and verified during testing of the e-data receipts.	Highly Recommended
2	Site Identifier	SITEID (*required*)	Unique identifier for the site.	Record your clinical site's identifier as defined by the sponsor.	This is typically pre-printed in the header of each CRF page. In an EDC study, this should be pre-populated in the screens provided to the site. For data received from electronic data providers (i.e., central lab) this information should be provided to the e-data provider and verified during testing of the e-data receipts.	Highly Recommended
3	Subject	SUBJID (*required*)	Subject identifier	Record the identifier for the subject.	This is typically recorded in the header of each CRF page. In an EDC study the subject identifiers may be provided to the site using a pre-populated list in the system. For data received from electronic data providers (i.e., central lab) this information should be provided to the e-data provider and verified during testing of the e-data receipts. The subject identifier recorded in the CRF may be combined with other identifiers to produce the SUBJID, or may map directly to the SUBJID.	Highly Recommended
4	Investigator	INVID (*permissible*)	Investigator identifier	Record the sponsor defined identifier for your site investigator.	Study level – Not needed if SITEID is equivalent to INVID.	Optional

References: SCDM's GCDMP (v.4 2005) and GlaxoSmithKline CRF Principles

LAB STREAM

Harmonized Version

Stream Leaders:

Gary G. Walker, Quintiles
Kim Truett, KCT Data, Inc.

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Section 2. Lab Stream Harmonized Version

1. Introduction and Background

The Lab Stream is composed of 33 volunteer members representing many job functions from across the pharmaceutical, biotech, CRO industries, and academia. The Lab case report form (CRF) samples submitted by stream members were compared, consistently collected variables were identified, the necessity of each variable was determined and regulatory and safety compliance were evaluated and confirmed.

Team Members	Affiliation	Location
Melissa Binz	Wyeth	BinzM@wyeth.com
Mary Busha	Boston Scientific	Mary.Busha@bsci.com
Cynthia Cooper	Novartis Pharma. Corp	cynthia.cooper@novartis.com
Roger Duguid	PharmaNet	RDuguid@pharmanet.com
John Estrada	Nextrials, Inc	estrada@nextrials.com
Nate Freimark	OmniCare	Nate.Freimark@OmnicareCR.com
Nicole Galegos	Schering Plough	nicole.gallegos@spcorp.com
Tony Harrington	Cambridge Cognition	Tony.Harrington@camcog.com
Eric L. Hiltebeitel	Cephalon, Inc	ehiltebe@cephalon.com
Paula Jones	Astellas Pharma US, Inc	paula.jones@us.astellas.com
Dawn Kaminski	Octagon Research Solutions	DKaminski@OCTAGONRESEARCH.com
Dinesh Kasthuril	Cognizant	Dinesh.Kasthuril@cognizant.com
Jagruthi Kasuganti	TAKE Solutions Inc	jagruthi.kasuganti@takesolutions.com
Terry Katz	ImClone Systems Incorporated	terry.katz@imclone.com
Shannon Labout	CSS Informatics/PPD	slabout@csscomp.com
Lisa Leubner Cashman	Genzyme Corp	Lisa.Cashman@genzyme.com
Tang Li	Cephalon	tli@cephalon.com
Erik Lickerman M.D.	Daedalus Software, Inc	elickerman@daedalussoftware.com
Yun Lu, Ph.D	Kai Research	ylu@kai-research.com
David Meehan	ICON Clinical Research	meehand@iconus.com
David Norris	Brown University	David_Norris@brown.edu
Linda Pedersen	Astellas Pharma US, Inc	linda.pederson@us.astellas.com
Phillip Reeder	The University of Texas Health Science Center at Houston	Phillip.Reeder@uth.tmc.edu
Diane Reeves	NIH	reevesd@mail.nih.gov
Lorraine Spencer	Takeda Global Research & Development Centre (Europe) Ltd	lspencer@tgrd.com
Susan Taleho	Organon	s.taleho@organonusa.com
Kim Truett	KCT Data, Inc	kim.truett@kctdm.com
Eudoro van der Biest, MS	LabConnect, LLC	evanderbiest@labconnectllc.com
Alec Vardy	Consultant	a.vardy@comcast.net
Gary Walker	Quintiles	gary.walker@quintiles.com
Karen Whitson	Abbott	karen.whitson@abbott.com
Patty Yost	RTI International	Yost@rti.org

The SDTM variables served as the target for deliverable data. At the initial CDASH meeting, categories for identifying those data that need to be collected (highly recommended), might be collected

(recommended/conditional) and some variables which, under certain circumstances, in order to map to the essential SDTM data were agreed upon, and are being used consistently across all streams.

The Lab Stream collected Lab CRFs from participating organizations, and compiled all of the variables from those CRFs into a table. The Stream then reviewed all of the variables in the table, and came to a consensus on which ones should be included in the ICV. The reasons for excluding specific variables from the standard are documented in the Notes section. The Stream then worked to develop appropriate CRF completion instructions and implementation guidelines for the variables included in the standard.

2. Scenarios

The tables below are provided for three different scenarios.

