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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This Document is Referenced by the Following Draft Guidance Document: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

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U.S. FOOD & DRUG
ADMINISTRATION

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Revision History

| Date | Version | Summary of Changes |
|-------------|----------------|--|
| 12/28/2017 | 1.0 | Original Version |
| 07/23/2020 | 2.0 | <ol style="list-style-type: none">1. Corrected footnote hyperlinks2. Edited variable names in examples and tables to maintain consistency across document3. Clarified document, listings, and data requests4. Deleted request for SITEFFE and SITEFFS variables in clinsite.xpt5. Added COHORT variable6. Revised PROTVIOL variable to IMPDEV and NOIMPDEV variables7. Provided additional instructions for placement of files per eCTD format |
| 08/11/2022 | 3.0 | <ol style="list-style-type: none">1. Rename BIMO Review Guide to BIMO Data Review Guide.2. Renamed TRTEFFR to TRTEFFR13. Added EFFPOP, TRTEFFR2, and CENSOR2 Variables4. Deleted request for TRTEFFS5. Change instructions for use of ISO codes to use of Geopolitical Entities, Names and Codes (GENC) codelist.6. Minor editorial changes. |

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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 applications² (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>.

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40 email address) for the individual(s) who can provide updated location information upon request.
41 This information ensures that when CDER issues an inspection assignment for the application,
42 the inspection is of the most responsible entity for a given regulatory responsibility, and that the
43 inspection assignment is issued for the location where records are present for review.
44

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

45
46
47 The protocol and protocol amendments, with associated versions of the case report form, and the
48 final version of the annotated case report form (case report form containing Clinical Data
49 Interchange Standards Consortium and Study Data Tabulation Model (SDTM) annotations) are
50 generally included in Appendix 16³ of the Clinical Study Report or in the datasets folder for each
51 study. When these items are included in an appendix to the Clinical Study Report or the dataset
52 folder for the study, there is no need to resubmit them. If the applicant is submitting a BIMO
53 Data Reviewer's Guide,⁴ the applicant should note that these items are present in an appendix of
54 the Clinical Study Report or the dataset folder where they are placed.
55

56 These items are included in the background materials provided to the Office of Regulatory
57 Affairs for BIMO inspections; it is important to provide all versions of these documents so that
58 the field investigator performing the inspection can reference the correct versions of protocols
59 and case report forms in place at the time of the conduct of specific study procedures.
60

II. SUBJECT-LEVEL DATA LINE LISTINGS BY CLINICAL SITE

A. Organization of the Subject-Level Data Line Listings

61
62
63
64
65
66 Examples of the formatting for the PDF of subject-level data line listings provided for each
67 major (i.e., pivotal) study used to support safety and efficacy in the application, including studies
68 with different treatment indications, are provided in Appendix 2 of this Guide. If the sponsor
69 believes alternative listings or formats are preferable for its submission, proposed alternatives
70 should be discussed with the Office of Scientific Investigations in advance of the application
71 submission—for example, before or during pre-NDA or pre-BLA meetings.
72

73 For clinical investigator sites involved in multiple studies in support of an application, the
74 subject listings should be provided independently for each study within the study-associated
75 PDF.
76

77 Subject-level data line listings, by clinical site, should include consented subjects, treatment
78 assignment, discontinuations, study population, inclusion and exclusion criteria, adverse events,
79 protocol deviations, efficacy endpoints, concomitant medications, and safety monitoring, as
80 further described below.
81

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>.

