Standard for Exchange of Nonclinical Data Implementation Guide: Developmental and Reproductive Toxicology

Version 1.0

Prepared by the

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[redacted]

Notes to Readers

- This is the implementation guide for nonclinical Developmental and Reproductive Toxicology study data and is based upon Version 1.6 of the CDISC Study Data Tabulation Model (SDTM).
- This document should be used in conjunction with Version 3.1 of the CDISC Standard for Exchange of Nonclinical Data (SEND) and Domain Models. It includes proposed enhancements for Developmental and Reproductive Toxicology (DART) data submission. The information here will remain as a separate document and will not be integrated into a later version of the SEND Implementation Guide.

Revision History

Date	Version	Summary of Changes
tbd	1.0 Final	Final version per SDTM v1.6
2016-08-01	1.0 Provisional	Provisional version reflecting changes and corrections identified during review period
2015-07-07	1.0 Draft	Initial draft for public review

Please see Appendix F for Representations and Warranties, Limitations of Liability, and Disclaimers.

CONTENTS

1 Introduction

1.1 Purpose

This Implementation Guide (IG) defines recommended standards for the submission of data from nonclinical Developmental and Reproductive Toxicology (DART) studies, and is referred to as the SENDIG-DART. This IG is based on and should be used in close concert with Version 3.1 of the Standard for Exchange of Nonclinical Data Implementation Guide (SENDIG) and Version 1.6 of the CDISC Study Data Tabulation Model (SDTM), available at www.cdisc.org. Individuals responsible for the structure and format of SEND datasets should read and have a comprehensive understanding of the concepts and principles in the SDTM and SENDIG documents prior to reading the SENDIG-DART.

The SENDIG-DART provides specific concepts, domain models, assumptions, business rules, and examples for preparing standard tabulation of DART study data. This includes DART-specific endpoints and the use of new variables for existing domains not previously included or demonstrated in the SENDIG.

Principles in this document are specialized and relevant to the individuals in organizations that perform DART studies and submit DART study data to a regulatory authority such as the US Food and Drug Administration (FDA). The assessment of nonclinical developmental and reproductive toxicity is guided by the International Conference on Harmonization (ICH) S5(R2) document (available at http://www.ich.org/products/guidelines/safety/article/safety-guidelines.html).

Version 1.0 of this document is intended to support the creation of domain datasets for Embryo-Fetal Development (EFD) study data. Subsequent versions of the SENDIG-DART will introduce additional DART concepts and study types (e.g., Fertility, Postnatal Development and Multi-generational).

This document does not contain all of the domains necessary for data providers to implement CDISC SEND-based standards for DART studies. Specifically, this document does not discuss existing domains that may be common to both DART and general toxicology studies (e.g., Exposure). Such domains are found in the SENDIG (available for download at http://www.cdisc.org/send). In addition, not all domains defined in the SENDIG-DART are required; data providers should ensure the domains represent the data necessary to address the appropriate scientific and regulatory needs.

The terminologies used in some examples are for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should refer to the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

1.2 Organization of this Document

This document is organized into the following sections:

- Section 1, Introduction, includes the overall purpose of the document
- Section 2, SDTM-Based Domains, provides an overview of the domains and endpoints
- Section 3, Assumptions for Domain Models, introduces Reproductive Phase and timing variables
- Section 4, Special-Purpose Domains, describes implementation recommendations for the special-purpose domains
- Section 5, Findings Domains, describes implementation recommendations for the findings domains
- Section 6, Trial Design, introduces and provides implementation recommendations for Trial Design domains
- Section 7, Changes to Existing Domains, describes effects on existing SEND domains submitted for DART studies
- Appendices provide additional background material and other supplemental material relevant to implementation

1.3 Relationships to Other Documents

This document should be used in conjunction with the SENDIG v3.1 and SDTM v1.6. A single complete submission for a DART study would typically include domains from the SENDIG together with domains introduced in the SENDIG-DART (see Section 2.2). Variables from SDTM v1.6 can be added to all domains in a DART submission.

This document does not replace the foundational CDISC standards or their implementation guides. The user should read those standards and implementation guides before applying the advice in this document. Domains not explicitly represented within this document can still be used according to the rules of those domains as needed. Refer to the current SENDIG (available at http://www.cdisc.org/send) for implementation examples using those domains.

1.4 How to Read this Implementation Guide

The SENDIG-DART is best read online so the reader can benefit from the hyperlinks to both internal and external references.

The following guidelines may be helpful in reading this document.

1. First, read the SDTM and SENDIG to gain a general understanding of the concepts used in this document.
2. Next, read Section 1 and Section 2 of this document for the overall purpose and coverage of domains. Refer to the Glossary in Appendix B as necessary.
3. Read the Assumptions for Domain Models in Section 3 relevant to Reproductive Phases.
4. Read Section 6 to understand the fundamentals of Trial Repro Stages, Trial Repro Paths and Repro Phases and consider how to apply the concepts.
5. Read Section 4 and Section 5 in detail for the new domains introduced in the SENDIG-DART. Note: The implementation examples for each domain help to provide an understanding of how to apply the domain models for specific types of data.
6. Review Section 7 for examples of changes to existing SEND domains.
7. Review applicable SEND CDISC Controlled Terminology (CT) (available at http://www.cancer.gov/research/resources/terminology/cdisc).
8. Review the Appendices as appropriate for information about new variables and study design diagrams.

1.5 Known Issues

The RPRFDY variable may have values of 0 or 1 (see RPRFDY in the Trial Repro Paths domain, Section 6.3.1) per timing conventions for Reproductive Toxicology studies in ICH Guidelines. This flexibility for a single variable may be reevaluated in a subsequent version of the SENDIG-DART.

1.6 Submitting Comments

Comments on this document can be submitted through the CDISC Discussion Forum (http://www.cdisc.org/forum).

2 SDTM-Based Domains

2.1 Domains and their Observation Classes

Table 2.1 is an overview of the domains introduced in this document.

Table 2.1 Domains Introduced in this Document

Domain Code	Domain	Domain Class	Description
*TP	Trial Repro Paths	Trial Design	Provides the complete planned sequence of Repro Stages within each Repro Path.
*TT	Trial Repro Stages	Trial Design	Descriptions of, and rules for, the start and end of planned blocks of time known as Repro Stages (e.g., Gestation 15Day, Gestation 28Day).
*SJ	Subject Repro Stages	Special-Purpose	Actual subject-level periods of time known as Repro Stages that a subject experiences (e.g., Premating1, Pairing1, Gestation_20D).
IC	Implantation Classification	Findings	Individual implantation classifications for the C-section component of DART studies.
PY	Nonclinical Pregnancy Results	Findings	Pregnancy results for female subjects, determined via a C-section.
FX	Fetal Pathology Findings	Findings	Individual findings for fetal pathology examinations.
FM	Fetal Measurements	Findings	Individual fetal weights and measurements, and fetal characteristics (e.g., Fetal Sex).

** Required domain*

2.2 SENDIG vs. SENDIG-DART Domain Data

2.2.1 Embryo-Fetal Development Study (EFD)

In a typical EFD toxicity study, females are bred pre-study. The start of Gestation is the female's confirmed mating date. Study design typically includes pre-treatment and/or post-treatment periods. The treatment period typically occurs during the implanted embryo's major organogenesis period. The duration of treatment varies between species.

The following endpoints and respective domains have been identified for EFD toxicity studies:

- Maternal toxicity (BW, BG, FW, CL, PC, PP, DD, DS)
- Pregnancy status, number of implantations, and corpora lutea counts (PY)
- Individual implantation viability (IC).
- Fetal examinations (FX) and measurements (FM).
- Organ weights, including gravid and non-gravid uterine weights (OM).
- Macroscopic examinations (MA).
- Any other findings data would be submitted in a SENDIG domain with SDTM v1.6 Repro Phase timing variables, as appropriate.

Table 2.2.1 is an overview of the combination of domains defined in the SENDIG and SENDIG-DART that may be submitted for an EFD study, depending on the study protocol.