Scenario 1: **Central processing:** In this scenario, patient 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, patient 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, patient 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. This scenario also applies when results are captured directly via an electronic device – not recorded on the CRF.

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.

3. Scenario 1 / Table 1: Data Collection Variables

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Date of collection	LBDTC *(expected)*	Date of sample collection	Record the date collection occurred.	This is intended to be used as a data management tool to verify that lab data is provided in the electronic data for each date that lab data was collected The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required.	Highly Recommended
2	Lab Status	LBSTAT *(permissible)*	Status of whether or not lab was done.	Indicate whether or not lab was done.	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 results provided.	Highly Recommended
3	Panel Name	LBCAT *(expected)* LBSCAT *(permissible)*	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	Examples: such as HEMATOLOGY, URINALYSIS, CHEMISTRY	Optional
4	Planned Time point	LBTPT *(permissible)*	Relative time 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	Optional
5	Time of collection	LBDTC *(expected)*	Time of collection	Record time of collection.	Especially important when multiple assessments are done on one day.	Optional
6	Protocol defined testing conditions met	LBFAST (for example) *(permissible)*	Conditions for sampling defined in the protocol.	The specific testing conditions required should be pre-printed on the CRF, such as "Did patient meet fasting requirements?". Record whether protocol defined testing conditions were met.	Results may be affected by whether conditions for sample were properly met. Example: fasting	Optional

	CDASH CRF Label/Question	Clinical Database Variable Name ***CDASH variables shaded***	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
7	Accession number	LBREFID *(permissible)*	Internal or external specimen identifier.	Record the sample or accession number assigned.	Example: Specimen ID	Optional

4. Scenario 1 / Table 2: Data Collection Variables Considered Not Necessary to Collect on CRF

These are either expected to be received from the Central lab or are not considered necessary.

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Test Name	LBTEST *(required)*	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.	Record the wording of the lab test, if not pre-printed on the CRF	Not required when lab data is not recorded on CRF. This data may be obtained from the central lab or the electronic equipment.	NA
2	Test Result	LBORRES *(expected)*	Result of the measurement or finding as originally received or collected.	Record test results.		NA
3	Lab Name	LBNAM *(permissible)*	Name of lab analyzing sample	Record the laboratory name.		NA
4	Sample Status	LBSPCCND *(permissible)*	Free or standardized text describing the condition of the specimen.	Record condition of sample		NA
5	Clinical Significance	SUPPQUAL domain	Whether lab test results were clinically significant.	Record whether lab results were clinically significant.	Not required when lab data is not recorded on CRF.	NA
6	Abnormal flag	LBNRIND *(expected)*	Reference Range Indicator Indicates where value falls with respect to reference range defined by high and low ranges.	Record whether sample was within range.	Not required when lab data is not recorded on CRF. This data may be obtained from the central lab or the electronic equipment.	NA
7	Units	LBORRESU *(expected)*	Original units in which the data were collected.	Record the units of the lab test, if not pre-printed on the CRF	Not required when lab data is not recorded on CRF. This data may be obtained from the central lab or the electronic equipment.	NA
8	Normal Range	LBORNRLO LBORNRHI *(expected)*	Normal range for continuous measurements in original units.	Record the normal range of the lab test.	Should be populated only for continuous results. This data may be obtained from the central lab or the electronic equipment. Not required when lab data is not recorded on CRF.	NA

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
9	Investigator Comment		Investigator comment on lab test or results.		Not needed.	NA

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

5. Scenario 2 / Table 1: Data Collection Variables

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Date of collection	LBDTC *(expected)*	Date of sample collection	Record the date collection occurred.	The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required.	Optional
2	Lab Status	LBSTAT *(permissible)*	Status of whether or not lab was done.	Indicate whether or not lab was done.	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 results provided.	Highly Recommended
3	Panel Name	LBCAT *(expected)* LBSCAT *(permissible)*	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. Examples: such as HEMATOLOGY, URINALYSIS, CHEMISTRY	Optional
4	Planned Timepoint	LBTPT *(permissible)*	Relative time for use when multiple sequential assessments are done	Record the planned timepoint labels for the lab test, if not pre-printed on the CRF	Planned Time Point would be needed to differentiate for multiple sequential assessments	Optional
5	Time of collection	LBDTC *(expected)*	Time of collection	Record time of collection.	Especially important when multiple assessments are done on one day.	Optional
6	Protocol defined testing conditions met	LBFAST (for example) *(permissible)*	Conditions for sampling defined in the protocol.	Record whether protocol defined testing conditions were met.	Results may be affected by whether conditions for sample were properly met. Example: fasting	Optional
7	Sample Status	LBSPCCND *(permissible)*	Free or standardized text describing the condition of the specimen.	Record condition of sample	Example: such as HEMOLYZED, ICTERIC, LIPEMIC etc.	Optional