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82 1. *Consented Subjects*

83
84 This by-subject, by-clinical site listing includes all subjects that consented to enroll in the study.
85 Consented subjects that were screen failures should also be included. For subjects that consented
86 but were not randomized to treatment or did not receive investigational product, the specific
87 reason they were not randomized or treated should be included in this listing.
88

89 2. *Treatment Assignment*

90
91 This by-subject, by-clinical site listing includes the treatment assignment to which the subject
92 was randomized. If a subject mistakenly received treatment different from the subject's assigned
93 treatment for any duration of time, the actual treatment received should also be included.
94

95 3. *Discontinuations*

96
97 This by-subject, by-clinical site listing includes:
98

- 99 • All subjects that discontinued during run-in period (if applicable)
 - 100 • All subjects that discontinued from study treatment
 - 101 • All subjects that discontinued from the study completely
- 102

103 For each subject, the date of and reason for discontinuation should be provided.
104

105 4. *Study Population*

106
107 This by-subject, by-clinical site listing identifies the protocol-defined study population in which
108 each subject was analyzed (e.g., intent-to-treat, safety, per protocol). For subjects that did not
109 meet criteria for inclusion in the per-protocol population, the reason they were excluded from the
110 per-protocol population should be provided.
111

112 5. *Inclusion and Exclusion Criteria*

113
114 This by-subject, by-clinical site listing should display whether each subject met each inclusion
115 and exclusion criterion defined in the protocol.
116

117 6. *Adverse Events*

118
119 This by-subject, by-clinical site listing should include all adverse events (i.e., nonserious adverse
120 events and serious adverse events, including deaths), date of occurrence and time if collected,
121 treatment(s) administered, severity, whether considered serious by the clinical investigator,
122 whether considered serious by the sponsor, action taken, whether the event led to discontinuation
123 of study therapy, and outcome/date of resolution.
124

125 7. *Protocol Deviations*

126

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

130

131 8. *Efficacy Endpoints*

132

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

142

143 9. *Concomitant Medications*

144

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

148

149 10. *Safety Monitoring*

150

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

156

157 **B. Site-Specific Listings Format**

158

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

163

164 Although listings are currently requested in PDF format, CDER is in the process of developing
165 tools to extract site-specific listings, needed for inspectional purposes, from submitted Clinical
166 Data Interchange Standards Consortium, SDTM, and Analysis Data Model (ADaM) datasets and
167 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>.

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168 specifications to include details for the submission of SDTM and ADaM datasets, including
169 controlled terminology standards. In anticipation of the development of CDER tools for
170 extraction of by-site, by-subject data listings, sponsors should ensure that they are prepared to
171 submit clinical study data using standards specified in the Data Standards Catalog.⁷
172

173

174

III. SUMMARY-LEVEL CLINICAL SITE DATASET

175

176

A. Organization of the Site-Level Dataset

177

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

181

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

185

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

188

189

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

190

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

193

194 • Safety Population (SAFPOP) — Total number of subjects in safety population at a given
195 site by treatment arm. When a subject has transferred from one site to another, the
196 applicant should handle reporting of such subjects consistently across sites and include in
197 the define file, or the BIMO Data Review Guide when one is provided, the reporting
convention used.

198

199 • Primary Efficacy Population (EFFPOP) — Total number of subjects in the primary efficacy
200 population, as defined in the clinical study report, at a given site by treatment arm to support
201 the proposed indication in the application. The efficacy population used should be identified
202 in the define file provided for the clinsite.xpt (e.g., Full Analysis Set, Per Protocol, Intent to
Treat, Modified Intent to Treat).

203

204 • Treatment Efficacy Result One (TRTEFFR1) — The summary statistic for each primary
205 efficacy endpoint, by treatment arm at a site, based subjects in the SAFPOP. Values reported
206 in TRTEFFR1 generally reflect simple summary statistics for the primary efficacy
207 endpoint(s). The method used for deriving the TRTEFFR1, including a description of which
208 analysis datasets and associated variables are used to derive the TRTEFFR1, should be
209 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>.

