Contains Nonbinding Recommendations

BIORESEARCH MONITORING TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is Referenced by the Following Draft Guidance Document:

Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions

For questions regarding this technical specifications document, contact CDER-BIMO-NDA-BLA-request@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

August 11, 2022

Contains Nonbinding Recommendations

BIORESEARCH MONITORING TECHNICAL CONFORMANCE GUIDE

August 11, 2022

Contains Nonbinding Recommendations

Revision History

Date	Version	Summary of Changes
12/28/2017	1.0	Original Version
07/23/2020	2.0	1. Corrected footnote hyperlinks 2. Edited variable names in examples and tables to maintain consistency across document 3. Clarified document, listings, and data requests 4. Deleted request for SITEFFE and SITEFFS variables in clinsite.xpt 5. Added COHORT variable 6. Revised PROTVIOL variable to IMPDEV and NOIMPDEV variables 7. Provided additional instructions for placement of files per eCTD format
08/11/2022	3.0	1. Rename BIMO Review Guide to BIMO Data Review Guide. 2. Renamed TRTEFFR to TRTEFFR1 3. Added EFFPOP, TRTEFFR2, and CENSOR2 Variables 4. Deleted request for TRTEFFS 5. Change instructions for use of ISO codes to use of Geopolitical Entities, Names and Codes (GENC) codelist. 6. Minor editorial changes.

Contains Nonbinding Recommendations

TABLE OF CONTENTS

Bioresearch Monitoring Technical Conformance Guide

This technical conformance guide, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for this technical conformance guide. If you cannot identify the appropriate FDA staff, send an email to cder-edata@fda.hhs.gov or cber.cdisc@fda.hhs.gov.

This Bioresearch Monitoring Technical Conformance Guide (Guide) provides current FDA specifications, recommendations, and general considerations for preparing and submitting Clinical Study-Level Information, Subject-Level Data Line Listings by Clinical Site, and a Summary-Level Clinical Site Dataset that are used by the Center for Drug Evaluation and Research (CDER) for planning of Bioresearch Monitoring (BIMO) inspections in electronic format for new drug applications (NDAs), biologics license applications (BLAs), and NDA or BLA supplemental applications containing clinical data that are regulated by CDER.[1] It also applies when these data and information are submitted under certain investigational new drug applications[2] (INDs) in advance of a planned NDA, BLA, or supplemental submission.

I. CLINICAL STUDY-LEVEL INFORMATION

A. Comprehensive and Readily Located List of All Clinical Sites

The recommended format for the portable document format (PDF) of the comprehensive and readily located list(s) of all clinical sites that participated in clinical studies for each major (i.e., pivotal) study is provided in Appendix 1 of this Guide.

B. Table Listing All Entities To Whom Sponsor Has Contracted Clinical Study-Related Activities

In the table(s) listing entities to whom the sponsor has contracted clinical study-related activities, which are provided in a PDF for each pivotal study, the applicant should identify the location of study-related documents for each study and whether they are sponsor- or Contract Research Organization-generated. For example, these documents may include, but are not limited to, monitoring plans and reports, training records, and data analysis plans (e.g., items that some applicants organize in a Trial Master File). When the location of study-related documents has not been finalized, the applicant should provide contact information (i.e., phone number and

[1] We update technical conformance guides periodically. For the most recent version of this Guide, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[2] See FDA guidance for industry *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (February 2020). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

email address) for the individual(s) who can provide updated location information upon request. This information ensures that when CDER issues an inspection assignment for the application, the inspection is of the most responsible entity for a given regulatory responsibility, and that the inspection assignment is issued for the location where records are present for review.

C. Protocol, Protocol Amendments, and Annotated Case Report Form

The protocol and protocol amendments, with associated versions of the case report form, and the final version of the annotated case report form (case report form containing Clinical Data Interchange Standards Consortium and Study Data Tabulation Model (SDTM) annotations) are generally included in Appendix 16[3] of the Clinical Study Report or in the datasets folder for each study. When these items are included in an appendix to the Clinical Study Report or the dataset folder for the study, there is no need to resubmit them. If the applicant is submitting a BIMO Data Reviewer's Guide,[4] the applicant should note that these items are present in an appendix of the Clinical Study Report or the dataset folder where they are placed.

These items are included in the background materials provided to the Office of Regulatory Affairs for BIMO inspections; it is important to provide all versions of these documents so that the field investigator performing the inspection can reference the correct versions of protocols and case report forms in place at the time of the conduct of specific study procedures.

II. SUBJECT-LEVEL DATA LINE LISTINGS BY CLINICAL SITE

A. Organization of the Subject-Level Data Line Listings

Examples of the formatting for the PDF of subject-level data line listings provided for each major (i.e., pivotal) study used to support safety and efficacy in the application, including studies with different treatment indications, are provided in Appendix 2 of this Guide. If the sponsor believes alternative listings or formats are preferable for its submission, proposed alternatives should be discussed with the Office of Scientific Investigations in advance of the application submission—for example, before or during pre-NDA or pre-BLA meetings.

For clinical investigator sites involved in multiple studies in support of an application, the subject listings should be provided independently for each study within the study-associated PDF.

Subject-level data line listings, by clinical site, should include consented subjects, treatment assignment, discontinuations, study population, inclusion and exclusion criteria, adverse events, protocol deviations, efficacy endpoints, concomitant medications, and safety monitoring, as further described below.

[3] See ICH guidance for industry *E3 Structure and Content of Clinical Study Reports* (July 1996).

[4] A specific template for a BIMO Data Reviewer's Guide is not specified. However, an example can be found at https://advance.phuse.global/display/WEL/Deliverables.

1. Consented Subjects

This by-subject, by-clinical site listing includes all subjects that consented to enroll in the study. Consented subjects that were screen failures should also be included. For subjects that consented but were not randomized to treatment or did not receive investigational product, the specific reason they were not randomized or treated should be included in this listing.

2. Treatment Assignment

This by-subject, by-clinical site listing includes the treatment assignment to which the subject was randomized. If a subject mistakenly received treatment different from the subject's assigned treatment for any duration of time, the actual treatment received should also be included.

3. Discontinuations

This by-subject, by-clinical site listing includes:

- All subjects that discontinued during run-in period (if applicable)
- All subjects that discontinued from study treatment
- All subjects that discontinued from the study completely

For each subject, the date of and reason for discontinuation should be provided.

4. Study Population

This by-subject, by-clinical site listing identifies the protocol-defined study population in which each subject was analyzed (e.g., intent-to-treat, safety, per protocol). For subjects that did not meet criteria for inclusion in the per-protocol population, the reason they were excluded from the per-protocol population should be provided.