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
8	Test Name	LBTESTCD And / Or LBTEST *(required)*	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.	Record the wording of the lab test, if not pre-printed on the CRF	Required to identify the test. Required to identify the test. It is recommended that the test names e pre-printed on the CRF.	Highly Recommended
9	Test Result	LBORRES *(expected)*	Result of the measurement or finding as originally received or collected.	Record test results.	Key data collected.	Highly Recommended
10	Units	LBORRESU *(expected)*	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 normals' file.	May be included if not standardized.	Recommended/ conditional
11	Normal Range	LBORNRLO LBORNRHI *(expected)*	Normal range for continuous measurements in original units.	Record the normal range of the lab test.	May be included if not obtained from lab documentation.	Optional
12	Abnormal flag	LBNRIND *(expected)*	Reference Range Indicator Indicates where value falls with respect to reference range defined by high and low ranges.	Record whether sample was within range.	May be included if not derived.	Optional
13	Clinical Significance	SUPPQUAL domain	Whether lab test results were clinically significant.	Record whether lab results were clinically significant.	May be included if required by the protocol.	Optional
14	Lab Name	LBNAM *(permissible)*	Name of lab analyzing sample	Record the laboratory name.	May be included on CRF if not standardized by clinical trial site.	Optional
15	Accession number	LBREFID *(permissible)*	Internal or external specimen identifier.	Record the sample or accession number assigned.	May be included for linking back to samples. Example: Specimen ID	Optional

6. Scenario 2 / Table 2: Data Collection Variables Considered Not Necessary to Collect on CRF

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Investigator Comment		Investigator comment on lab test or results.		Not needed.	NA

Scenario 3: Central processing but CRF includes site assessment of clinical significance: In this scenario, data is 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, but the CRF includes the data necessary to identify and rate the clinical significance of the abnormal results.

7. Scenario 3 / Table 1: Data Collection Variables

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Date of collection	LBDTC *(expected)*	Date of sample collection	Record the date collection occurred.	The date of collection may be derived from the date of visit and if so, a separate assessment date field is not required.	Highly Recommended
2	Lab Status	LBSTAT *(permissible)*	Status of whether or not lab was done.	Indicate whether or not lab was done.	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 results provided.	Highly Recommended
3	Panel Name	LBCAT *(expected)* LBSCAT *(permissible)*	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. Examples: such as HEMATOLOGY, URINALYSIS, CHEMISTR	Optional
4	Planned Timepoint	LBTPT *(permissible)*	Relative time for use when multiple sequential assessments are done	Record the planned timepoint labels for the lab test, if not pre-printed on the CRF	Planned Time Point would be needed to differentiate for multiple sequential assessments	Optional
5	Time of collection	LBDTC *(expected)*	Time of collection	Record time of collection.	Especially important when multiple assessments are done on one day.	Optional
6	Protocol defined testing conditions met	LBFAST (for example) *(permissible)*	Conditions for sampling defined in the protocol.	Record whether protocol defined testing conditions were met.	Results may be affected by whether conditions for sample were properly met. Example: fasting	Optional
7	Test Name	LBTEST *(required)*	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.	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 e pre-printed on the CRF.	Highly Recommended

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
8	Test Result	LBORRES *(expected)*	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	SUPPQUAL domain	Whether lab test results were clinically significant.	Record whether lab results were clinically significant.	Key data collected in this scenario.	Highly Recommended
10	Lab Name	LBNAM *(permissible)*	Name of lab analyzing sample	Record the laboratory name.	May be included on CRF if not standardized by clinical trial site.	Optional
11	Accession number	LBREFID *(permissible)*	Internal or external specimen identifier.	Record the sample or accession number assigned.	May be included for linking back to samples. Example: Specimen ID	Optional

8. Scenario 3 / Table 2: Data Collection Variables Considered Not Necessary to Collect on CRF

	CDASH CRF Label/Question	Clinical Database Variable Name *CDASH variables shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Sample Status	LBSPCCND *(permissible)*	Free or standardized text describing the condition of the specimen.	Record condition of sample	Not needed. Example: such as HEMOLYZED, ICTERIC, LIPEMIC etc.	NA
2	Abnormal flag	LBNRIND *(expected)*	Reference Range Indicator Indicates where value falls with respect to reference range defined by high and low ranges.	Record whether sample was within range.	Not required when lab data is not recorded on CRF.	NA
3	Units	LBORRESU *(expected)*	Original units in which the data were collected.	Record the units of the lab test, if not pre-printed on the CRF	Not required when lab data is not recorded on CRF.	NA
4	Normal Range	LBORNRLO LBORNRHI *(expected)*	Normal range for continuous measurements in original units.	Record the normal range of the lab test.	Not required when lab data is not recorded on CRF.	NA
5	Investigator Comment		Investigator comment on lab test or results.		Not needed.	NA

ECG STREAM

Harmonized Version

Stream Leaders:
Gary G. Walker, Quintiles
Lauren Shinaberry, PRA International

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Section 3. ECG Stream Harmonized Version

1. Introduction and Background

The ECG Stream is composed of 20 volunteer members representing many job functions from across the pharmaceutical, biotech, CRO industries, and academia. The ECG case report form (CRF) samples submitted by stream members were compared, consistently collected variables were identified, the necessity of each variable was determined and regulatory and safety compliance were evaluated and confirmed.