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

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

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

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

228
229 To accommodate the variety of endpoint types that can be used in analyses, it is critical that the
230 following endpoint type definitions be referenced, and summaries be provided when tabulating
231 the site-specific summary statistic by treatment arm (for TRTEFFR1 and TRTEFFR2):

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

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

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249 When more than one primary efficacy endpoint exists, additional rows should be added to the
250 dataset to report additional ENDPOINT, Primary Endpoint Type (ENDPTYPE), TRTEFFR1,
251 and TRTEFFR2 values by arm for each site.
252

253 It is anticipated that efficacy data for all subjects included in the SAFPOP and EFFPOP variables
254 will be included in TRTEFFR1 and TRTEFFR2 variables reported, respectively. If efficacy data
255 is not available for all subjects reported in the SAFPOP or EFFPOP variables, then efficacy data
256 for these subjects should be reported as specified in the study Data Analysis Plan, and the
257 method used for calculation of efficacy variables should be described in the data define table
258 provided with the clinsite.xpt file.
259

260 The summary-level clinical site dataset should be accompanied by a data definition file. The
261 contents of the define file for a dataset and fictional examples are presented in Appendix 3 and
262 Appendix 4 of this Guide.
263

C. Creating the Data File (Template and Structure)

264
265
266 A sample summary-level clinical site data submission using the variables identified in Appendix
267 3 of this Guide is provided in Appendix 4.
268
269

IV. SUBMITTING BIMO CLINICAL DATA IN THE eCTD FORMAT

270
271
272 Clinical study-level information, subject-level data line listings by clinical site, and the
273 summary-level clinical site dataset submitted with an application, in Electronic Common
274 Document (eCTD) format, should be placed in eCTD Module 5 (M5) — Clinical Study Reports,
275 using the following conventions:

A. Study Tagging File

276
277
278 Construct a BIMO study tagging file (STF) and place it in eCTD Module 5.3.5.4, “Other Study
279 reports and related information.” The study identifier (ID) for this STF is “BIMO.” Files
280 described in section III (e.g., Description of Clinical Study-Level Information, Subject-Level
281 Data Line Listings by Clinical Site, and Summary-Level Clinical Site Dataset) of the draft
282 guidance *Standardized Format for Electronic Submission of NDA and BLA Content for the*
283 *Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions* (February
284 2018) are linked to this BIMO STF using file tags as indicated below.⁸ Leaf titles for these data
285 are named “BIMO [list study ID, followed by brief description of file being submitted].”
286

287 **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.

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| 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 |

288

289

290

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

291

292

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.

293

294

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

295

296

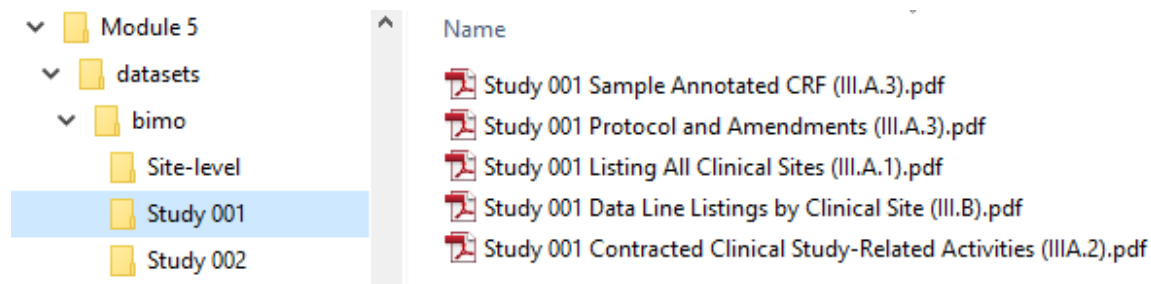
Figure 2: Place Clinical Study-Level Information and Subject-Level Line Listings by Clinical Site in the M5 Folder

297

298

299

300



301

302

303

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

304

305

For the site-level dataset, use the filename “clinsite.xpt.” A single file containing data from all major (i.e., pivotal) studies⁹ used to support safety and efficacy in the application should be provided.

