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Clinical Site Dataset in eSubmissions to the FDA

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ABSTRACT

To verify the integrity of the data, submitted to the FDA, is the cause for CDER to perform on-site inspections of clinical trial sites. For an early planning of on-site inspections, CDER recommends the applicants to submit data on clinical site level. In December 2012 the draft guidance "Providing Submissions in Electronic Format - Summary Level Clinical Site Data for CDER's Inspection Planning" was published by the FDA, describing the requirements for the clinical site dataset.

The poster will provide information about the regulatory background and an overview on how to prepare and submit the clinical site dataset. This covers the information included in the dataset, as well as the clinical site submission package that is send to the FDA.

INTRODUCTION

As part of NDA and BLA submission packages to the FDA, it is required to submit study specific data.

Additionally, CDER prefers to receive summary level clinical site data within new drug applications (NDAs), biologics licensing applications (BLAs), and NDA and BLA supplemental applications containing new clinical study reports. CDER is developing an inspection site selection tool which uses this summary level clinical site data for an early planning of on-site inspections, to verify the integrity of the data collected by these sites. For this reason the FDA recommends to submit the summary level clinical site dataset in a standardized electronic format which is described in the draft guidance "Providing Submissions in Electronic Format - Summary Level Clinical Site Data for CDER's Inspection Planning" and the related document "Specifications for Preparing and Submitting Summary Level Clinical Site Data for CDER's Inspection Planning".

The summary level clinical site dataset is intended to

- characterize individual clinical investigator sites,
- describe aspects of the studies with which those clinical investigator sites are associated and
- present the characteristics and outcomes of the study on the site level.

The draft guidance was published in December 2012 by the FDA and the comment period was closed in February 2013. The comments are still under review and a re-drafted version of the guidance is planned.

SPECIFICATIONS

The detailed specifications for preparing and submitting of the summary level clinical site dataset are described in the document "Specifications for Preparing and Submitting Summary Level Clinical Site Data for CDER's Inspection Planning".

The summary level clinical site dataset contains all studies used to support safety and efficacy in the application. For each study the data should be submitted by site and treatment arm for the ITT population. If a site is involved in different studies the site has to be included in the dataset for each study.

The requested variables of the summary level clinical site dataset can be divided into 3 groups:

- Variables for general information and information about included studies:
  - ⇨ The values of these variables are unique in each record within a study.

Variable Name	Description	Type
STUDY	Study identification number	Char
STUDYTL	Study title as listed in clinical study report	Char
DOMAIN	Domain abbreviation	Char
SPONNO	Total number of sponsors	Num

Variable Name	Description	Type
SPONNAME	Name of the sponsor organization at the time of study completion	Char
IND	Investigational new drug application number	Num
UNDERIND	Study was conducted under an IND or not (N/Y)	Char
NDA	FDA new drug application number	Num
BLA	FDA identification number for biologics license application	Num
SUPPNUM	Serial number for supplemental application	Num
ENDPOINT	Plain text to describe the primary endpoint	Char
ENDTYPE	Variable type of ENDPOINT (continuous, discrete, time to event, or other)	Char

- Variables for site information
  - ⇨ The values of these variables are unique in each record by site within a study.

Variable Name	Description	Type
SITEID	Site identification number	Char
SCREEN	Total number of patients screened	Num
SITEEFFE	Site-specific treatment effect reported	Num
SITEEFFS	Standard deviation of SITEEFFE	Num
LASTNAME	Last name of investigator	Char
FRSTNAME	First name of investigator	Char
MINITIAL	Middle initial of the investigator	Char
PHONE	Phone number of primary investigator	Char
FAX	Fax number of primary investigator	Char
EMAIL	Email address of the primary investigator	Char
COUNTRY	Country code	Char
STATE	Unabbreviated state or province	Char
CITY	Unabbreviated city, county or village	Char
POSTAL	Postal code	Char
STREET	Street address and office number	Char
FINLMAX	Maximum financial disclosure amount ($USD) by any single investigator	Num
FINLDISC	Total financial disclosure amount ($USD)	Num

- Variables for characteristics and outcomes by study, site and treatment arm

Variable Name	Description	Type
ARM	Plain text for the treatment arm	Char
ENROLL	Total number of patients enrolled	Num
DISCONT	Number of patients discontinuing after being enrolled	Num
TRTEFFE	Summary statistic for primary efficacy endpoint	Num
TRTEFFS	Standard deviation of TRTEFFE	Num
CENSOR	Number of censored observations	Num
NSAE	Total number of non-serious adverse events	Num
SAE	Total number of serious adverse events excluding deaths	Num
DEATH	Total number of deaths	Num
PROTVIOL	Number of protocol violations	Num

The order of the variables, the labels and the associated formats are specified in the specifications document "Specifications for Preparing and Submitting Summary Level Clinical Site Data for CDER's Inspection Planning".