Table 2.2.1 Example Domains for an Embryo-Fetal Development Study

SENDIG Domains	SENDIG-DART Domains
Trial Design	
TS - Trial Summary	TP - Trial Repro Paths
TA - Trial Arms	TT - Trial Repro Stages
TE - Trial Elements	
TX – Trial Sets	
Special-Purpose	
DM - Demographics	SJ - Subject Repro Stages
SE - Subject Elements	

SENDIG Domains	SENDIG-DART Domains
Interventions, Events, Findings	
EX - Exposure	PY - Nonclinical Pregnancy Results
BW - Body Weights	IC - Implantation Classification
BG - Body Weight Gain	FX - Fetal Pathology Findings
FW - Food and Water Consumption	FM - Fetal Measurements
CL - Clinical Observations	
PC - Pharmacokinetics Concentrations	
PP - Pharmacokinetics Parameters	
DS - Disposition	
DD - Death Diagnosis	
MA - Macroscopic Observations	
OM - Organ Measurements	

3 Assumptions for Domain Models

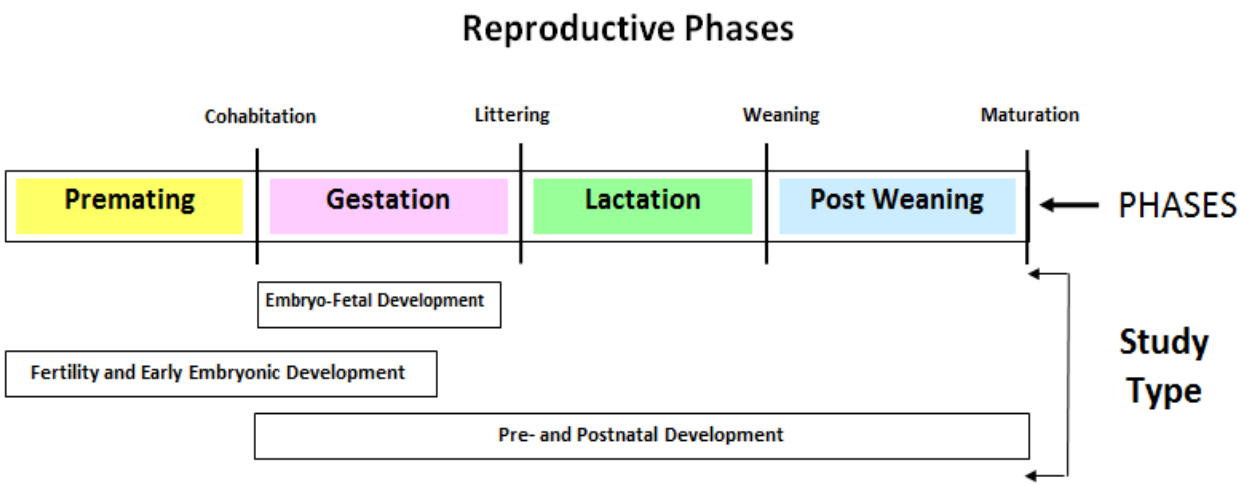
3.1 Reproductive Phase (Repro Phase)

A Repro Phase (also referred to as "Phase" in this document) is a component of the DART Trial Design (Section 6) that serves a purpose in the study as a whole. Examples of a Repro Phase include Premating, Gestation, and Lactation. The Repro Phases in a study are defined by the RPHASE variable in the Trial Repro Paths (TP) domain (Section 6.3).

Assessments are scheduled and data analyzed relative to the Repro Phase day rather than relative to the start of treatment (or RFSTDTC). Epochs or Elements (defined in the SENDIG available at http://www.cdisc.org/send) can span multiple Phases, therefore Repro Phase day timing variables are used to provide the planned and/or actual day within a Phase in domains for DART studies.

Figure 3.1 below illustrates a high-level overview of the relationship between reproductive study types and Phases. The start and end of the treatment period depends on the study type and is not illustrated in this diagram.

Figure 3.1 Reproductive Phases Example



3.2 Assumptions for Repro Phase Day Timing Variables

1. Timing variables introduced in SDTM v1.6 for the SENDIG-DART define the planned and actual days within a Repro Phase (RPHASE) in subject-level domains.
2. RPDY is the actual day number from the beginning of a Repro Phase. Phases are associated with the planned and actual reporting intervals.
3. Phase days may begin with 0 or 1. The Repro Phase Start Reference Day (RPRFDY) variable, defined in the Trial Repro Paths (TP) domain (Section 6.3.1) indicates which day number is used for the start of the Phase. Data providers should refer to scientific conventions to designate the RPRFDY.
4. Repro Phase timing variables can only be included if TP and TT domains are provided. The TP domain defines the Repro Phases along the Repro Path and the TT domain defines Repro Stages within the Phases along the Path. The SJ (Subject Repro Stages) domain provides the actual Stages individual subjects experienced within each Phase. See the TP and TT (Sections 6.3 and 6.2, respectively), and SJ (Section 4.1) domains for examples on Trial Design and the SJ special-purpose domain.
5. Each Repro Phase contains at least one Repro Stage. The start and end date of each Stage for a subject is the Start Date/Time of Stage (SJSTDTC) variable in the SJ domain. If there are multiple Stages within a Phase, the actual start date of a Phase is anchored in SJSTDTC for the first Stage in the Phase. For

example, if there are three Stages (A (early), B (mid), and C (late)) on a Path within a Phase (e.g., Gestation), then the reference start date of the Gestation Phase is the SJSTDTC for Stage A (early).

6. Typically there is only one Stage on a Path within a Phase; however, the model can accommodate multiple Stages within a Phase. For example, 'Prior to Cohabitation' and during 'Cohabitation' (prior to confirmation of mating) in a fertility study could be considered as two stages within the Premating Phase.
7. The Planned Repro Phase Day (RPPLDY) can be used to group records allowing data that were planned to be collected on different phase days to be grouped. Planned assessments may be scheduled to occur over a range of phase days (i.e., grace days). In such cases, a single value for RPPLDY should be chosen.
8. The Core (permissibility) of each of the timing variables will be dependent on the domain. For existing domains, this is indicated in the 'Existing Domains Affected' table in Section 7.1. Repro Phase Day timing variables can be used in place of or in conjunction with Study Day (--DY) variables.

3.2.1 The Actual Repro Phase Day Calculation

--RPDY = (date portion of --DTC) - (date portion of SJSTDTC) + RPRFDY where --DTC is the actual observation date and SJSTDTC is the earliest stage start date for any given phase, and RPRFDY is the first Phase Day reference (0 or 1).

- This also applies to the --RPSTDY and --RPENDY.

3.2.2 The Planned Repro Phase Day Calculation

RPPLDY= planned event date - (date portion of SJSTDTC) + RPRFDY

- This should also apply to the RPPLSTDY and RPPLENDY.

3.2.3 Parallels for Study Day and Repro Phase Day Variables

Table 3.2.3 illustrates the Study Day variables in the SENDIG v3.1 on the left side, and the Phase Day timing variables introduced in the SENDIG-DART on the right. See Section 7.1 for Core (permissibility)

Table 3.2.3 Study Day vs. Repro Phase (RPHASE) Day per Domain Examples

	[1] Actual and Nominal Study Day Variables					[2] Planned and Actual Phase (RPHASE) Day Variables			
	Actual		Nominal			Planned		Actual	
Domain	--DY or --STDY	--ENDY	--NOMDY	--NOMLBL	(TP)	RPPLDY or RPPLSTDY	RPPLENDY	--RPDY or --RPSTDY	--RPENDY
EX	EXSTDY	EXENDY			RPRFDY	RPPLSTDY	RPPLENDY	EXRPSTDY	EXRPENDY
BW	BWDY		BWNOMDY	BWNOMLBL	RPRFDY	RPPLDY		BWRPDY	
BG	BGDY	BGENDY			RPRFDY	RPPLDY	RPPLENDY	BGRPDY	BGRPENDY
CL	CLDY	CLENDY	CLNOMDY	CLNOMLBL	RPRFDY	RPPLDY		CLRPDY	CLRPENDY
FW	FWDY	FWENDY			RPRFDY	RPPLDY	RPPLENDY	FWRPDY	FWRPENDY
LB	LBDY	LBENDY	LBNOMDY	LBNOMLBL	RPRFDY	RPPLDY	RPPLENDY	LBRPDY	LBRPENDY
PC	PCDY	PCENDY	PCNOMDY	PCNOMLBL	RPRFDY	RPPLDY	RPPLENDY	PCRPDY	PCRPENDY
PP			PPNOMDY	PPNOMLBL	RPRFDY	RPPLDY		PPRPDY	
DS	DSSTDY		DSNOMDY	DSNOMLBL	RPRFDY	RPPLSTDY		DSRPSTDY	
DD	DDDY				RPRFDY			DDRPDY	
MA	MADY				RPRFDY	RPPLDY		MARPDY	
OM	OMDY		OMNOMDY	OMNOMLBL	RPRFDY	RPPLDY		OMRPDY	
CO	CODY				RPRFDY			CORPDY	

[1] *Anchored by RFSTDTC (DM domain)*

[2] *Anchored by SJSTDTC (SJ domain)*

4 Special-Purpose Domains

4.1 Subject Repro Stages – SJ

SJ is a Special-Purpose domain. Stages in a reproductive study are planned blocks of time (i.e., developmental and reproductive segments) within a Repro Phase (RPHASE). The SJ domain contains the Trial Repro Stages (defined in the TT domain) that each subject actually experienced within a RPHASE which is defined in the TP domain. A subject's assignment to a Trial Repro Path (TP) is recorded in the RPATHCD in the Demographics (DM) domain.