5. Inclusion and Exclusion Criteria

This by-subject, by-clinical site listing should display whether each subject met each inclusion and exclusion criterion defined in the protocol.

6. Adverse Events

This by-subject, by-clinical site listing should include all adverse events (i.e., nonserious adverse events and serious adverse events, including deaths), date of occurrence and time if collected, treatment(s) administered, severity, whether considered serious by the clinical investigator, whether considered serious by the sponsor, action taken, whether the event led to discontinuation of study therapy, and outcome/date of resolution.

7. Protocol Deviations

This by-subject, by-clinical site listing should include all protocol deviations. The listing should include a description of the deviation and identify whether the sponsor considered the deviation to be an important or non-important protocol deviation.[5]

8. Efficacy Endpoints

This by-subject, by-clinical site listing(s) should contain primary and key secondary efficacy parameters or events. For derived or calculated endpoints, the raw data points used to generate the derived or calculated endpoint should be provided. For example, when efficacy endpoints are assessed based on a laboratory, imaging, components of a clinical outcome assessment(s), or other study procedures, the by-subject, by-clinical site listing should include all testing results that contribute to the derived efficacy endpoint. When efficacy endpoints are collected as clinical events, a by-subject, by-clinical site listing should be provided that includes clinical event, date of event, and when adjudicated, the date of adjudication and the outcome of the adjudication process.

9. Concomitant Medications

This by-subject, by-clinical site listing should contain all concomitant medications as specified by the protocol. The date started, date stopped, dose, route of administration, and reason for administration should be included.

10. Safety Monitoring

This by-subject, by-clinical site listing(s) should contain results of tests (e.g., laboratory, electrocardiogram) performed for safety monitoring as defined in the protocol. When safety endpoints are collected as clinical events, a by-subject, by-clinical site listing should be provided that includes clinical event, date of event, and when adjudicated, the outcome of the adjudication process.

B. Site-Specific Listings Format

The specified data line listings are anticipated to fit reporting requirements for most applications. If a sponsor believes additional listings are needed to permit FDA to verify key study data during inspections, additional listings should be included. If the size of the PDF file exceeds 500 megabytes, it should be split into smaller components.[6]

Although listings are currently requested in PDF format, CDER is in the process of developing tools to extract site-specific listings, needed for inspectional purposes, from submitted Clinical Data Interchange Standards Consortium, SDTM, and Analysis Data Model (ADaM) datasets and intends to make those tools available in the future. FDA intends to update these technical

[5] See ICH guidance for industry *E3 Structure and Content of Clinical Study Reports — Questions and Answers (R1)* (January 2013).

[6] See ICH guideline *Specification for Submission Formats for eCTD v1.3* (June 2021) at https://www.ich.org/page/ich-m8-specification-submission-formats-ectd.

specifications to include details for the submission of SDTM and ADaM datasets, including controlled terminology standards. In anticipation of the development of CDER tools for extraction of by-site, by-subject data listings, sponsors should ensure that they are prepared to submit clinical study data using standards specified in the Data Standards Catalog.[7]

III. SUMMARY-LEVEL CLINICAL SITE DATASET

A. Organization of the Site-Level Dataset

A single summary-level clinical site dataset that contains data from all major (i.e., pivotal) studies used to support safety and efficacy in the application, including studies with different treatment indications, should be provided.

For each major (i.e., pivotal) study used to support safety and efficacy, data by clinical site and treatment arm for the safety population (SAFPOP) and primary efficacy population (EFFPOP) should be provided.

For clinical investigator sites involved in multiple studies in support of an application, the site data should be reported independently for each study within the dataset.

B. Variables and Variable Names for Site-Specific Efficacy Results

For each study and investigator site, it is critical to submit the following variables associated with efficacy and their variable names:

- Safety Population (SAFPOP) — Total number of subjects in safety population at a given site by treatment arm. When a subject has transferred from one site to another, the applicant should handle reporting of such subjects consistently across sites and include in the define file, or the BIMO Data Review Guide when one is provided, the reporting convention used.
- Primary Efficacy Population (EFFPOP) — Total number of subjects in the primary efficacy population, as defined in the clinical study report, at a given site by treatment arm to support the proposed indication in the application. The efficacy population used should be identified in the define file provided for the clinsite.xpt (e.g., Full Analysis Set, Per Protocol, Intent to Treat, Modified Intent to Treat).
- Treatment Efficacy Result One (TRTEFFR1) — The summary statistic for each primary efficacy endpoint, by treatment arm at a site, based subjects in the SAFPOP. Values reported in TRTEFFR1 generally reflect simple summary statistics for the primary efficacy endpoint(s). The method used for deriving the TRTEFFR1, including a description of which analysis datasets and associated variables are used to derive the TRTEFFR1, should be described in the define file provided with the clinsite.xpt (see discussion below for examples of summary statistics according to different types of efficacy endpoints).

[7] Available at http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm.

- Treatment Efficacy Result Two (TRTEFFR2) —The summary statistic for each primary efficacy endpoint, by treatment arm at a site, based subjects in the EFFPOP. Values reported in TRTEFFR2 generally reflect simple summary statistics for the primary efficacy endpoint(s). The method used for deriving the TRTEFFR2, including a description of which analysis datasets and associated variables are used to derive the TRTEFFR2, should be described in the define file provided with the clinsite.xpt (see discussion below for examples of summary statistics according to different types of efficacy endpoints).
- Endpoint (ENDPOINT) — A plain-text label that describes the primary endpoint as described in the data definition file data dictionary included with each application.
- Treatment Arm (ARM) — A plain-text label for the treatment arm that is used in the Clinical Study Report.

In addition, for studies whose primary endpoint is a time-to-event endpoint, it is critical to include the following data element:

- Censored Observations (CENSOR1 and CENSOR2) — The number of censored observations for the given site and by treatment arm for the SAFPOP and EFFPOP, respectively.

If a study does not contain a time-to-event endpoint, this data element should be recorded as a missing value (if not applicable, leave blank in clinsite.xpt).