Team Members	Affiliation	Location
Beverly J. Smith	InterMune, Inc.	bsmith@intermune.com
Charlene Dark	Statistics & Data Corporation	cdark@statisticsanddata.com
Christine Connolly	Millennium Pharmaceuticals, Inc	Christine.Connolly@mpi.com
Donalee Obrien	QIMR	Donalee.OBrien@qimr.edu.au
Eric L. Hiltebeitel	Cephalon, Inc	ehiltebe@cephalon.com
Jagruthi Kasuganti	TAKE Solutions Inc	jagruthi.kasuganti@takesolutions.com
Kati Melzer	SCHWARZ BIOSCIENCES (UCB)	Kati.Melzer@ucb-group.com
Lisa Leubner Cashman	Genzyme Corp	Lisa.Cashman@genzyme.com
Marie Rosenfeld	Abbott	Marie.rosenfeld@abbott.com
Mark Hrvoje Medvedovic, MD	CliniPharma Consulting	mroche@infoway-inforoute.ca
Mary Busha	Boston Scientific	Mary.Busha@bsci.com
Melissa Binz	Wyeth	BinzM@wyeth.com
Nate Freimark	OmniCare	Nate.Freimark@OmnicareCR.com
Sally Huebner	Boston Scientific	sally.huebner@bsci.com
Sarah McLaughlin	Biogen Idec	Sarah.McLaughlin@biogenidec.com
Sunil Agarwal	Cognizant Technology Solutions	sunil.agarwal@cognizant.com
Susan Nunn	Abbott	susan.e.nunn@abbott.com
Susan Taleho	Organon	s.taleho@organonusa.com
Xingi Han	Novartis	xingji.han@novartis.com
Huayu Xiong, PhD	Novartis	huayu.xiong@novartis.com
Lauren Shinaberry	PRA International	ShinaberryLauren@PRAIntl.com
Gary Walker	Quintiles	gary.walker@quintiles.com
Dianne Reeves	NIH/NCI	reevesd@mail.nih.gov

The SDTM variables served as the target for deliverable data. At the initial CDASH meeting, categories for identifying those data that need to be collected (highly recommended), might be collected (recommended/conditional) and some variables which, under certain circumstances, in order to map to the essential SDTM data were agreed upon, and are being used consistently across all streams.

The ECG Stream collected ECG CRFs from participating organizations, and compiled all of the variables from those CRFs into a table. The Stream then reviewed all of the variables in the table, and came to a consensus on which ones should be included in the ICV. The reasons for excluding specific variables from the standard are documented in the Notes section. The Stream then worked to develop appropriate CRF completion instructions and implementation guidelines for the variables included in the standard.

2. Scenarios

The ECG Stream decided not to specify which ECG measurements should be collected as this is a medical and scientific decision that should be based on the needs of the protocols.

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.

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

Scenario 3: **Central reading with assessment of clinical significance:** Central reading scenario (scenario 1) but in addition, the CRF includes a site assessment of clinical significance

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

3. Scenario 1 / Table 1: Data Collection Variables

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Date of ECG	EGDTC *(expected)*	Date of ECG	Record the date ECG occurred. A complete date is expected for ECGs that occur during the study. May be collected elsewhere, such as a study visit date.	This is intended to be used as a data management tool to verify results provided.	Highly Recommended
2	ECG Status	EGSTAT *(permissible)*	Status of whether or not ECG was done.	Indicate whether or not ECG was done.	This is intended to be used as a data management tool to verify that results missing from the electronic transfer were intentional.	Highly Recommended
3	Time of ECG	EGDTC *(expected)*	Clock time of ECG	Record the time the ECG was done, using a 24 hour clock in HH:MM format, as needed. Midnight should be recorded as 00:00 and starts the new date. Seconds (SS) may be collected where deemed appropriate.	Especially important when multiple assessments are done on one day.	Recommended/ Conditional
4	Time Point	EGTPT *(permissible)*	Relative time for use when multiple sequential assessments are done	Record the time point labels for the ECG test, if not pre-printed on the CRF	Planned Time point would be needed to differentiate for multiple sequential assessments	Recommended/ Conditional
5	Internal or external reference number	EGREFID *(permissible)*	Internal or external identifier.	Record the identifier number assigned.	Example: UUID for external waveform file	Recommended/ Conditional

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
6	Subject Position	EGPOS *(permissible)*	Position of the subject during ECG	Record the position of the subject during the ECG	Results may be affected by whether conditions for ECG were properly met. If the protocol requires that the position of the subject be known, then this item may be included to confirm that the protocol requirements for the subject's position were met. If the position of the subject is not critical to the protocol or the risk of sites not consistently performing the ECG then this item is unnecessary. If this data is being provided in the electronic data transfer then it is not necessary to include it on the CRF.	Recommended/ Conditional

4. Scenario 1 / Table 2: Data Collection Variables Considered Not Necessary to Collect on CRF

These are either expected to be received from the Central ECG vendor or are not considered necessary. For central ECG processing these data are expected to be provided separately by the ECG vendor or are not considered necessary to be collected.