4.1.1 Specification for Subject Repro Stages (SJ) Domain Model

sj.xpt, Subject Repro Stages - Special-Purpose. One record per actual Repro Stage per subject, Tabulation

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	SJ	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
SJSEQ	Sequence Number	Num		Identifier	Sequence number given to ensure uniqueness of subject records within a USUBJID within this domain in chronological order. May be any valid number.	Req
RSTGCD	Repro Stage Code	Char		Topic	RSTGCD (the companion to RSTAGE) is limited to 8 characters and does not have special character restrictions.	Req
RSTAGE	Description of Repro Stage	Char		Synonym Qualifier	Name of the Repro Stage. If RSTGCD has the value of UNPLAN, then RSTAGE should be null.	Perm
SJSTDTC	Start Date/Time of Repro Stage	Char	ISO 8601	Timing	Start date/time for a Reproductive Stage for each subject in ISO 8601 character format.	Req
SJENDTC	End Date/Time of Repro Stage	Char	ISO 8601	Timing	End date/time for a Reproductive Stage for each subject in ISO 8601 character format.	Exp
RPHASE	Repro Phase	Char	(NCDPHASE)	Timing	Name of the reproductive phase to which this Repro Stage of the Repro Path is associated. Defined in the TP domain. The RPHASE variable is required when any Repro Phase Day variable is used.	Req
SJUPDES	Description of Unplanned Repro Stage	Char		Synonym Qualifier	Description of what happened to the subject during an unplanned Repro Stage. Used only if RSTGCD has the value of UNPLAN.	Perm

(Parentheses indicate CDISC controlled terminology codelist)

4.1.2 Assumptions for Subject Repro Stages (SJ) Domain Model

1. The Subject Repro Stages domain allows the submission of data on each subject's actual timing and sequence of Repro Stages in a DART study. There are, by definition, no time gaps between Stages; therefore, the value of SJENDTC for one Stage will always be the same as the value of SJSTDTC for the next Stage.

2. Reference the Trial Repro Stages and Trial Repro Paths domains, as these define a study's planned Stages and describe the planned sequences of Stages for the Paths of the study.
3. For any subject, the dates in the SJ dataset are the dates when the transition events identified in the Trial Repro Stages table occurred.
4. If a Stage start or end date/time was not collected directly, the method used to infer the date/time should be explained in the Comments column of the define file.
5. If the subject's experience for a particular period of time cannot be represented with one of the planned Stages, then that period of time should be represented as an unplanned Stage.
6. The value of RSTGCD for an unplanned Stage is "UNPLAN" and SJUPDES should be populated with a description of the unplanned Stage. The RSTAGE value should be null in this case.
7. The values of SJSTDTC provide the chronological order of the actual subject Stages. SJSEQ should be assigned to be consistent with the chronological order of the Stages per subject. Note: The requirement that SJSEQ be consistent with chronological order is more stringent than in most other domains where --SEQ values need only be unique within subject.
8. RPHASE is required so that subjects are always assigned to a Phase, even when experiencing an unplanned Stage.

4.1.3 Examples for Subject Repro Stages (SJ) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1
EFD Toxicity and Toxicokinetic (TK) Study in Rabbits

Below is the Subject Repro Stages example followed by Subject Elements for the same study to illustrate SJ and SE. SE is defined in the SENDIG.
In this example, there is only one planned Stage per subject. Females are scheduled for sacrifice either on Gestation Day (GD) 16 or 28. Regardless of treatment Arms and Elements, the only planned Stages are Gestation for 28 days or 16 days.

Subject Stages (SJ) for subjects 0001, 0010, 0003, 0030: Each subject experiences one Stage. Subjects are in the Gestation Phase during all Trial Elements.

Rows 1, 3: Experienced Gestation for 28 days, from start of study to scheduled sacrifice C-section on GD 28.
Rows 2, 4: Experienced Gestation for 16 days, from start of study to scheduled sacrifice for TK sampling on GD 16.

sj.xpt

Row	STUDYID	DOMAIN	USUBJID	SJSEQ	RSTGCD	RSTAGE	SJSTDTC	SJENDTC	RPHASE
1	EFD111	SJ	EFD111-0001	1	GEST	Gestation28D	2007-03-01	2007-03-29T07:44	GESTATION
2	EFD111	SJ	EFD111-0010	1	GESTTK	Gestation16D	2007-03-01	2007-03-17T08:35	GESTATION
3	EFD111	SJ	EFD111-0003	1	GEST	Gestation28D	2007-03-01	2007-03-29T08:00	GESTATION
4	EFD111	SJ	EFD111-0030	1	GESTTK	Gestation16D	2007-03-01	2007-03-17:T08:05	GESTATION

"Treatment" related Subject Elements (SE) examples for subjects 001, 0010, 0003, 0030:

Rows 1-3: Subject 0001 experienced three Elements (Pre-treatment, Vehicle Control, Post-treatment).

Rows 4-5: Subject 0010 experienced two Elements (Pre-treatment, Vehicle Control).
Rows 6-8: Subject 0003 experienced three Elements (Pre-treatment, Treatment [X], Post-treatment).
Rows 9-10: Subject 0030 experienced two Elements (Pre-treatment, Treatment [X]).

se.xpt

Row	STUDYID	DOMAIN	USUBJID	SESEQ	ETCD	ELEMENT	SESTDTC	SEENDTC
1	EFD111	SE	EFD111-0001	1	PRETXT	Pre-treatment	2007-03-01T00:00	2007-03-07T08:01
2	EFD111	SE	EFD111-0001	2	CONTROL	Vehicle Control	2007-03-07T08:01	2007-03-21T08:40
3	EFD111	SE	EFD111-0001	3	POSTTXT	Post-treatment	2007-03-21T:08:40	2007-03-29T07:44
4	EFD111	SE	EFD111-0010	1	PRETXT	Pre-treatment	2007-03-01T00:00	2007-03-07T08:15
5	EFD111	SE	EFD111-0010	2	CONTROL	Vehicle Control	2007-03-07T08:15	2007-03-17T08:35
6	EFD111	SE	EFD111-0003	1	PRETXT	Pre-treatment	2007-03-01T00:00	2007-03-07T07:55
7	EFD111	SE	EFD111-0003	2	TXTMT_X	Treatment [X]	2007-03-07T07:55	2007-03-21T07:31
8	EFD111	SE	EFD111-0003	3	POSTTXT	Post-treatment	2007-03-21T07:31	2007-03-29T08:00
9	EFD111	SE	EFD111-0030	1	PRETXT	Pre-treatment	2007-03-01T00:00	2007-03-07T08:20
10	EFD111	SE	EFD111-0030	2	TXTMT_X	Treatment [X]	2007-03-07T08:20	2007-03-17T08:05