To accommodate the variety of endpoint types that can be used in analyses, it is critical that the following endpoint type definitions be referenced, and summaries be provided when tabulating the site-specific summary statistic by treatment arm (for TRTEFFR1 and TRTEFFR2):

- Discrete Endpoints — Endpoints based on efficacy observations that can take on a discrete number of values (e.g., binary, categorical). Summarize discrete endpoints by an event frequency (i.e., number of events), proportion of patients with an event, proportion of patients responding to treatment, or similar method at the site for the given treatment.
- Continuous Endpoints — Endpoints based on efficacy observations that can take on an infinite number of values. Summarize continuous endpoints by the mean, median, or other distributional quantile of the observations at the site for the given treatment.
- Time-to-Event Endpoints — Endpoints where the time to occurrence of an event is the primary efficacy measurement. Summarize time-to-event endpoints by two data elements: the number of events that occurred (TRTEFFR1 and TRTEFFR2) and the number of censored observations (CENSOR1 and CENSOR2).
- Other — If the primary efficacy endpoint cannot be summarized in terms of the previous guidelines, a single value or multiple values with precisely defined variable interpretations should be submitted as part of the dataset.

In all cases, the endpoint description provided in the ENDPOINT plain-text label should be expressed clearly to interpret the value provided in the TRTEFFR1 and TRTEFFR2 variables.

When more than one primary efficacy endpoint exists, additional rows should be added to the dataset to report additional ENDPOINT, Primary Endpoint Type (ENDPTYPE), TRTEFFR1, and TRTEFFR2 values by arm for each site.

It is anticipated that efficacy data for all subjects included in the SAFPOP and EFFPOP variables will be included in TRTEFFR1 and TRTEFFR2 variables reported, respectively. If efficacy data is not available for all subjects reported in the SAFPOP or EFFPOP variables, then efficacy data for these subjects should be reported as specified in the study Data Analysis Plan, and the method used for calculation of efficacy variables should be described in the data define table provided with the clinsite.xpt file.

The summary-level clinical site dataset should be accompanied by a data definition file. The contents of the define file for a dataset and fictional examples are presented in Appendix 3 and Appendix 4 of this Guide.

C. Creating the Data File (Template and Structure)

A sample summary-level clinical site data submission using the variables identified in Appendix 3 of this Guide is provided in Appendix 4.

IV. SUBMITTING BIMO CLINICAL DATA IN THE eCTD FORMAT

Clinical study-level information, subject-level data line listings by clinical site, and the summary-level clinical site dataset submitted with an application, in Electronic Common Document (eCTD) format, should be placed in eCTD Module 5 (M5) — Clinical Study Reports, using the following conventions:

A. Study Tagging File

Construct a BIMO study tagging file (STF) and place it in eCTD Module 5.3.5.4, "Other Study reports and related information." The study identifier (ID) for this STF is "BIMO." Files described in section III (e.g., Description of Clinical Study-Level Information, Subject-Level Data Line Listings by Clinical Site, and Summary-Level Clinical Site Dataset) of the draft guidance *Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions* (February 2018) are linked to this BIMO STF using file tags as indicated below.[8] Leaf titles for these data are named "BIMO [list study ID, followed by brief description of file being submitted]."

Table 1: STF File Tags

Requested Item	STF File Tag	Used For	Required File Formats
III.A.*1-2*	data-listing-dataset	General clinical study-level information	.pdf

[8] When final, this guidance will represent the FDA's current thinking on this topic.

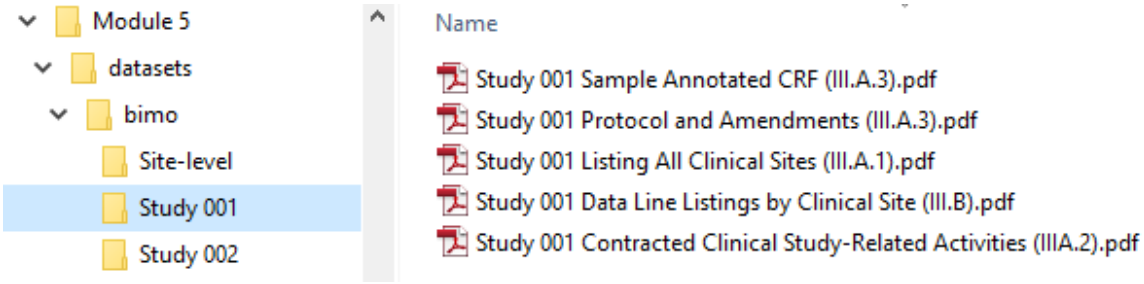
Requested Item	STF File Tag	Used For	Required File Formats
III.A.*3*	Protocol-or-amendment	Protocol and Protocol Amendments, by study	.pdf
III.A.*3*	annotated-crf	Sample annotated case report form, by study	.pdf
III.B	data-listing-dataset	Data listings, by study (Line listings, by site)	.pdf
III.C	data-listing-dataset	Site-level dataset, across studies	.xpt
III.C	data-listing-data-definition	Define file	.xml
Optional	data-listing-dataset	BIMO Data Reviewer's Guide	.pdf

B. eCTD Folder Structure for Clinical Study-Level Information and Subject-Level Line Listings by Clinical Site

Clinical study-level information and subject-level line listings by clinical site are submitted for each major (i.e., pivotal) study used to support safety and efficacy in the application.

Within the eCTD folder structure, place clinical study-level information and subject-level line listings by clinical site in the M5 folder as follows:

Figure 2: Place Clinical Study-Level Information and Subject-Level Line Listings by Clinical Site in the M5 Folder



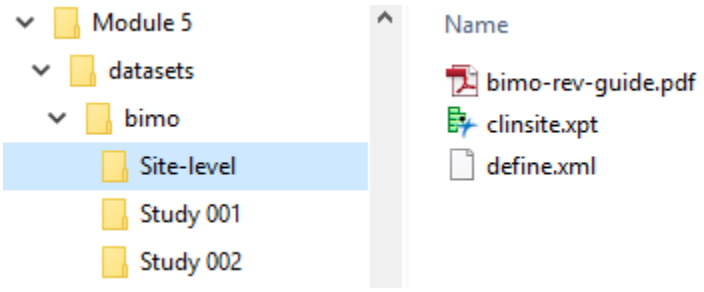
C. eCTD Folder Structure for Summary-Level Clinical Site Dataset

For the site-level dataset, use the filename "clinsite.xpt." A single file containing data from all major (i.e., pivotal) studies[9] used to support safety and efficacy in the application should be provided.

[9] For questions regarding whether a study is considered major (i.e., pivotal), applicants should consult the relevant Office of New Drugs review division during Type C Integrated Summary of Safety or pre NDA/BLA meetings.