306

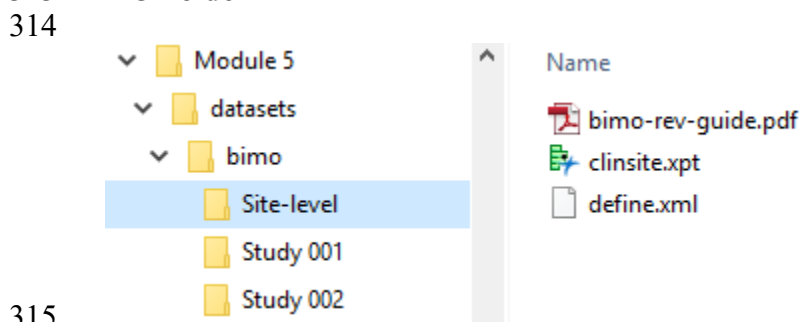
307

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.

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308
309 Within the eCTD folder structure, place the site-level dataset define file and BIMO Data
310 Reviewer’s Guide, if it is being submitted, in the M5 folder as follows:

311
312 **Figure 2: Place the Site-Level Dataset Define File and BIMO Data Reviewer’s Guide in the**
313 **M5 Folder**



315

316

317 **D. File Format**

318

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

325 **E. Leaf Titles**

326

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

331

332 **F. Submission**

333

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

336

337 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>.

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

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353 **APPENDIX 1: CLINICAL STUDY-LEVEL INFORMATION**

354
355 *Format for comprehensive and readily located list of all clinical sites that participated in each*
356 *clinical study. A separate table should be provided for each clinical study.*

357 **Table A: Format for Clinical Site Lists**

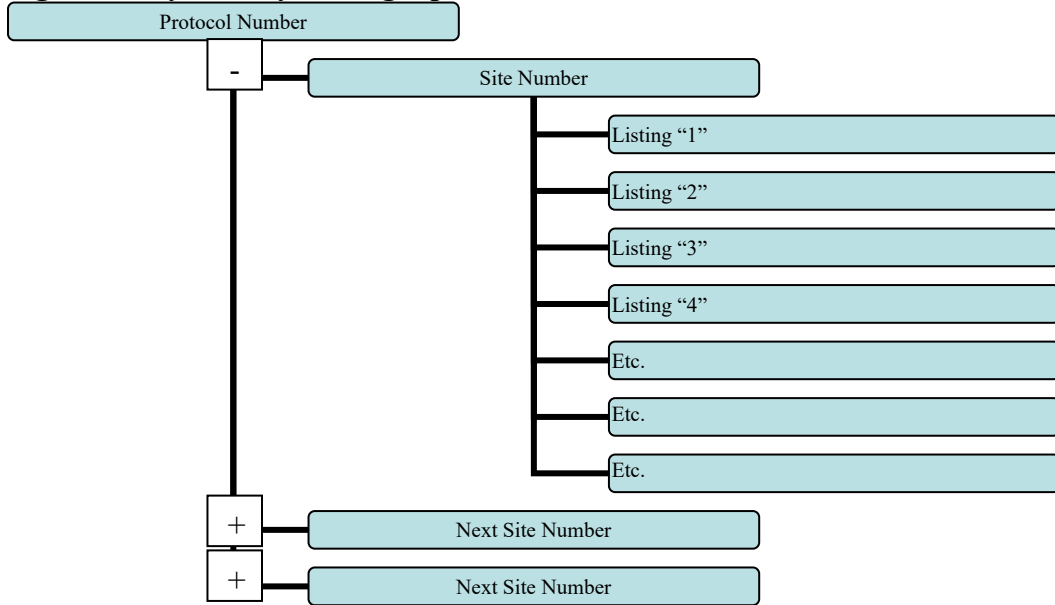
| Protocol Number: Protocol Title | | | |
|---|---|--|--|
| Site Identifier | Investigator Name (Prior Clinical Investigator(s)) | Site Address at Time of Clinical Study (Updated Site Address when exists and available) | Site Contact Information at Time of Clinical Study (Updated Contact Information when exists and available) |
| SITEID | LASTNAME, FRSTNAME, MINITAL | 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. | | | |