5 Findings Domains

5.1 Implantation Classification – IC

5.1.1 Specification for Implantation Classification (IC) Domain Model

ic.xpt, Implantation Classification – Findings. One record per implantation site per fetus per subject, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	IC	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
FETUSID	Unique Fetus Identifier	Char		Identifier	Identifier used to identify a fetus from a maternal subject for prenatal evaluations. Unique per USUBJID across a study.	Exp
ICSEQ	Sequence Number	Num		Identifier	Sequence number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
ICTESTCD	Test Short Name	Char	(ICTESTCD)	Topic	Short name of the measurement, test, or examination described in ICTEST. It can be used as a column name when converting a dataset from a vertical format to a horizontal format. The value in ICTESTCD cannot be longer than 8 characters, nor can it start with a number.	Req
ICTEST	Implantation Exam Name	Char	(ICTEST)	Synonym Qualifier	Long name for ICTESTCD (e.g., Implantation Site Characterization). The value in ICTEST cannot be longer than 40 characters.	Req
ICORRES	Result or Findings as Collected	Char		Result Qualifier	Implantation Classification finding or observation as originally received or collected.	Exp
ICSTRESC	Standardized Results in Character Format	Char	(ICFINDRS)	Result Qualifier	Contains the result value for all findings, copied or derived from ICORRES in a standard format. ICSTRESC should store all results or findings in character format.	Exp
ICIMPLBL	Implantation Site Label	Char		Record Qualifier	Label or identifier that describes the location or position of an implantation site in the uterus (or uterine horn). e.g., Sponsor 1: 1L, 2L, 3L, 1R, 2R e.g., Sponsor 2: 1L, 2L, 3L, 4R, 5R e.g., Sponsor 3: 1, 2, 3, 4, 5	Req
ICRESCAT	Result Category	Char	(ICRESCAT)	Variable Qualifier	Used to categorize the result of the finding (e.g., FETUS, RESORPTION, EMBRYO).	Exp
ICRESLOC	Result Location of Finding	Char		Result Qualifier	Location where the result was observed (as opposed to the location specified for examination), if collected. In IC this is the uterine horn location of the implantation site in species that have a Left and Right Uterine Horn. Should be populated if ICIMPLBL is not unique per horn.	Exp

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
ICSTAT	Completion Status	Char	(ND)	Record Qualifier	Used to indicate when a test or examination was not done or result is missing. Should be null if a result exists in ICORRES.	Perm
ICREASND	Reason Not Done	Char		Record Qualifier	Describes why ICSTAT is NOT DONE. Use only in conjunction with ICSTAT when value is NOT DONE.	Perm
ICSPEC	Specimen Material Type	Char	(SPEC)	Record Qualifier	Should always be the controlled term for Uterus when used.	Perm
RPHASE	Repro Phase	Char		Timing	Name of the reproductive phase associated with date/time of the observation.	Exp
RPPLDY	Planned Repro Phase Day of Observation	Num		Timing	Reproductive phase day the uterine examination was scheduled to occur, relative to RPRFDY in the TP domain. Should be an integer.	Exp
ICDTC	Date/Time	Char	ISO 8601	Timing	Collection date and time of the uterine examination represented in ISO 8601 character format.	Exp
ICDY	Study Day	Num		Timing	Study day of the uterine examination expressed in integer days relative to the protocol-defined RFSTDTC.	Perm
ICRPDY	Actual Repro Phase Day of Observation	Num		Timing	Reproductive phase day the uterine examination occurred, relative to SJSTDTC for the phase and the start value in RPRFDY (TP). Should be an integer.	Exp

(Parentheses indicate CDISC controlled terminology codelist)

5.1.2 Assumptions for Implantation Classification (IC) Domain Model

1. IC Definition
    a. The Implantation Classification domain is for capturing individual implantation results for pregnant females, if collected, in a C-section component of a DART study. This domain individually classifies the viability status of each implantation per site. By definition, each record represents an implantation site observed in utero.
    b. In most cases there should be one record per implantation site. In cases where two or more fetuses share the same implantation site, there should be one record per fetus, each uniquely identified by FETUSID.
    c. Implantation results on a litter (aggregate) basis should be submitted in the PY (Pregnancy Results) domain.
    d. This domain is not for capturing uterine contents collected as a general gross examination (MA domain) or litter based tabulation (PY domain). In cases where unscheduled deaths do not have individual implantation classifications collected, uterine contents may be collected as a gross observation in the MA domain or an aggregate basis to be tabulated by the test codes in the PY domain.
2. Subject / Implantation Identification:
    a. The subject of the observation (USUBJID) is the maternal subject. Female subjects confirmed as not pregnant at C-section should not be included in this domain.
    b. FETUSID is a unique embryo/fetus identifier that must be unique per subject within a study. It may be equivalent to the ICIMPLBL, but that is not an assumption. FETUSID should be populated for implantations that have individual fetal examinations or measurements that will be captured in other domains. The USUBJID / FETUSID combination is consistent across domains within a study.
    c. FETUSID can be null for implantations where no other findings are scheduled or collected (e.g., resorptions, fertility studies with scheduled mid-gestation C-sections).
3. Test Definition:

a. The ICTEST extensible controlled terminology value is Implantation Site Characterization. Fetal characteristics and measurements are captured in the FM domain. Fetal morphology findings are captured in the FX domain.

4. Results:
   a. Controlled terminology values for ICSTRESC are in the ICFINDRS CT list.
   b. ICIMPLBL is not considered a unique identification since multiple embryos/fetuses may share the same implantation site as in the case of twins. The ICIMPLBL must be populated for each result, i.e. for each implantation site. In the situation where the implantations were not evaluated (ICSTAT = NOT DONE) per protocol, the artificial label, ALL, is used to represent missing results (see Example 5).
   c. The ICRESCAT is a categorization of implantation classification results that is less granular than ICSTRESC.
5. Timing Variables:
   a. If not collected, ICDTC may be assigned as the date/time of C-section or the subject's disposition date/time (DSDTC).

5.1.3 Examples for Implantation Classification (IC) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1

This example represents implantation classifications for a female subject in a rodent EFD toxicology study.

Rows 1-8: Represent implantation classification results for implantation sites (ICIMPLBL) 1 through 8. The original result as collected is represented in ICORRES. SEND standardized results are represented in ICSTRESC and ICRESCAT.

Rows 9-10: Represent two fetuses that share the same implantation site (twins). There are two records for the ICIMPLBL value of 9, one per fetus (FETUSID). The original results collected "Twin, Dead" (Row 9) and "Twin, Alive" (Row 10) are standardized in ICSTRESC as Dead and Alive, respectively.

ic.xpt

Row	STUDYID	DOMAIN	USUBJID	FETUSID	ICSEQ	ICTESTCD	ICTEST	ICORRES	ICSTRESC
1	TST01	IC	TST01-014		1	IMPSCHCT	Implantation Site Characterization	Early Resorption	EARLY INTRAUTERINE DEATH
2	TST01	IC	TST01-014		2	IMPSCHCT	Implantation Site Characterization	Late Resorption	LATE INTRAUTERINE DEATH
3	TST01	IC	TST01-014	1	3	IMPSCHCT	Implantation Site Characterization	Alive	ALIVE
4	TST01	IC	TST01-014	2	4	IMPSCHCT	Implantation Site Characterization	Alive	ALIVE
5	TST01	IC	TST01-014		5	IMPSCHCT	Implantation Site Characterization	Early Resorption	EARLY INTRAUTERINE DEATH
6	TST01	IC	TST01-014	3	6	IMPSCHCT	Implantation Site Characterization	Dead	DEAD
7	TST01	IC	TST01-014	4	7	IMPSCHCT	Implantation Site Characterization	Alive	ALIVE
8	TST01	IC	TST01-014	5	8	IMPSCHCT	Implantation Site Characterization	Alive	ALIVE
9	TST01	IC	TST01-014	6	9	IMPSCHCT	Implantation Site Characterization	Twin, Dead	DEAD
10	TST01	IC	TST01-014	7	10	IMPSCHCT	Implantation Site Characterization	Twin, Alive	ALIVE

Row	ICIMPLBL	ICRESCAT	ICRESLOC	ICSPEC	RPHASE	RPPLDY	ICDTC	ICDY	ICRPDY
1 (cont)	1	RESORPTION	Left Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
2 (cont)	2	RESORPTION	Left Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
3 (cont)	3	FETUS	Left Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20

Row	ICIMPLBL	ICRESCAT	ICRESLOC	ICSPEC	RPHASE	RPPLDY	ICDTC	ICDY	ICRPDY
4 (cont)	4	FETUS	Left Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
5 (cont)	5	RESORPTION	Left Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
6 (cont)	6	FETUS	Right Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
7 (cont)	7	FETUS	Right Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
8 (cont)	8	FETUS	Right Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
9 (cont)	9	FETUS	Right Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20
10 (cont)	9	FETUS	Right Horn	UTERUS	GESTATION	20	2004-12-08T08:03	21	20

Example 2

This example represents implantation classifications for a female subject in a rabbit EFD toxicology study.