Within the eCTD folder structure, place the site-level dataset define file and BIMO Data Reviewer's Guide, if it is being submitted, in the M5 folder as follows:

Figure 2: Place the Site-Level Dataset Define File and BIMO Data Reviewer's Guide in the M5 Folder



D. File Format

The Clinical Study-Level Information and Subject-Level Data Line Listings by Clinical Site should be submitted in PDF (*.pdf). When submitting a BIMO Data Reviewer's Guide, it should also be submitted in PDF (*.pdf). The summary-level clinical site data should be submitted in SAS transport file format (*.xpt). The define file for the summary-level clinical site data should be submitted in Extensible Markup Language (define.xml) format. For more information, see the *Study Data Technical Conformance Guide*.[10]

E. Leaf Titles

Leaf titles for study-level information and study-level, subject-level data line listings by clinical site are named "BIMO [list study ID, followed by brief description of file being submitted]." For the leaf representing the clinsite.xpt dataset, please clearly identify it with the leaf title "BIMO summary-level clinical site data."

F. Submission

See the technical specifications in *Transmitting Electronic Submissions Using eCTD Specifications* for details on electronic transmission or physical media submissions.[11]

The following are helpful references for eCTD submission:

[10] Available at https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources.

[11] Available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM163567.pdf.

- ICH eCTD STF Specification V 2.6.1, *The eCTD Backbone File Specification for Study Tagging Files* (June 2008) (available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM163560.pdf).
- FDA guidance for industry *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (February 2020) (available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents).
- FDA eCTD web page (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm).
- For general help with eCTD submissions, submit your questions to the following email address: ESUB@fda.hhs.gov.

APPENDIX 1: CLINICAL STUDY-LEVEL INFORMATION

Format for comprehensive and readily located list of all clinical sites that participated in each clinical study. A separate table should be provided for each clinical study.

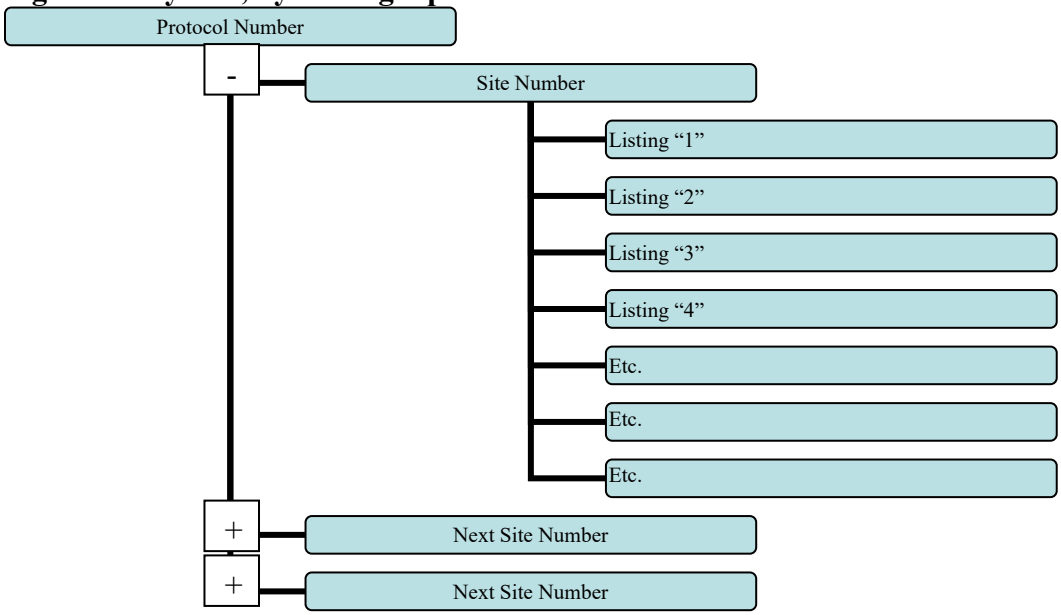
Table A: Format for Clinical Site Lists

Protocol Number: Protocol Title			
Site Identifier	**Investigator Name (Prior Clinical Investigator(s))**	**Site Address at Time of Clinical Study (Updated Site Address when exists and available)**	**Site Contact Information at Time of Clinical Study (Updated Contact Information when exists and available)**
SITEID	**LASTNAME, FRSTNAME, MINITIAL**	**FACILITY NAME STREET CITY, STATE, POSTAL COUNTRY**	**PHONE FAX EMAIL**
0001*	Doe, John M.	Doe University Department of Medicine 1 Main St., Suite 100 Silver Spring, MD 20850 USA	Phone: 1-555-555-5555 Fax: 1-555-555-5555 Email: john.doe@mail.com
0002	Doe, Jean (Smith, John)	Doe University Department of Medicine 1 Main St., Suite 100 Silver Spring, MD 20850 USA	Phone: 1-555-555-5555 Fax: 1-555-555-5555 Email: john.smith@mail.com (Phone: 1-555-555-5554 Email: jean.doe@mail.com)
003	Dietric-Fischer, Inge	Hartmannstrasse 7 5300 Bonn 1 Germany	Phone:49-555-555-5555 Fax: 49-555-555-5555 Email: Dietric.Fischer@web.de
* Site terminated, or clinical investigator changed, at request of sponsor before study completion.			

APPENDIX 2: FORMATTING SUBJECT-LEVEL DATA LINE LISTINGS BY CLINICAL SITE

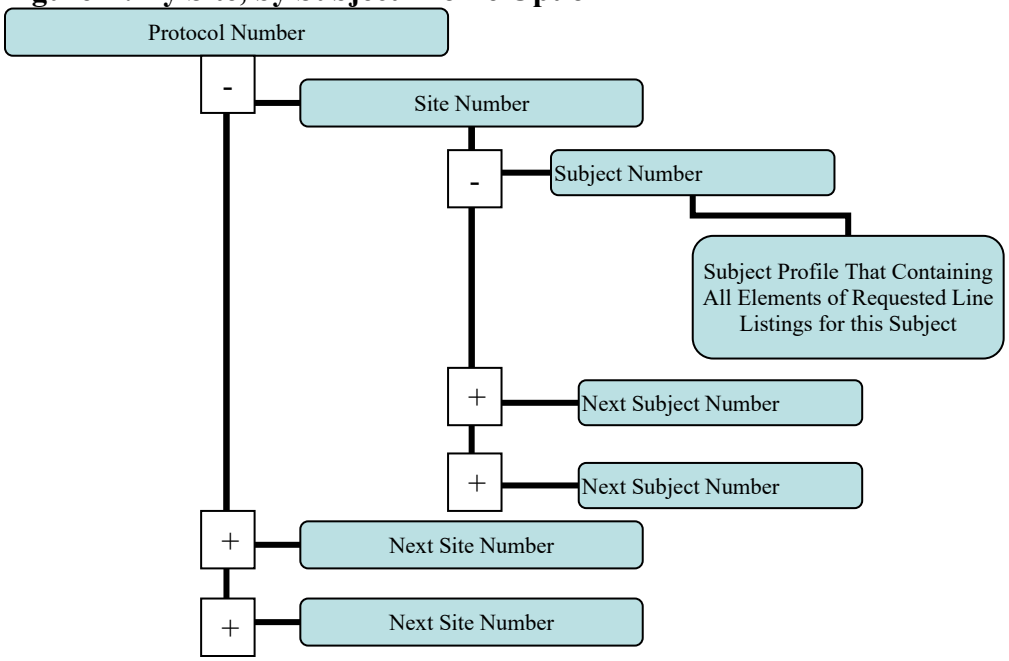
By Site, by Listing Option A:

Figure A: By Site, by Listing Option A



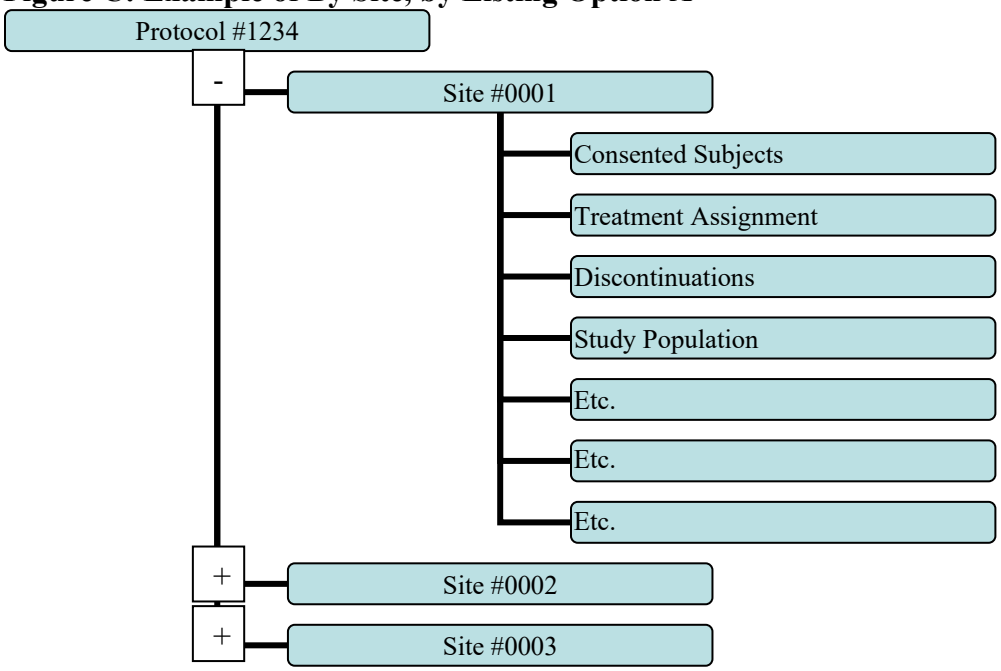
By Site, by Subject Profile Option B:

Figure B: By Site, by Subject Profile Option B



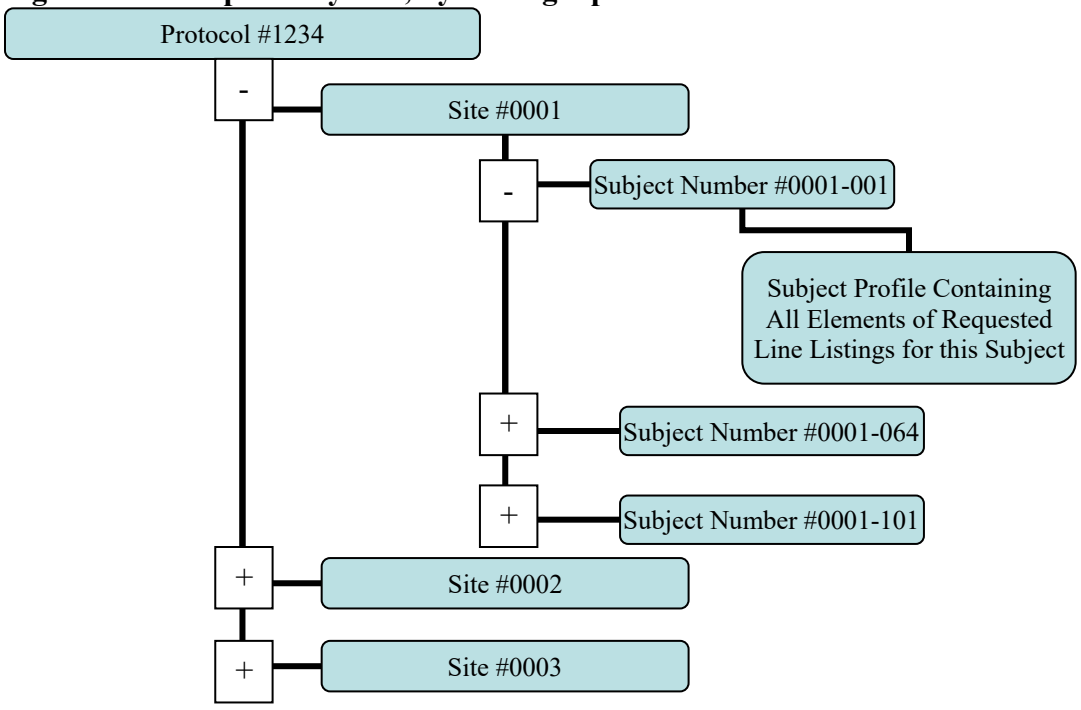
Example of By Site, by Listing Option A:

Figure C: Example of By Site, by Listing Option A



Example of By Site, by Listing Option B:

Figure D: Example of By Site, by Listing Option B



APPENDIX 3: CLINICAL SITE DATA ELEMENTS SUMMARY LISTING

Table B: Clinical Site Data Elements Summary Listing

Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
1	STUDYID	Study Identifier	Char	String	Study or trial identification number.	ABC-123
2	TITLE	Study Title	Char	String	Title of the study as listed in the clinical study report (limit 200 characters). If the title exceeds 200 characters, provide shortened title and define (e.g., use the abbreviated title from clinicaltrial.gov).	Double blind, randomized, placebo-controlled clinical study on the influence of drug X on indication Y
3	SPONCNT	Sponsor Count	Num	Integer	Total count of sponsors throughout the study. If there was a change in the sponsor while the study was ongoing, with sponsors as defined in § 312.3 (21 CFR 312.3), enter an integer indicating the total count of sponsors. If there was no change in the sponsor while the study was ongoing, enter "1."	1
4	SPONSOR	Sponsor Name	Char	String	Full name of the sponsor organization conducting the study at the time of study completion, as sponsor is defined in § 312.3. If the sponsor name exceeds 200 characters, provide short-form sponsor name and define.	DrugCo, Inc.
5	IND	IND Number	Num	6 digit identifier	IND number. If study not performed under IND, leave blank.	010010
6	UNDERIND	Under IND	Char	String	Value should equal "Y" if study at the site was conducted under an IND (i.e., a Form FDA 1572 was signed by the investigator) and "N" if study was not conducted under an IND at the site (i.e., a Form FDA 1572 was not signed by the investigator).	Y
7	NDA	NDA Number	Num	6 digit identifier	FDA NDA number, if available/applicable. If not applicable, leave blank.	021212
8	BLA	BLA Number	Num	6 digit identifier	FDA identification number for BLA, if available/applicable. If not applicable, leave blank.	123456
9	SUPPNUM	Supplement Number	Num	Integer	Serial number for supplemental application, if applicable. If no information is available, leave blank.	4
10	SITEID	Study Site Identifier	Char	String	Investigator site identifier assigned by the sponsor.	50
11	ARM	Description of Planned Treatment Arm	Char	String	Plain-text label for the name given to an arm or treatment group as referenced in the clinical study report (limit 200 characters). When no arm or treatment group is available due to only screen failure subjects at site, use label "Screen Failure."	Active name and dose (e.g., "Active 25mg"), Comparator product name (e.g., "Drug x"), Placebo, Screen Failure

Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
12	COHORT	Description of Planned Cohort	Char	String	For cohort studies, the plain-text label given to a cohort as referenced in the clinical study report (limit 200 characters). When not a cohort study, leave blank.	A
13	SAFPOP	Number of Subjects in Safety Population	Num	Integer	Total number of subjects in safety population at a given site by treatment arm. When a subject has transferred from one site to another, the applicant should handle reporting of such subjects consistently across sites and include in the define file the reporting convention used. The applicant may opt to further explain the reasons subjects transferred between sites in the BIMO Data Reviewer's Guide, if a guide will be provided.	20
14	EFFPOP	Number of Subjects in Efficacy Population	Num	Integer	Total number of subjects in primary efficacy population as reported in the Clinical Study Report at a given site by treatment arm. Further describe the population reported as EFFPOP (e.g.,. Per Protocol, Full Analysis Set, Intent to Treat, modified Intent to Treat) in the clinsite define.html. When a subject has transferred from one site to another, the applicant should handle reporting of such subjects consistently across sites and include in the define file the reporting convention used. The applicant may opt to further explain the reasons subjects transferred between sites in the BIMO Data Reviewer's Guide, if a guide will be provided.	18
15	SCREEN	Number of Subjects Screened	Num	Integer	Total number of subjects screened (and consented) at a given site (overall number per site as subjects have not yet been assigned to treatment arm). When a subject has transferred from one site to another, the applicant should handle reporting of such subjects consistently across sites and include the reporting convention used in the define file or the BIMO Data Reviewer's Guide (if provided). The applicant may opt to further explain the reasons subjects transferred between sites in the BIMO Data Reviewer's Guide, if provided.	100
16	DISCSTUD	Number Subjects Discont. Study	Num	Integer	Number of subjects in the safety population who discontinued from the study by treatment arm at a given site.	5
17	DISCTRT	Number Subjects Discont. Study Treatment	Num	Integer	Number of subjects in the safety population who discontinued from the study treatment by treatment arm at a given site.	10
18	ENDPOINT	Primary Endpoint	Char	String	Plain-text label used to describe the primary endpoint as described in the define file included with each application (limit 200 characters).	Average increase in blood pressure

Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
19	ENDPTYPE	Primary Endpoint Type	Char	String	Variable type of the primary endpoint (i.e., “continuous,” “discrete,” “time to event,” or “other”).	Continuous
20	TRTEFFR1	Treatment Efficacy Result for SAFPOP	Num	Floating Point	Summary statistic for each primary efficacy endpoint by treatment arm at a given site for subjects in SAFPOP.	1.00
21	TRTEFFR2	Treatment Efficacy Result for EFFPOP	Num	Floating Point	Summary statistic for each primary efficacy endpoint by treatment arm at a given site for subjects in EFFPOP.	0.98
22	CENSOR1	Censored Observations in SAFPOP	Num	Integer	Total number of censored observations in SAFPOP at a given site by treatment arm for primary endpoint (e.g., applicable to time-to-event). If not applicable, leave blank.	5
23	CENSOR2	Censored Observations in EFFPOP	Num	Integer	Total number of censored observations in EFFPOP at a given site by treatment arm for primary endpoint (e.g., applicable to time-to-event). If not applicable, leave blank.	3
24	NSAE	Number of Non-Serious Adverse Events	Num	Integer	Total number of nonserious adverse events at a given site by treatment arm for subjects in the SAFPOP. This value should include multiple events per subject and all event types (i.e., **not limited to** only those that are deemed related to study drug or that are treatment emergent events). When events with the same preferred term have occurred on different dates for a subject, each event should be counted separately in event count.	10
25	SAE	Number of Serious Adverse Events	Num	Integer	Total number of serious adverse events, excluding deaths, at a given site by treatment arm for subjects in the SAFPOP. This value should include multiple events per subject. When events with the same preferred term have occurred on different dates for a subject, each event should be counted separately in event count.	5
26	DEATH	Number of Deaths	Num	Integer	Total number of deaths at a given site by treatment arm for subjects in the SAFPOP.	1
27	IMPDEV	Number of Important Protocol Deviations	Num	Integer	Total number of important protocol deviations at a given site by treatment arm for subjects in the SAFPOP. A protocol deviation is any change, divergence, or departure from the study design or procedures defined in the protocol or associated investigational plans that is not implemented or intended as a systematic change. This value should include multiple deviations per subject and all major deviation types. Important deviations are those deviations that might significantly affect the completeness, accuracy, and/or reliability of the study data or that might significantly affect a subject's rights, safety, or well-being.	2

Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
28	NOIMPDEV	Number of Non-Important Protocol Deviations	Num	Integer	Total number of protocol deviations, excluding important protocol deviations, at a given site by treatment arm for subjects in the SAFPOP. A protocol deviation is any change, divergence, or departure from the study design or procedures defined in the protocol or associated investigational plans that is not implemented or intended as a systematic change.	98
29	FINLDISC	Financial Disclosure Amount	Char	String	Total financial disclosure amount (US$) by site calculated as the sum of disclosures for the clinical investigator and all sub-investigators, to include all required parities under the applicable regulations (21 CFR 54, 312, 314, 320, 330, 601, 807, 812, 814, and 860). Enter ">=$25,000," "< $25,000," "unknown" if a proper value is applicable but is not known (i.e., unable to obtain information from investigator at site), or "masked" if information on this item is available but it has not been provided by the sender due to security, privacy, or other reasons.	>= $25,000
30	LASTNAME	Investigator Last Name	Char	String	Last name of the clinical investigator as it appears on the Form FDA 1572 or the signed investigator agreement. At sites where the clinical investigator has changed during the course of the study, the most recent clinical investigator should be listed.	Doe
31	FRSTNAME	Investigator First Name	Char	String	First name of the clinical investigator as it appears on the Form FDA 1572 or the signed investigator agreement.	John
32	MINITIAL	Investigator Middle Initial	Char	String	Middle initial of the clinical investigator, if any, as it appears on the Form FDA 1572 or the signed investigator agreement.	M
33	PHONE	Investigator Phone Number	Char	String	Phone number of the clinical investigator. Include country code for non-U.S. numbers.	44-555-555-5555
34	FAX	Investigator Fax Number	Char	String	Fax number of the clinical investigator. Include country code for non-U.S. numbers. If not available, leave blank.	44-555-555-5555
35	EMAIL	Investigator Email Address	Char	String	Email address of the clinical investigator.	John.doe@mail.com
36	COUNTRY	Country	Char	Geopolitical Entities, Names and Codes (GENC)	GENC code for the country in which the site is located.	USA

Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
37	STATE	State	Char	GENC	GENC subdivision unabbreviated preferred name in which the site is located. If not applicable, enter "NA."	Maryland
38	CITY	City	Char	String	Unabbreviated city or village in which the site is located.	Silver Spring
39	POSTAL	Postal Code	Char	String	Postal code in which the site is located. If not applicable, enter "NA."	20850
40	STREET	Street Address	Char	String	Street address and office number at which the site is located (limit 200 characters).	2005 John Fitzgerald Kennedy Boulevard Northwest, International Technology Center, Department of Medicine and Pharmacokinetics, National Institute of Clinical Research Twin Towers Building,
41	STREET1	Street Address Continued	Char	String	Street address and office number at which the site is located. Use this field when the STREET variable does not permit sufficient space to fully describe street address and office number at which the site is located.	The Executive Wing, Suite # 209

APPENDIX 4: EXAMPLES

The following is a fictional example of a dataset for a placebo-controlled trial. Four international sites enrolled a total of 205 subjects who were randomized in a 1:1 ratio to active or placebo. In the first example there is a single primary endpoint (percent of responders). In the second example there are co-primary endpoints (percent of responders and change from baseline). Note that since there were two treatment arms, in the first example, each site contains two rows and there are a total of eight rows for the entire dataset. In the second example, each site contains a total of 4 rows, and there are a total of 16 rows for the entire dataset.

Table C: Example for Clinical Site Data Elements Summary Listing with One Endpoint

STUDYID	TITLE	SPONCNT	SPONSOR	IND	UNDER-IND	NDA	BLA	SUPP-NUM	SITEID	ARM	COHORT	SAFPOP	EFFPOP	SCREEN	DISCSTUD	DISCTRT
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	001	Active	-	26	54	61	3	2
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	001	Placebo	-	25	54	61	4	1
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	002	Active	-	23	44	54	2	1
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	002	Placebo	-	25	43	54	4	3
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	003	Active	-	27	55	62	3	0
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	003	Placebo	-	26	56	62	5	3
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	004	Active	-	26	49	60	2	2
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	·	·	004	Placebo	-	27	50	60	1	0

ENDPOINT	ENDPTYPE	TRTEFFR1	TRTEFFR2	CENSOR1	CENSOR2	NSAE	SAE	DEATH	IMPDEV	NOIMPDEV	FINLDISC	LASTNAME	FRSTNAME
Percent Responders	Binary	0.48	0.64	·	-	0	2	0	1	4	< $25,000	Doe	John
Percent Responders	Binary	0.14	0.19	·	-	2	2	0	1	6	< $25,000	Doe	John
Percent Responders	Binary	0.48	0.42	·	-	3	2	1	0	9	>= $25,000	Washington	George
Percent Responders	Binary	0.14	0.20	·	-	0	2	0	3	11	>= $25,000	Washington	George
Percent Responders	Binary	0.54	0.48	·	-	2	2	0	1	4	>= $25,000	Jefferson	Thomas
Percent Responders	Binary	0.19	0.32	·	-	3	6	0	0	7	>= $25,000	Jefferson	Thomas
Percent Responders	Binary	0.46	0.45	·	-	4	1	0	0	8	unknown	Lincoln	Abraham
Percent Responders	Binary	0.12	0.16	·	-	1	2	0	1	13	unknown	Lincoln	Abraham

MINITIAL	PHONE	FAX	EMAIL	COUNTRY	STATE	CITY	POSTAL	STREET	STREET1
M	555-123-4567	555-123-4560	John@mail.com	RUS	Moskovskaya Oblast'	Moscow	103009	Kremlin Road 1	
M	555-123-4567	555-123-4560	John@mail.com	RUS	Moskovskaya Oblast'	Moscow	103009	Kremlin Road 1	
	020-3456-7891	020-3456-7890	george@mail.com	GBR	Westminster	London	SW1A 2	10 Downing St	

	020-3456-7891	020-3456-7890	george@mail.com	GBR	Westminster	London	SW1A 2	10 Downing St	
	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FRA	Paris	Paris	75002	1, Rue Road	
	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FRA	Paris	Paris	75002	1, Rue Road	
	555-987-6543	555-987-6540	abe@mail.com	USA	Maryland	Rockville	20852	10903 New Hampshire Avenue, Office of Medical Products and Tobacco, Center for Drug Evaluation and Research	Building 4, Room 1375
	555-987-6543	555-987-6540	abe@mail.com	USA	Maryland	Rockville	20852	10903 New Hampshire Avenue, Office of Medical Products and Tobacco, Center for Drug Evaluation and Research	Building 4, Room 1375

Table D: Example for Clinical Site Data Elements Summary Listing with Multiple Primary Endpoints