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Test Name	EGTEST *(required)*	Verbatim name of the test or examination used to obtain the measurement or finding.	Record the wording of the ECG measurement	Not required when ECG data is not recorded on CRF. This data may be obtained from the central ECG vendor or the electronic equipment. If Clinical Significance is not present in the electronic data and the sponsor needs to collect this on the CRF instead, Scenario 3 should be used.	NA
2	Test Result	EGORRES *(expected)*	Result of the measurement or finding as originally received or collected.	Record test results.		NA
3	Vendor Name	EGNAM *(permissible)*	Name of vendor providing ECG data	Record the vendor name.		NA
4	Evaluator	EGEVAL *(expected)*	Role of the person who provided the evaluation. This should only be used for results that are subjective (e.g. assigned by a person or a group) and do not apply to quantitative results (i.e. ADJUDICATION COMMITTEE, VENDOR)	Record the role of the person evaluating the results.		NA
5	Clinical Significance	SUPPQUAL domain	Whether ECG results were clinically significant.	Record whether ECG results were clinically significant.		NA
6	Abnormal flag	EGNRIND *(expected)*	Reference Range Indicator Indicates where value falls with respect to reference range defined by high and low ranges, or by an expected character result (i.e. NORMAL).	Record whether measurement was within range.		NA
7	Units	EGORRESU *(expected)*	Original units in which the data were collected.	Record the units of the ECG test		NA

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
8	Investigator Comment		Investigator comment on ECG test or results.		Not needed. Details of collecting comments are covered under the CDASH Comments Stream. It is expected that comments related to specific tests will be coming from the electronic data, not collected on the CRF.	NA

Scenario 2: Local reading: When results of ECG are reported directly on the CRF.

5. Scenario 2 / Table 1: Data Collection Variables

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Date of ECG	EGDTC *(expected)*	Date of ECG	Record the date ECG occurred. A complete date is expected for ECGs that occur during the study. May be collected elsewhere, such as a study visit date.	Key data collected.	Highly Recommended
2	Test Name	EGTESTCD And / Or EGTEST *(required)*	Verbatim name of the test or examination used to obtain the measurement or finding.	Record the wording of the ECG test, if not pre-printed on the CRF	Required to identify the result. May be preprinted.	Highly Recommended
3	Test Result	EGORRES *(expected)*	Result of the measurement or finding as originally received or collected.	Record test results.	Key data collected.	Highly Recommended
4	ECG Status	EGSTAT *(permissible)*	Status of whether or not ECG was done.	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 missing results are intentionally missing.	Highly Recommended
5	Time of ECG	EGDTC *(expected)*	Clock time of ECG	Record the time the ECG was done, using a 24 hour clock in HH:MM format, as needed. Midnight should be recorded as 00:00 and starts the new date. Seconds (SS) may be collected where deemed appropriate.	Especially important when multiple assessments are done on one day.	Recommended/ Conditional
6	Time Point	EGTPT *(permissible)*	Relative time for use when multiple sequential assessments are done	Record the time point labels for the ECG, if not pre-printed on the CRF.	Planned Time point would be needed to differentiate for multiple sequential assessments	Recommended/ Conditional

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
7	Clinical Significance	SUPPQUAL domain	Whether ECG results were clinically significant.	Record whether ECG results were clinically significant.	May be included if required by the protocol.	Recommended/ Conditional
8	Units	EGORRESU *(permissible)*	Original units in which the data were collected.	Units should be pre-printed on the CRF.	May be included if quantitative results are recorded. Because units for quantitative ECG results are limited to seconds or milliseconds, units should be pre-printed on the CRF rather than having the sites record the units.	Recommended/ Conditional
9	Subject Position	EGPOS *(permissible)*	Position of the subject during ECG	Record the position of the subject during the ECG	Results may be affected by whether conditions for ECG were properly met. If the protocol requires that the position of the subject be known, then this item should be included to confirm that the protocol requirements for the subject's position were met. If the position of the subject is not critical to the protocol, or the risk of sites not consistently performing the ECG then this item is unnecessary.	Recommended/ Conditional
10	Evaluator	EGEVAL *(expected)*	Role of the person who provided the evaluation. This should only be used for results that are subjective (e.g. assigned by a person or a group) and do not apply to quantitative results (i.e. ADJUDICATION COMMITTEE, INVESTIGATOR)	Record the role of the person evaluating the results.	May be included if required by the protocol.	Recommended/ Conditional
11	Reason Not Done	EGREASND *(permissible)*	Describes why the ECG was not done (i.e. BROKEN EQUIPMENT, SUBJECT REFUSED)	Record the reason that the ECG was not done.	May be included if required by the protocol. Examples of when this may be necessary are cardiac studies or thorough QT studies.	Recommended/ Conditional