- Each implantation site (ICIMPLBL) was given a sequential identification number in either the left or the right uterine horn. The number started with 1 in each horn as opposed to Example 1 which continued sequentially from left to right. In this case, the sponsor includes L (left) or R (right) as part of the ICIMPLBL value to distinguish left from right. The uterine horn location is represented in the ICRESLOC variable as collected.
- FETUSIDs were only given to implantations with an ICRESCAT value of Fetus.

ic.xpt

Row	STUDYID	DOMAIN	USUBJID	ICSEQ	FETUSID	ICTESTCD	ICTEST	ICORRES	ICSTRESC
1	TST02	IC	TST02-2200	1	1	IMPSCHCT	Implantation Site Characterization	Alive	ALIVE
2	TST02	IC	TST02-2200	2	2	IMPSCHCT	Implantation Site Characterization	Dead	DEAD
3	TST02	IC	TST02-2200	3		IMPSCHCT	Implantation Site Characterization	Early Resorption	EARLY INTRAUTERINE DEATH
4	TST02	IC	TST02-2200	4		IMPSCHCT	Implantation Site Characterization	Late Resorption	LATE INTRAUTERINE DEATH
5	TST02	IC	TST02-2200	5	3	IMPSCHCT	Implantation Site Characterization	Alive	ALIVE
6	TST02	IC	TST02-2200	6	4	IMPSCHCT	Implantation Site Characterization	Dead	DEAD
7	TST02	IC	TST02-2200	7	5	IMPSCHCT	Implantation Site Characterization	Alive	ALIVE
8	TST02	IC	TST02-2200	8		IMPSCHCT	Implantation Site Characterization	Early Resorption	EARLY INTRAUTERINE DEATH

Row	ICIMPLBL	ICRESCAT	ICRESLOC	ICSPEC	RPHASE	RPPLDY	ICDTC	ICDY	ICRPDY
1 (cont)	1L	FETUS	LEFT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27
2 (cont)	2L	FETUS	LEFT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27
3 (cont)	3L	RESORPTION	LEFT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27
4 (cont)	4L	RESORPTION	LEFT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27
5 (cont)	1R	FETUS	RIGHT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27
6 (cont)	2R	FETUS	RIGHT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27
7 (cont)	3R	FETUS	RIGHT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27
8 (cont)	4R	RESORPTION	RIGHT	UTERUS	GESTATION	27	2007-04-08T09:15	28	27

Example 3

This example represents implantation classification data for a subject with a scheduled end-of-gestation C-section.

Rows 1-9: Represent implantation results for Subject 1000. The Early or Late Intrauterine Deaths (Rows 3 and 6) were categorized in ICRESCAT as Resorptions. The Empty Implantation Site finding (Row 5) does not have a value for ICRESCAT. FETUSID was recorded only for results categorized as Fetus in ICRESCAT.

Two fetuses in Rows 8, 9 that share the same implantation site in the left uterine horn were labeled (ICIMPLBL) as 8 and 8a. Each fetus was assigned a different FETUSID.

Rows 10-13: Subject 1001 was found dead. The female was C-sectioned and all implantations were collected as intrauterine deaths. There were no recorded observations as to timing (early, late, at term) of the implant deaths to indicate category, therefore ICRESCAT is null.

ic.xpt

Row	STUDYID	DOMAIN	USUBJID	FETUSID	ICSEQ	ICTESTCD	ICTEST	ICORRES	ICSTRESC
1	TST04	IC	TST04-1000	1	1	IMPSCHCT	Implantation Site Characterization	Live Fetus	ALIVE
2	TST04	IC	TST04-1000	2	2	IMPSCHCT	Implantation Site Characterization	Live Fetus	ALIVE
3	TST04	IC	TST04-1000		3	IMPSCHCT	Implantation Site Characterization	Early Intrauterine Death	EARLY INTRAUTERINE DEATH
4	TST04	IC	TST04-1000	4	4	IMPSCHCT	Implantation Site Characterization	Live Fetus	ALIVE
5	TST04	IC	TST04-1000		5	IMPSCHCT	Implantation Site Characterization	Empty Implantation Site	EMPTY IMPLANTATION SITE
6	TST04	IC	TST04-1000		6	IMPSCHCT	Implantation Site Characterization	Late Intrauterine Death	LATE INTRAUTERINE DEATH
7	TST04	IC	TST04-1000	7	7	IMPSCHCT	Implantation Site Characterization	Dead Fetus	DEAD
8	TST04	IC	TST04-1000	8	8	IMPSCHCT	Implantation Site Characterization	Live Twin (L8 and L9)	ALIVE
9	TST04	IC	TST04-1000	9	9	IMPSCHCT	Implantation Site Characterization	Live Twin (L8 and L9)	ALIVE
10	TST04	IC	TST04-1001		10	IMPSCHCT	Implantation Site Characterization	Intrauterine Death	INTRAUTERINE DEATH
11	TST04	IC	TST04-1001		11	IMPSCHCT	Implantation Site Characterization	Intrauterine Death	INTRAUTERINE DEATH
12	TST04	IC	TST04-1001		12	IMPSCHCT	Implantation Site Characterization	Intrauterine Death	INTRAUTERINE DEATH
13	TST04	IC	TST04-1001		13	IMPSCHCT	Implantation Site Characterization	Intrauterine Death	INTRAUTERINE DEATH

Row	ICIMPLBL	ICRESCAT	ICRESLOC	ICSPEC	RPHASE	RPPLDY	ICDTC	ICDY	ICRPDY
1 (cont)	1	FETUS	Right	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
2 (cont)	2	FETUS	Right	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
3 (cont)	3	RESORPTION	Right	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
4 (cont)	4	FETUS	Right	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
5 (cont)	5		Right	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
6 (cont)	6	RESORPTION	Right	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
7 (cont)	7	FETUS	Left	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
8 (cont)	8	FETUS	Left	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
9 (cont)	8a	FETUS	Left	UTERUS	GESTATION	20	2008-09-28T08:30	21	20
10 (cont)	1		Right	UTERUS	GESTATION	20	2008-09-20T08:50	21	20
11 (cont)	2		Right	UTERUS	GESTATION	20	2008-09-20T08:50	21	20
12 (cont)	3		Right	UTERUS	GESTATION	20	2008-09-20T08:50	21	20
13 (cont)	4		Right	UTERUS	GESTATION	20	2008-09-20T08:50	21	20

Example 4

This example shows implantation classifications for a female subject in a rat fertility study with a mid-term gestation C-section.

- Since the embryos are not fully developed mid-term, their implantation classification is being assessed for the particular stage of gestation. Each implantation site was characterized either as a Normally Developing Implant or an Early Resorption. SEND Standardized results are captured in ICSTRESC and ICRESCAT.
- In this case, the sponsor does not record a FETUSID and there were no other individual embryo / fetal findings collected in the study. Since FETUSID is an expected variable, the column is included in the structure of the dataset, but the values are null.

ic.xpt

Row	STUDYID	DOMAIN	USUBJID	FETUSID	ICSEQ	ICTESTCD	ICTEST	ICORRES
1	TST03	IC	TST03-1023		1	IMPSCHCT	Implantation Site Characterization	Normally Developing Implant
2	TST03	IC	TST03-1023		2	IMPSCHCT	Implantation Site Characterization	Normally Developing Implant
3	TST03	IC	TST03-1023		3	IMPSCHCT	Implantation Site Characterization	Early Resorption
4	TST03	IC	TST03-1023		4	IMPSCHCT	Implantation Site Characterization	Normally Developing Implant
5	TST03	IC	TST03-1023		5	IMPSCHCT	Implantation Site Characterization	Early Resorption
6	TST03	IC	TST03-1023		6	IMPSCHCT	Implantation Site Characterization	Early Resorption
7	TST03	IC	TST03-1023		7	IMPSCHCT	Implantation Site Characterization	Early Resorption