358
359

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

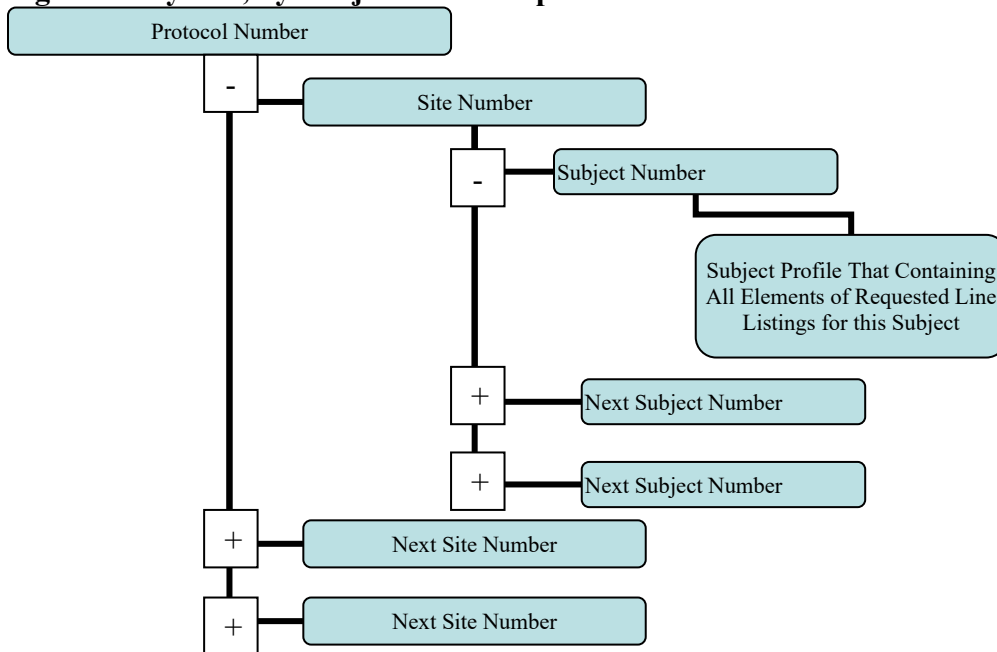
362
363 By Site, by Listing Option A:
364

365 **Figure A: By Site, by Listing Option A**



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368
369 By Site, by Subject Profile Option B:
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371 **Figure B: By Site, by Subject Profile Option B**