6. Scenario 2 / Table 2: Data Collection Variables Considered Not Necessary to Collect on CRF

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Investigator Comment		Investigator comment on ECG results.	None	Not needed. If Investigator is providing comments that are actually an interpretation of the ECG as a whole or indicating the presence of a particular condition, this is expected to be collected as a result of the ECG. Details of collecting general comments are covered under the CDASH Comments Stream.	NA
2	Vendor Name	EGNAM *(permissible)*	Name of vendor	None	If ECG is read locally, vendor name does not apply.	NA
3	ECG Reference ID	EGREFID *(permissible)*	Internal or external ECG identifier.	None	If ECG is read locally, external reference does not apply	NA

Scenario 3: Central processing but CRF includes site assessment of clinical significance

7. Scenario 3 / Table 1: Data Collection Variables

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Date of ECG	EGDTC *(expected)*	Date of ECG	Record the date ECG was performed. A complete date is expected for ECGs that occur during the study. May be collected elsewhere, such as a study visit date.	Key data collected. Used to link clinical significance to corresponding result in electronic ECG data.	Highly Recommended
2	Test Name	EGTEST *(required)*	Verbatim name of the test or examination used to obtain the measurement or finding.	Record the description of the ECG result, if not pre-printed on the CRF	Required to identify the test. May be preprinted.	Highly Recommended
3	ECG Status	EGSTAT *(permissible)*	Status of whether or not ECG was done.	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.	Highly Recommended
4	Clinical Significance	SUPPQUAL domain	Whether ECG results were clinically significant.	Record whether ECG results were clinically significant.	Key data collected in this scenario.	Highly Recommended
5	Test Result	EGORRES *(expected)*	Result of the measurement or finding as originally received or collected.	Record test results.	Optional if already provided from central ECG data.	Recommended/ Conditional
6	Vendor Name	EGNAM *(permissible)*	Name of central ECG vendor	Record the vendor name.	May be included on CRF if not standardized by clinical trial site.	Recommended/ Conditional
7	Time of ECG	EGDTC *(expected)*	Clock time of ECG	Record the time the ECG was done, using a 24 hour clock in HH:MM format, as needed. Midnight should be recorded as 00:00 and starts the new date. Seconds (SS) may be collected where deemed appropriate.	Planned Time point would be needed to differentiate for multiple sequential assessments	Recommended/ Conditional
8	Time Point	EGTPT *(permissible)*	Relative time for use when multiple sequential assessments are done	Record the time point labels for the ECG, if not pre-printed on the CRF.	Especially important when multiple assessments are done on one day.	Recommended/ Conditional

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
9	Protocol defined testing conditions met	EGPOS, EGMETHOD (for example) *(permissible)*	Conditions for testing defined in the protocol.	Record whether protocol defined testing conditions were met.	Results may be affected by whether conditions for test were properly met. Example: Subject position during ECG, whether ECG was 12-Lead or 1-Lead	Recommended/ Conditional
10	ECG Reference ID	EGREFID *(permissible)*	Internal or external ECG identifier.	Record the ECG Reference ID assigned.	May be included for linking back to external data file	Recommended/ Conditional

8. Scenario 3 / Table 2: Data Collection Variables Considered Not Necessary to Collect on CRF

	CDASH CRF Label/Question	Clinical Database Variable name *CDASH variables Shaded*	Definition	Instruction to Clinical Site	Implementation / Rationale to Sponsors	CDASH Core
1	Abnormal flag	EGNRIND *(permissible)*	Reference Range Indicator Indicates where value falls with respect to reference range defined by high and low ranges.	Record whether ECG result was out of range or abnormal.	Not required when ECG data is not recorded on CRF.	NA
2	Units	EGORRESU *(permissible)*	Original units in which the data were collected.	Record the units of the ECG result, if not pre-printed on the CRF	Not required when ECG data is not recorded on CRF.	NA
3	Investigator Comment		Investigator comment on ECG test or results.	None	Not needed. Details of collecting comments are covered under the CDASH Comments Stream. It is expected that comments related to specific tests will be coming from the electronic data, not collected on the CRF.	NA
4	Evaluator	EGEVAL *(expected)*	Role of the person who provided the evaluation. This should only be used for results that are subjective (e.g. assigned by a person or a group) and do not apply to quantitative results (i.e. ADJUDICATION COMMITTEE, VENDOR)	None	Not required when ECG data is not recorded on CRF.	NA

Section 4. Appendices

Appendix 1 Project Background

The Clinical Data Acquisition Standards Harmonization (CDASH) project is addressing FDA's Critical Path Opportunity (#45) whose purpose is 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. (Critical Path Opportunities List (Innovation/Stagnation) link: http://www.fda.gov/oc/initiatives/criticalpath/opportunities06.html)*

Standards can substantially reduce time and resource needs for clinical research studies, particularly when they are implemented in the start-up stage. (*Applied Clinical Trials, June 2007*). In addition, they have been reported to improve project team communication and resulting data quality.

Through standardization of basic data collection fields, 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 continues 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, ACRO. CDISC has expertise in standards development demonstrated by former CDISC work, such as in the development of the Study Data Tabulation Model (SDTM) for reporting results in regulatory submissions to FDA, can be leveraged in the CDASH project.