STUDYID	TITLE	SPONCNT	SPONSOR	IND	UNDER-IND	NDA	BLA	SUPP-NUM	SITEID	ARM	COHORT	SAFPOP	EFFPOP	SCREEN	DISCSTUD	DISCTRT
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	001	Active	A	26	22	61	3	2
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	001	Active	B	26	22	61	3	2
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	001	Placebo	A	25	23	61	4	1
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	001	Placebo	B	25	23	61	4	1
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	002	Active	A	23	19	54	2	1
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	002	Active	B	23	19	54	2	1
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	002	Placebo	A	25	23	54	4	3
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	002	Placebo	B	25	23	54	4	3
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	003	Active	A	27	26	62	3	0
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	003	Active	B	27	26	62	3	0
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	003	Placebo	A	26	23	62	5	3
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	003	Placebo	B	26	23	62	5	3
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	004	Active	A	26	19	60	2	2
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	004	Active	B	26	19	60	2	2
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	004	Placebo	A	27	20	60	1	0
ABC-123	Double blind…	1	DrugCo, Inc.	000001	Y	200001	.	.	004	Placebo	B	27	20	60	1	0

ENDPOINT	ENDPTYPE	TRTEFFR1	TRTEFFR2	CENSOR1	CENSOR2	NSAE	SAE	DEATH	IMPDEV	NOIMPDEV	FINLDISC	LASTNAME	FRSTNAME
Percent Responders	Binary	0.48	0.58	.	.	0	2	0	1	5	< $25,000	Doe	John
Change from Baseline	Continuous	0.74	0.76	.	.	0	2	0	1	8	< $25,000	Doe	John
Percent Responders	Binary	0.14	0.12	.	.	2	2	0	1	5	< $25,000	Doe	John
Change from Baseline	Continuous	0.14	0.16	.	.	2	2	0	1	8	< $25,000	Doe	John
Percent Responders	Binary	0.48	0.44	.	.	3	2	1	0	11	>= $25,0000	Washington	George

ENDPOINT	ENDPTYPE	TRTEFFR1	TRTEFFR2	CENSOR1	CENSOR2	NSAE	SAE	DEATH	IMPDEV	NOIMPDEV	FINLDISC	LASTNAME	FRSTNAME
Change from Baseline	Continuous	0.67	0.63	.	.	3	2	1	0	13	>= $25,0000	Washington	George
Percent Responders	Binary	0.14	0.15	.	.	0	2	0	3	11	>= $25,0000	Washington	George
Change from Baseline	Continuous	0.14	0.16	.	.	0	2	0	3	13	>= $25,0000	Washington	George
Percent Responders	Binary	0.54	0.50	.	.	2	2	0	1	9	>= $25,0000	Jefferson	Thomas
Change from Baseline	Continuous	0.65	0.61	.	.	2	2	0	1	5	>= $25,0000	Jefferson	Thomas
Percent Responders	Binary	0.19	0.22	.	.	3	6	0	0	9	>= $25,0000	Jefferson	Thomas
Change from Baseline	Continuous	0.19	0.26	.	.	3	6	0	0	5	>= $25,0000	Jefferson	Thomas
Percent Responders	Binary	0.46	0.51	.	.	4	1	0	0	0	unknown	Lincoln	Abraham
Change from Baseline	Continuous	0.71	0.81	.	.	4	1	0	0	3	unknown	Lincoln	Abraham
Percent Responders	Binary	0.12	0.17	.	.	1	2	0	0	0	unknown	Lincoln	Abraham
Change from Baseline	Continuous	0.15	0.19	.	.	1	2	0	1	3	unknown	Lincoln	Abraham

MINITIAL	PHONE	FAX	EMAIL	COUNTRY	STATE	CITY	POSTAL	STREET	STREET1
M	555-123-4567	555-123-4560	John@mail.com	RUS	Moskovskaya Oblast'	Moscow	103009	Kremlin Road 1	
M	555-123-4567	555-123-4560	John@mail.com	RUS	Moskovskaya Oblast'	Moscow	103009	Kremlin Road 1	
M	555-123-4567	555-123-4560	John@mail.com	RUS	Moskovskaya Oblast'	Moscow	103009	Kremlin Road 1	
M	555-123-4567	555-123-4560	John@mail.com	RUS	Moskovskaya Oblast'	Moscow	103009	Kremlin Road 1	
.	020-3456-7891	020-3456-7890	george@mail.com	GBR	Westminster	London	SW1A 2	10 Downing St Suite 2058	
.	020-3456-7891	020-3456-7890	george@mail.com	GBR	Westminster	London	SW1A 2	10 Downing St Suite 2058	
.	020-3456-7891	020-3456-7890	george@mail.com	GBR	Westminster	London	SW1A 2	10 Downing St Suite 2058	
.	020-3456-7891	020-3456-7890	george@mail.com	GBR	Westminster	London	SW1A 2	10 Downing St Suite 2058	
.	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FRA	Paris	Paris	75002	1, Rue Road	
.	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FRA	Paris	Paris	75002	1, Rue Road	
.	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FRA	Paris	Paris	75002	1, Rue Road	
.	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FRA	Paris	Paris	75002	1, Rue Road	
.	555-987-6543	555-987-6540	abe@mail.com	USA	Maryland	Rockville	20852	2005 John Fitzgerald Kennedy Boulevard Northwest, International Technology Center, Department of Medicine and Pharmacokinetics, National Institute of Clinical Research Twin Towers Building,	The Executive Wing, Suite # 209
.	555-987-6543	555-987-6540	abe@mail.com	USA	Maryland	Rockville	20852	2005 John Fitzgerald Kennedy Boulevard Northwest, International Technology Center, Department of Medicine and Pharmacokinetics, National Institute of Clinical Research Twin Towers Building,	The Executive Wing, Suite # 209
.	555-987-6543	555-987-6540	abe@mail.com	USA	Maryland	Rockville	20852	2005 John Fitzgerald Kennedy Boulevard Northwest, International Technology Center, Department of Medicine and Pharmacokinetics, National Institute of Clinical Research Twin Towers Building,	The Executive Wing, Suite # 209
.	555-987-6543	555-987-6540	abe@mail.com	USA	Maryland	Rockville	20852	2005 John Fitzgerald Kennedy Boulevard Northwest,	The Executive

MINITIAL	PHONE	FAX	EMAIL	COUNTRY	STATE	CITY	POSTAL	STREET	STREET1
								International Technology Center, Department of Medicine and Pharmacokinetics, National Institute of Clinical Research Twin Towers Building,	Wing, Suite # 209