Row	ICSTRESC	ICIMPLBL	ICRESLOC	ICRESCAT	ICSPEC	RPHASE	RPPLDY	ICDTC	ICDY	ICRPDY
1 (cont)	ALIVE	1	LEFT	EMBRYO	UTERUS	GESTATION	15	2008-02-15T07:45	16	15
2 (cont)	ALIVE	2	LEFT	EMBRYO	UTERUS	GESTATION	15	2008-02-15T07:45	16	15
3 (cont)	EARLY INTRAUTERINE DEATH	3	LEFT	RESORPTION	UTERUS	GESTATION	15	2008-02-15T07:45	16	15
4 (cont)	ALIVE	4	LEFT	EMBRYO	UTERUS	GESTATION	15	2008-02-15T07:45	16	15
5 (cont)	EARLY INTRAUTERINE DEATH	5	RIGHT	RESORPTION	UTERUS	GESTATION	15	2008-02-15T07:45	16	15
6 (cont)	EARLY INTRAUTERINE DEATH	6	RIGHT	RESORPTION	UTERUS	GESTATION	15	2008-02-15T07:45	16	15
7 (cont)	EARLY INTRAUTERINE DEATH	7	RIGHT	RESORPTION	UTERUS	GESTATION	15	2008-02-15T07:45	16	15

Example 5

This example shows a record for a dam that was scheduled to have a uterine examination per the data provider's protocol, but the implantation sites were inadvertently not recorded after the dam was confirmed pregnant via C-section. To indicate that it applies to the entire uterus, this record is given an Implantation Site Label (ICIMPLBL) value of 'ALL'.

ic.xpt

Row	STUDYID	DOMAIN	USUBJID	FETUSID	ICSEQ	ICTESTCD	ICTEST	ICORRES	ICSTRESC	ICIMPLBL	ICSTAT
1	TST05	IC	TST05-015		1	IMPSCHCT	Implantation Site Characterization			ALL	NOT DONE

Row	ICREASND	ICRESCAT	ICRESLOC	ICSPEC	RPHASE	RPPLDY	ICDTC	ICDY	ICRPDY
1 (cont)	Results not recorded			UTERUS	GESTATION	20	2009-05-14T10:05	21	20

5.2 Nonclinical Pregnancy Results – PY

5.2.1 Specification for Nonclinical Pregnancy Results (PY) Domain Model

py.xpt, Nonclinical Pregnancy Results — Findings. One record per test per subject per finding, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	PY	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
PYSEQ	Sequence Number	Num		Identifier	Sequence number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
PYTESTCD	Test Short Name	Char	(PYTESTCD)	Topic	Short name of the measurement, test, or examination described in PYTEST. The value in PYTESTCD cannot be longer than 8 characters, nor can it start with a number. PYTESTCD cannot contain characters other than letters, numbers, or underscores.	Req
PYTEST	Pregnancy Result Test Name	Char	(PYTEST)	Synonym Qualifier	Long name for PYTESTCD. The value in PYTEST cannot be longer than 40 characters. Examples: Pregnancy Status, Corpora Lutea Count, Postimplantation Loss, Number of Implantations.	Req
PYORRES	Result or Findings as Collected	Char		Result Qualifier	Result of the measurement or finding as originally received or collected.	Exp
PYORRESU	Unit of the Original Result	Char	(UNIT)	Variable Qualifier	The unit of the original result if applicable for a numeric result. The unit of the original result should be mapped to a synonymous unit on the Controlled Terminology list.	Exp
PYSTRESC	Standardized Results in Character Format	Char	(PYFINDRS)	Result Qualifier	Contains the result value for all findings, copied or derived from PYORRES in a standard format or in standard units. PYSTRESC should store all results or findings in character format; if results are numeric, they should also be stored in numeric format in PYSTRESN. When PYTESTCD is PREGSTAT, PYSTRESC must use the controlled terminology list for PYSTRESC.	Exp
PYSTRESN	Standardized Results in Numeric Format	Num		Result Qualifier	Used for continuous or numeric results or findings in standard format; copied in numeric format from PYSTRESC. PYSTRESN should store all numeric test results or findings.	Exp
PYSTRESU	Unit of the Standardized Result	Char	(UNIT)	Variable Qualifier	Standardized unit used for PYSTRESC and PYSTRESN	Exp
PYRESCAT	Result Category	Char	(PYRESCAT)	Variable Qualifier	Used to categorize the result when PYTEST is Pregnancy Status.	Exp
PYRESLOC	Result Location of Finding	Char		Result Qualifier	Location where the result was observed, if collected. Examples: Left Uterine Horn, Right Uterine Horn if the test is Number of Implantations.	Perm
PYSTAT	Completion Status	Char	(ND)	Record Qualifier	Used to indicate when a test or examination was not done or a result is missing. Should be null if a result exists in PYORRES.	Perm

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
PYREASND	Reason Not Done	Char		Record Qualifier	Describes why PYSTAT is NOT DONE. Use only in conjunction with PYSTAT when value is NOT DONE.	Perm
PYMETHOD	Method of Test or Examination	Char		Record Qualifier	Method of test or examination. Example: Ammonium Sulfide Stain	Perm
PYEXCLFL	Exclusion Flag	Char	(NY)	Record Qualifier	Y if the result should be excluded from all calculations, otherwise null. PYEXCLFL should not be used when PYSTAT is NOT DONE.	Perm
PYREASEX	Reason for Exclusion	Char		Record Qualifier	The reason the result should be excluded from all calculations. Used in conjunction with PYEXCLFL when its value is Y.	Perm
RPHASE	Repro Phase	Char		Timing	Name of the reproductive phase associated with date/time of the observation.	Exp
RPPLDY	Planned Repro Phase Day	Num		Timing	Reproductive phase day the observation was scheduled to occur, relative to RPRFDY in the TP domain. Should be an integer.	Exp
PYDTC	Date/Time	Char	ISO 8601	Timing	Collection date and time of the observation represented in ISO 8601 character format.	Exp
PYDY	Study Day	Num		Timing	Study day of the observation expressed in integer days relative to the protocol-defined RFSTDTC.	Perm
PYRPDY	Actual Repro Phase Day	Num		Timing	Reproductive phase day the observation occurred, relative to SJSTDTC for the phase and the start value in RPRFDY (TP). Should be an integer.	Exp

(Parentheses indicate CDISC controlled terminology codelist)

5.2.2 Assumptions for Nonclinical Pregnancy Results (PY) Domain Model

1. This domain captures pregnancy results for female subjects, collected or derived by the system, during C-section and parturition (i.e., birthing, delivery) in DART studies.
2. In studies with scheduled prenatal C-sections, there is typically a uterine examination to confirm pregnancy and observe implantation sites (e.g., Number of Implantations), as well as, an observation of the ovaries to count the number of corpora lutea (e.g., Corpora Lutea Count).
3. In PY the tabulated data are maternal subject (litter) based. Litter based results may represent individual implantation or fetus data captured in other domains (e.g., IC, FM).
4. PYORRES for the Pregnancy Status test can contain information collected that describes the pregnancy. When PYTEST is Pregnancy Status, SEND CT lists PYFINDRS (for PYSTRESC) and PYRESCAT exist. The other tests in this domain are typically litter based tabulations that are numeric.
5. Disposition data are captured in DS and DD domains. Terms in the PYFINDRS CT list do not include disposition or timing of disposition descriptors as part of the standardized result. If disposition descriptors (e.g., died early or found dead GD 12) are collected or provided with the result (e.g., Pregnant, died early) that information would exist in PYORRES.
6. The PYFINDRS and/or PYRESCAT term of UNDETERMINED should only be used if there was an examination and a result was collected. If there is a record for a subject that was not examined per protocol, PYSTAT should be NOT DONE, PYREASND should be provided, and PYORRES, PYSTRESC, and PYRESCAT should be null.
7. When the Corpora Lutea Count is recorded separate for each ovary there should be a record for each location (PYRESLOC). If PYRESLOC is null or not in the dataset, this is assumed to be a total count from both ovaries. This also applies to recording results separate for the left and right uterine horn vs. the total uterine count (e.g., Number of Implantations, Number of Resorptions, etc.).
8. In a study with scheduled C-sections at final disposition, PYDTC (if not collected) may be assigned as the date/time of C-section or the subject's disposition date/time (DSDTC).

5.2.3 Examples for Nonclinical Pregnancy Results (PY) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1
This example represents pregnancy results for a female subject in a rabbit EFD toxicology study.

Rows 1-10: Represent C-section results for a female subject that experienced a normal pregnancy. The results for Rows 2 and 3 are null, with a PYSTAT = NOT DONE with the reason indicated in PYREASND.