In June 2006 the initial Collaborative Group was announced by Dr. Woodcock at the Annual DIA Meeting in Philadelphia "Human Subject Protection/Bioresearch Monitoring Initiative and Critical Path Update".

CDASH strategy and resources are the responsibility 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
- Duke Clinical Research Institute (DCRI)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH)
    - The Clinical Research Policy Analysis and Coordination Program
    - The National Cancer Institute (NCI)

        - NCI-Cancer Bioinformatics Grid (caBIG)
        - NCI-Enterprise Vocabulary Service (EVS)
    - The National Clinical Research Resources (NCRR)
    - The National Institute of Child Health and Human Development (NICHD)
    - The National Library of Medicine (NLM)
- Pharmaceutical Research and Manufacturers Association (PhRMA)
- Society for Clinical Data Management (SCDM)

A CDISC Project Kick-off meeting was held in October 2006 to initiate the first CDASH three project work streams (sub-groups).

The primary goal of the CDASH project is the development of a set of 'content standards' for a basic set of global data collection fields that will support clinical research studies. These "content standards" consist of:

- Data Collection Fields
- Definitions
- Site Completion Instructions
- Implementation / Rationale

for a basic set of global data collection fields that will support clinical research studies.

The initial scope of the project is the development of 16 CRF content 'safety data/domains'

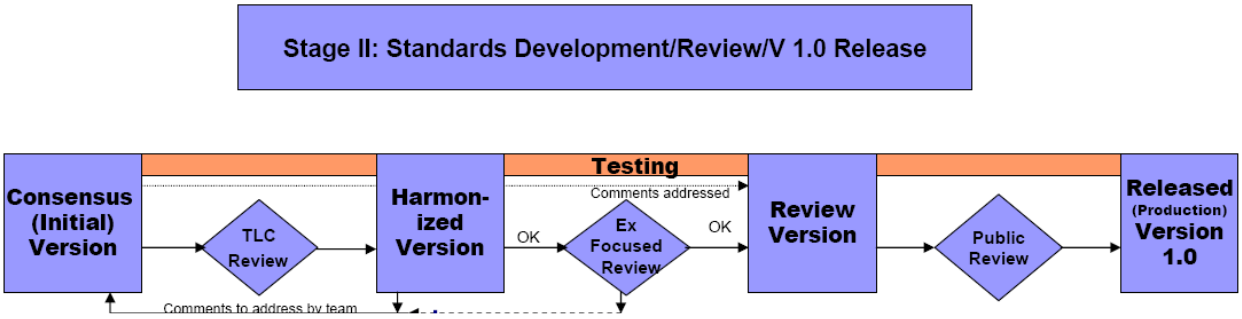
Domains	
Adverse Events (AE)	Inclusion and Exclusion Criteria (IE)
Concomitant Medications (CM)	Lab (LB)
Comments (CO)	Medical History (MH)
Demographics (DM)	Physical Examination (PE)
Disposition (DS)	Protocol Violations (DV)
Drug Accountability (DA)	Subject Characteristics (SC)
ECG (EG)	Substance Use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

These safety domains are common to all therapeutic areas. The initial scope is on CRF content not the physical layout of CRFs. Terminology is out of scope for the CDASH work streams; rather, terminology is incorporated through collaboration with the CDISC Terminology Team.

Basic data collection fields identified by CDASH project work streams (via the CDISC consensus process) are mapped into the Study Data Tabulated Model (SDTM) and are compliant with the SDTM Implementation Guide (SDTM IG). SDTM "required" data collection fields have been addressed in the CDASH recommendations.

Appendix 2 Project Process

The CDASH Project follows 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 describing the 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 (see section 2.0). The CDASH domain-specific recommendations from the workstreams are first reviewed by an internal CDISC Technical Leadership Committee (TLC) to ensure that they do not diverge from the other relevant CDISC standards. They are then combined into 'review packages' for external review by the Collaborative Group, an external focus group in the case of this Project. The entire set of domains will be reviewed together in an open public review process.

In the development of the Harmonized Versions (HV), the CDISC SDTM variable tables served as a starting/reference point. The CDASH and SDTM variables may differ in certain cases, however, because SDTM is a standard for standardizing results for regulatory submissions whereas CDASH variables are used in the collection of data. Another difference is that the CDASH project is designed to encourage collection of a minimal or basic set of required and necessary data fields whereas SDTM represents more of a 'superset' of variables for reporting results.

In addition to referring to the CDISC SDTM standard, CDASH volunteers were asked to collect CRF samples currently used by industry and to evaluate commonalities and/or differences of CRF samples and the SDTM standard. Work streams were also asked to document data points that they recommended be including or excluding in the CDASH domains, along with their justifications for these decisions.

2.1 Guiding Principles

The following *Guiding principles were provided to the work streams in developing their domains. Variables should –

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

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

2.2 Volunteers: Work Streams and Work Stream Procedures

The CDASH project work is performed primarily by volunteers, who are representing biopharmaceutical companies, contract research organizations, academia and government. Each work stream is responsible for one or more domains.