Some common derivation rules are the following:

- If a numeric variable is not applicable for a study, enter -1.
- For COUNTRY use the 3 letter ISO 3166 country code.

EXAMPLE OF A SUMMARY CLINICAL SITE DATASET

STUDY	STUDYTL	DOMAIN	SPONNO	SPONNAME	IND	UNDERIND	NDA	BLA	SUPPNUM	SITEID	ARM	ENROLL	SCREEN	DISCONT
ABC-123	Double blind ...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	001	Active	26	61	3
ABC-123	Double blind ...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	001	Placebo	25	61	4
ABC-123	Double blind ...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	002	Active	23	54	2
ABC-123	Double blind ...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	002	Placebo	25	54	1

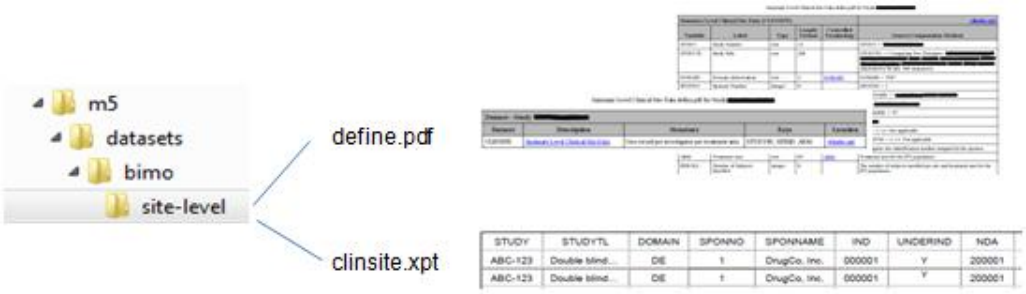
ENDPOINT	ENDTYPE	TRTEFFE	TRTEFFS	SITEEFFE	SITEEFFS	CENSOR	NSAE	SAE	DEATH	PROTVIOL
Percent Responders	Binary	0.48	0.0980	0.34	0.1405	-1	0	2	0	1
Percent Responders	Binary	0.14	0.0694	0.34	0.1405	-1	2	2	1	1
Percent Responders	Binary	0.46	0.0977	0.33	0.1275	-1	4	1	0	0
Percent Responders	Binary	0.12	0.0625	0.33	0.1275	-1	1	2	0	1

FINLMAX	FINLDISC	LASTNAME	FRSTNAME	MINITIAL	PHONE	FAX	EMAIL	COUNTRY	STATE	CITY	POSTAL	STREET
-1	-1	Doe	John	M	555-123	555-129	John@mail.com	RU	Moscow	Moscow	103009	Kremlin Rd. 1
-1	-1	Doe	John	M	555-123	555-129	John@mail.com	RU	Moscow	Moscow	103009	Kremlin Rd. 1
15000.00	25000.00	Lincoln	Abraham		020-3456	020-3459	abe@mail.com	US	Maryland	Rockville	20852	1 Rockville Pk.
15000.00	25000.00	Lincoln	Abraham		020-3456	020-3459	abe@mail.com	US	Maryland	Rockville	20852	1 Rockville Pk.

- Variables for general information and information about included studies
- Variables for site information
- Variables for characteristics and outcomes by study, site and treatment arm

SUBMITTING IN eCTD FORMAT

The clinical site dataset should be submitted in SAS transport file format with the name **clinsite.xpt**. An additional **define.pdf** should also be provided.
The files should be included in Module 5 – Clinical Study Reports:



REFERENCES

FDA Guidance Documents:

http://www.fda.gov/downloads/drugs/developmentapprovalprocess/formssubmissionrequirements/ucm332468.pdf

http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ucm332466.pdf

CONTACT INFORMATION

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