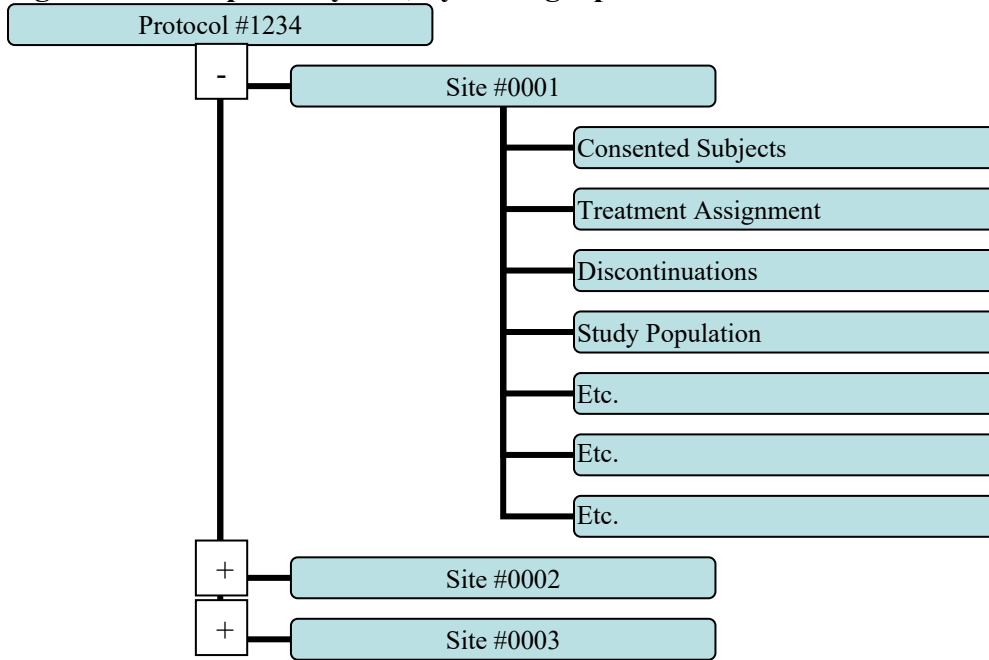
372
373

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374 Example of By Site, by Listing Option A:

375

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



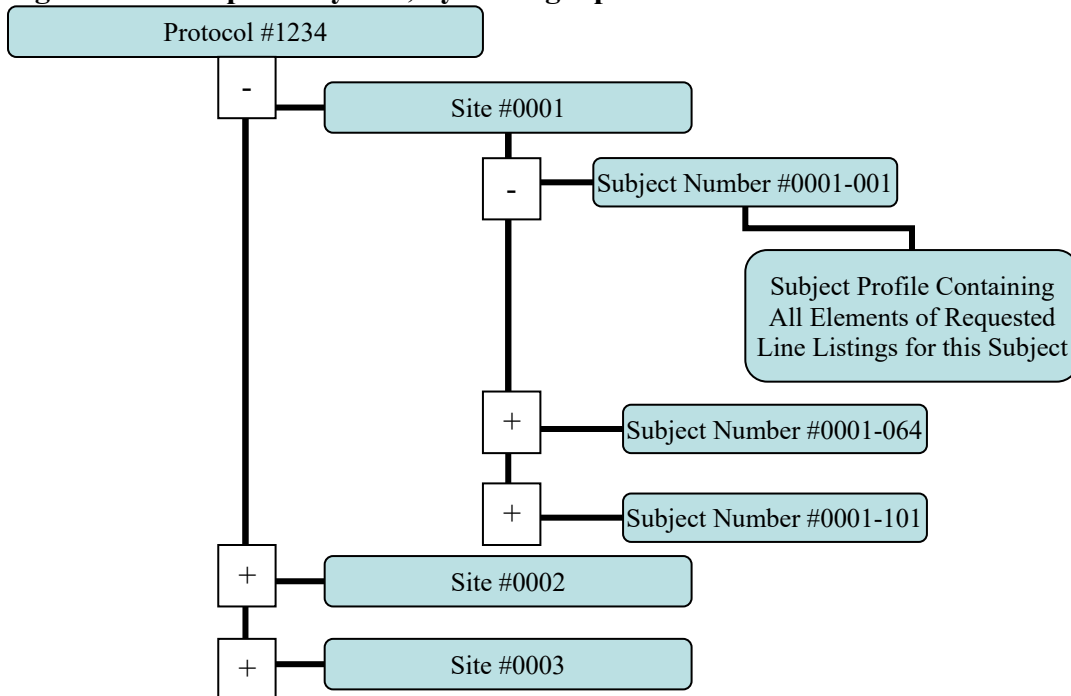
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378

379 Example of By Site, by Listing Option B:

380

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



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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 |

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| 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 | DISCRT | 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 |

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| 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 |

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| 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 parties 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 | INITIAL | 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 |

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| 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 |

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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 | DISCRT |
|---------|-----------------|---------|--------------|--------|-----------|--------|-----|--------------|--------|---------|--------|--------|--------|--------|----------|--------|
| 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 | FINLISC | 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 |

| INITIAL | 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 | |

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| | | | | | | | | | |
|--|----------------|----------------|-----------------|-----|-------------|-----------|--------|---|-----------------------|
| | 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 | DISCRT |
|---------|-----------------|---------|--------------|--------|-----------|--------|-----|--------------|--------|---------|--------|--------|--------|--------|----------|--------|
| 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 | >= \$25,000 | Washington | George |

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| 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 |

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| MINIMAL | 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 |