The CDASH Core Team, a qualified, multidisciplinary team of 10 members, leads each of the safety domain work stream listed above. The following table lists the members of the CDASH Core Team and their respective work streams (domains). The Core Team executes the project plan, holding regular conference calls and face-to-face meetings, as appropriate, to achieve the objectives. Each Core Team member led one or more work streams (or sub-group) of volunteer participants. Volunteers for each work stream were recruited via open invitation. Effort was made to ensure that representation on each work stream was from diverse companies, with various functional areas represented and that there was multinational representation whenever possible.

Work streams volunteers were recruited, and there were typically resulting in 10-40 members per work streams. An effort was made to ensure that there were various functional areas represented and that there was multinational representation whenever possible.

Work stream volunteers were asked to agree on basic data collection fields, map these fields to SDTM, to add definitions and to write instructions for investigative sites and to write implementation guidelines /rationales for study sponsors.

The work streams began by reviewing CRF samples supplied by ACRO (where available), as well as other CRF samples collected that are currently used by industry. Within each work stream, sub-groups were assigned and given the action items of scanning CRF samples and quality control (QC) of CRF examples and establishing the administrative procedures for the work streams. Weekly or bi-weekly teleconferences provided a communication forum to review and discuss the identification of basic data collection fields for a given domain.

The work streams collected feedback from numerous functional areas within their respective companies (including ex-US affiliates) to identify the purpose for their respective work streams' data collection focus (i.e., their domain). The work streams then focused the group discussions per the Guiding Principles (listed above). For each variable, a category was assigned (highly recommended/recommended/optional, variable labels and definitions were developed. The SDTM submission fields served as a target for deliverable data. Data collection fields were mapped to the SDTM variables as applicable.

Appendix 3 CDASH Core Designations

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 always be on the CRF (e.g., a regulatory requirement (if applicable)) and should be completed.

Recommended/Conditional= A data collection field that should always be collected on the CRF but may be left blank under certain circumstances described in the implementation notes in each table.

Optional = A data collection field that is available for use if needed.

Highly recommended and recommended/conditional data collection fields are expected to be present on the majority of CRFs, however, it is assumed that sponsors will determine which data fields will be collected based on TA specific data requirements, protocol and other considerations.

It is strongly recommended that standards are defined on the sponsor level taking into consideration the requirements of the stage of clinical development, the individual therapeutic area requirements and NOT on a trial-by-trial basis within the sponsor organization.

The SDTM core designation reflects the expectation of inclusion in an SDTM submission. As an aide to reviewers, SDTM Core Variables***** (Required, Expected and Permissible) are included in the CDASH tables. See the CDISC SDTM Implementation Guide: Human Clinical Trials (Version 3.1.2)

Appendix 4 Explanation of Table Headers

Following are explanations for column headers used in the tables:

CDASH CRF Label/Question – Provides descriptive text on the type of data to be collected on the CRF.

Clinical Database Variable Name – Lists the SDTM conforming variable name defined in the SDTM IG along with the SDTM "Core" designation.

Suggested CDASH collection variable names (e.g. CMONG and CMTTM) are shaded. These variable names are "SDTM-like variables" and can be used as a tool for deriving the SDTM variable needed for reporting.

Definition – Describes the purpose of the data collection field. The text may or may not mirror the text in the SDTM IG (under variable label or CDISC notes).

Instructions to Clinical Site –Contains information for the clinical site on how to enter collected information onto the CRF.

Implementation/rational to Sponsors –Contains further information on how to implement the CRF data collection fields.

Note: "Instructions for the Clinical Site" and "Implementation Guidelines" are provided only for those data collection fields that are considered "highly recommended" and "recommended/optional".

CDASH Core – Category designations. See Appendix 3 -CDASH Core Designations for a detailed explanation.

Appendix 5 Core Team and Stream Members

Core Team			
Work stream Leader	**Affiliation**	**Email address**	**Stream**
Rhonda Facile	CDISC	rfacile@cdisc.org	Project Director
Paul Bukoweic	Millennium Pharmaceuticals	Paul.Bukoweic@mpi.com	Physical Exam & Vital Signs
Dorothy Dorotheo	Intermune	DDorotheo@intermune.com	Concomitant Medications
Shannon Labout	CSS Informatics and SCDM	shannon.labout@csscomp.net	Inclusion/Exclusion
Jay Leeka	AstraZeneca	Jay.Leeka@astrazeneca.com	Comments & Protocol Deviations
Liz Nulton-Bodiford	GlaxoSmithKline	liz.m.nulton-bodiford@gsk.com	Drug Accountability & Exposure
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/Consultant	Alec.Vardy@cvt.com	Disposition/ End of Study
Gary Walker	Quintiles	gary.walker@quintiles.com	Demographics & Subject Characteristics and ECG

Stream Members *(to add later – alpha by company name)*

Stream Members		
Organization	**Name**	**Stream(s)**

Appendix 6 Revision History

None.

Appendix 7 Place holder for IP

Representation and Warranties; Limitations of Liability, and Disclaimers