Row 11: Represents a female scheduled for C-section that was confirmed not pregnant at C-section. Since the subject was not pregnant, this female has no other test records in this domain.

Row 12: Represents a female scheduled for TK sampling on GD 16; however, a grace period of GD 15 or 16 is specified in the protocol. The female was actually terminated for TK on GD 15. As per protocol for TK females, only pregnancy status was collected at C-section. There was no further examination. RPPLDY is 16 (for protocol plan of GD 15-16) and PYRPDY is 15.

Row 13: Represents a female scheduled for C-section on GD 28, but was found dead on GD 12. As per protocol for females found dead or sacrificed, only pregnancy status was collected at C-section. Gross examination of abdominal viscera was performed and captured in the MA domain. Found dead was collected as part of the pregnancy status in PYORRES. RPPLDY is 28 and PYRPDY is 12.

py.xpt

Row	STUDYID	DOMAIN	USUBJID	PYSEQ	PYTESTCD	PYTEST	PYORRES	PYORRESU	PYSTRESC
1	999333	PY	99933375	1	PREGSTAT	Pregnancy Status	Normal Pregnancy		PREGNANT
2	999333	PY	99933375	2	CRPLUTCT	Corpora Lutea Count			
3	999333	PY	99933375	3	PREIMLSS	Pre-implantation Loss			
4	999333	PY	99933375	4	PSTIMLSS	Postimplantation Loss	17	%	17
5	999333	PY	99933375	5	IMPLANTS	Number of Implantations	6		6
6	999333	PY	99933375	6	FETUSLIV	Number of Live Fetuses	5		5
7	999333	PY	99933375	7	FETUSDEA	Number of Dead Fetuses	0		0
8	999333	PY	99933375	8	RESORPCT	Number of Resorptions	1		1
9	999333	PY	99933375	9	FWAVGLF	Average Female Live Fetal Weight	35.40	g	35.4
10	999333	PY	99933375	10	FWAVGLM	Average Male Live Fetal Weight	35.34	g	35.34
11	999333	PY	99933376	11	PREGSTAT	Pregnancy Status	Not Pregnant		NOT PREGNANT
12	999333	PY	99933377	12	PREGSTAT	Pregnancy Status	Pregnant TK Sacrifice		PREGNANT
13	999333	PY	99933378	13	PREGSTAT	Pregnancy Status	Pregnant Found Dead		PREGNANT

Row	PYSTRESN	PYSTRESU	PYRESCAT	PYSTAT	PYREASND	RPHASE	RPPLDY	PYDTC	PYRPDY
1 (cont)			PREGNANT			GESTATION	28	2010-05-12T08:25:10	28
2 (cont)				NOT DONE	Loss of tissue definition	GESTATION	28	2010-05-12T08:25:10	28
3 (cont)				NOT DONE	Corpora Lutea unable to be counted	GESTATION	28	2010-05-12T08:25:10	28
4 (cont)	17	%				GESTATION	28	2010-05-12T08:25:10	28
5 (cont)	6					GESTATION	28	2010-05-12T08:25:10	28
6 (cont)	5					GESTATION	28	2010-05-12T08:25:10	28
7 (cont)	0					GESTATION	28	2010-05-12T08:25:10	28

Row	PYSTRESN	PYSTRESU	PYRESCAT	PYSTAT	PYREASND	RPHASE	RPPLDY	PYDTC	PYRPDY
8 (cont)	1					GESTATION	28	2010-05-12T08:25:10	28
9 (cont)	35.4	g				GESTATION	28	2010-05-12T08:25:10	28
10 (cont)	35.34	g				GESTATION	28	2010-05-12T08:25:10	28
11 (cont)			NOT PREGNANT			GESTATION	28	2010-05-12T08:45:10	28
12 (cont)			PREGNANT			GESTATION	16	2010-04-30T13:20:05	15
13 (cont)			PREGNANT			GESTATION	28	2010-04-26T09:10:05	12

Example 2

Rows 1-12: Represent a female that upon uterine examination had a litter that was all resorptions (PYSTRESC). The data provider captured this in PYORRES as part of the pregnancy status result. Row 9 shows the fetal sex ratio is null with PYSTAT = NOT DONE and PYREASND = No fetuses was recorded.

Row 13: Represents a female that aborted and was subsequently euthanized (PYORRES). Aborted is the standardized result in PYSTRESC and is categorized as Pregnant in PYRESCAT.

Row 14: Represents a mated female that was confirmed not pregnant at C-section.

py.xpt

Row	STUDYID	DOMAIN	USUBJID	PYSEQ	PYTESTCD	PYTEST	PYORRES	PYORRESU	PYSTRESC
1	99861	PY	99861-23	1	PREGSTAT	Pregnancy Status	Pregnant - All Resorptions		RESORBED OR DEAD LITTER
2	99861	PY	99861-23	2	CRPLUTCT	Corpora Lutea Count	6		6
3	99861	PY	99861-23	3	PREIMLSS	Pre-implantation Loss	17	%	17
4	99861	PY	99861-23	4	PSTIMLSS	Postimplantation Loss	100	%	100
5	99861	PY	99861-23	5	IMPLANTS	Number of Implantations	5		5
6	99861	PY	99861-23	6	FETUSCT	Number of Fetuses	0		0
7	99861	PY	99861-23	7	FETUSLIV	Number of Live Fetuses	0		0
8	99861	PY	99861-23	8	FETUSDEA	Number of Dead Fetuses	0		0
9	99861	PY	99861-23	9	FFSR	Fetal Female Sex Ratio			
10	99861	PY	99861-23	10	RESORPCT	Number of Resorptions	5		5
11	99861	PY	99861-23	11	RESORPE	Number of Early Resorptions	3		3
12	99861	PY	99861-23	12	RESORPL	Number of Late Resorptions	2		2
13	99861	PY	99861-24	13	PREGSTAT	Pregnancy Status	Aborted - Euthanized		ABORTED
14	99861	PY	99861-25	14	PREGSTAT	Pregnancy Status	Not Pregnant - Mated		NOT PREGNANT

Row	PYSTRESN	PYSTRESU	PYRESCAT	PYSTAT	PYREASND	RPHASE	RPPLDY	PYDTC	PYRPDY
1 (cont)			PREGNANT			GESTATION	28	2009-04-06T08:50:10	28
2 (cont)	6					GESTATION	28	2009-04-06T08:50:10	28
3 (cont)	17	%				GESTATION	28	2009-04-06T08:50:10	28
4 (cont)	100	%				GESTATION	28	2009-04-06T08:50:10	28
5 (cont)	5					GESTATION	28	2009-04-06T08:50:10	28
6 (cont)	0					GESTATION	28	2009-04-06T08:50:10	28
7 (cont)	0					GESTATION	28	2009-04-06T08:50:10	28
8 (cont)	0					GESTATION	28	2009-04-06T08:50:10	28
9 (cont)				NOT DONE	No fetuses	GESTATION	28	2009-04-06T08:50:10	28
10 (cont)	5					GESTATION	28	2009-04-06T08:50:10	28

Row	PYSTRESN	PYSTRESU	PYRESCAT	PYSTAT	PYREASND	RPHASE	RPPLDY	PYDTC	PYRPDY
11 (cont)	3					GESTATION	28	2009-04-06T08:50:10	28
12 (cont)	2					GESTATION	28	2009-04-06T08:50:10	28
13 (cont)			PREGNANT			GESTATION	28	2009-03-23T06:15:00	20
14 (cont)			NOT PREGNANT			GESTATION	28	2009-04-06T07:30:15	28

Example 3

Row 1: Represents the pregnancy status record for female subject 23.
Rows 2-4: Represent three results collected for the Corpora Lutea Count test. PYRESLOC specifies the location of the result for Rows 2 and 3. PYRESLOC is null for Row 4 as it is the total count from both ovaries.
Rows 5-7: Represent three results collected for the Number of Implantations test. PYRESLOC specifies the uterine horn location of the result for Rows 5 and 6. PYRESLOC is null for Row 7 as it is the total count from the left and right uterine horns.

py.xpt

Row	STUDYID	DOMAIN	USUBJID	PYSEQ	PYTESTCD	PYTEST	PYORRES	PYORRESU	PYSTRESC	PYSTRESN	PYSTRESU
1	99861	PY	99861-23	1	PREGSTAT	Pregnancy Status	Normal Pregnancy		PREGNANT		
2	99861	PY	99861-23	2	CRPLUTCT	Corpora Lutea Count	4		4	4	
3	99861	PY	99861-23	3	CRPLUTCT	Corpora Lutea Count	6		6	6	
4	99861	PY	99861-23	4	CRPLUTCT	Corpora Lutea Count	10		10	10	
5	99861	PY	99861-23	5	IMPLANTS	Number of Implantations	3		3	3	
6	99861	PY	99861-23	6	IMPLANTS	Number of Implantations	6		6	6	
7	99861	PY	99861-23	7	IMPLANTS	Number of Implantations	9		9	9	

Row	PYRESCAT	PYRESLOC	RPHASE	RPPLDY	PYDTC	PYRPDY
1 (cont)	PREGNANT		GESTATION	21	2012-05-21T07:05:10	21
2 (cont)		Left Ovary	GESTATION	21	2012-05-21T07:05:10	21
3 (cont)		Right Ovary	GESTATION	21	2012-05-21T07:05:10	21
4 (cont)			GESTATION	21	2012-05-21T07:05:10	21
5 (cont)		Left Horn	GESTATION	21	2012-05-21T07:05:10	21
6 (cont)		Right Horn	GESTATION	21	2012-05-21T07:05:10	21
7 (cont)			GESTATION	21	2012-05-21T07:05:10	21

5.3 Fetal Measurements – FM

5.3.1 Specification for Fetal Measurements (FM) Domain Model

fm.xpt, Fetal Measurements – Findings. One record per finding per fetus per subject per test, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	FM	Identifier	Two-character code for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
FETUSID	Unique Fetus Identifier	Char		Identifier	Identifier used to identify a fetus from a maternal subject for prenatal evaluations. Unique per USUBJID across a study.	Exp
FMSEQ	Sequence Number	Num		Identifier	Sequence number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
FMGRPID	Group Identifier	Char		Identifier	Optional group identifier, used to link together a block of related records within a subject in a domain. This is not the treatment group number.	Perm
FMTESTCD	Test Short Name	Char	(FMTESTCD)	Topic	Short name of the test described in FMTEST. The value in FMTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g. "1TEST"). FMTESTCD cannot contain characters other than letters, numbers, or underscores.	Req
FMTEST	Fetal Measurement Name	Char	(FMTEST)	Synonym Qualifier	Long name for FMTESTCD. The value in FMTEST cannot be longer than 40 characters. Example: Body Weight	Req
FMORRES	Result or Findings as Collected	Char		Result Qualifier	Result of the finding or measurement as originally received or collected. Should be null if examination or measurement was not done.	Exp
FMORRESU	Unit of the Original Result	Char	(UNIT)	Variable Qualifier	The unit of the original result if applicable for a numeric result. The unit of the original result should be mapped to a synonymous unit on the Controlled Terminology list.	Exp
FMSTRESC	Standardized Results in Character Format	Char		Result Qualifier	Contains the result value for all findings, copied or derived from FMORRES in a standard format or standard unit. If results are numeric, they should also be stored in numeric format in FMSTRESN.	Exp
FMSTRESN	Standardized Results in Numeric Format	Num		Result Qualifier	Used for results or findings in standard format; contains the numeric form of FMSTRESC. FMSTRESN should store all numeric test results or findings.	Exp
FMSTRESU	Unit of the Standardized Result	Char	(UNIT)	Variable Qualifier	Standardized unit used for FMSTRESC or FMSTRESN.	Exp
FMSTAT	Completion Status	Char	(ND)	Record Qualifier	Used to indicate when a test or examination was not done or a result is missing. Should be null if a result exists in FMORRES.	Perm
FMREASND	Reason Not Done	Char		Record Qualifier	Describes why FMSTAT is NOT DONE. Use only in conjunction with FMSTAT when value is NOT DONE.	Perm

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
FMANTREG	Anatomical Region	Char		Variable Qualifier	Defines the specific anatomical or biological region of a tissue, organ specimen or the region from which the specimen is obtained, as defined in the protocol, such as a section or part of what is described in the FMLOC variable. Examples: CORTEX, MEDULLA, MUCOSA	Perm
FMLOC	Location Used for the Measurement	Char	(LOC)	Record Qualifier	Anatomical location of the fetus relevant to the collection of the measurement. The protocol or procedural location targeted for examination. Examples: CAUDAL VERTEBRA, BODY	Exp
FMLAT	Laterality	Char	(LAT)	Record Qualifier	Qualifier for laterality of the test location (FMLOC). Example: LEFT, RIGHT, BILATERAL.	Perm
FMEXCLFL	Exclusion Flag	Char	(NY)	Record Qualifier	Indicates whether the "result" value for a record should be excluded from summary statistical calculations. Expected to be Y or Null. FMEXCLFL should not be used when FMSTAT is ND (Not Done).	Perm
FMREASEX	Reason for Exclusion	Char		Record Qualifier	The reason the result should be excluded from all calculations. Used only when FMEXCLFL value is Y.	Perm
RPHASE	Repro Phase	Char		Timing	Name of the reproductive phase associated with date/time of the observation.	Perm
RPPLDY	Planned Repro Phase Day	Num		Timing	Reproductive phase day the measurement was scheduled to occur, relative to RPRFDY in the TP domain. Should be an integer.	Perm
FMDTC	Date/Time	Char	ISO 8601	Timing	Collection date and time of the measurement represented in ISO 8601 character format. For post mortem observations, this is the date/time of subject disposition in ISO 8601 format.	Perm
FMDY	Study Day	Num		Timing	Study day of the measurement expressed in integer days relative to the protocol-defined RFSTDTC.	Perm
FMRPDY	Actual Repro Phase Day	Num		Timing	Reproductive phase day the measurement occurred, relative to SJSTDTC for the phase and the start value in RPRFDY (TP). Should be an integer.	Perm

(Parentheses indicate CDISC controlled terminology codelist)

5.3.2 Assumptions for Fetal Measurements (FM) Domain Model

1. The Fetal Measurements domain captures individual fetal body and tissue weights, as well as growth and body measurements and characteristics.
2. Tests include measurements that may be performed during a fetal pathology examination that are not otherwise recorded as malformations and variations, such as, vertebra counts and fetal sex.
3. The USUBJID in this domain is the maternal subject (i.e., female parent, litter). The FETUSID is the identifier of the fetus for the subject of the test.
4. Do not include fetal alterations / abnormality findings in this domain (e.g., malformations, variations).
5. The Nonclinical DART Sex (NCDSEX) CT list applies to FXSTRESC for Fetal Sex / SEXFETAL (TEST / TESTCD).

5.3.3 Examples for Fetal Measurements (FM) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1

This example represents individual rat fetal measurements and characteristics for three fetuses in a litter (maternal subject) in an EFD Toxicity study.

fm.xpt

Row	STUDYID	DOMAIN	USUBJID	FETUSID	FMSEQ	FMTESTCD	FMTEST	FMORRES	FMORRESU	FMSTRESC	FMSTRESN
1	113670	FM	113670-112321	1	1	SEXFETAL	Fetal Sex	Female		FEMALE	
2	113670	FM	113670-112321	1	2	FWT	Fetal Weight	5.07	g	5.07	5.07
3	113670	FM	113670-112321	1	3	FOWT	Fetal Organ Weight	2.25	g	2.25	2.25
4	113670	FM	113670-112321	1	4	CVCOUNT	Caudal Vertebra Count	9		9	9
5	113670	FM	113670-112321	1	5	VOLUME	Volume	0.72	mL	0.72	0.72
6	113670	FM	113670-112321	2	6	SEXFETAL	Fetal Sex	Male		MALE	
7	113670	FM	113670-112321	2	7	FWT	Fetal Weight	5.13	g	5.13	5.13
8	113670	FM	113670-112321	2	8	FOWT	Fetal Organ Weight	2.32	g	2.32	2.32
9	113670	FM	113670-112321	2	9	CVCOUNT	Caudal Vertebra Count	10		10	10
10	113670	FM	113670-112321	2	10	VOLUME	Volume	0.68	mL	0.68	0.68
11	113670	FM	113670-112321	3	11	SEXFETAL	Fetal Sex	Male		MALE	
12	113670	FM	113670-112321	3	12	FWT	Fetal Weight	5.34	g	5.34	5.34
13	113670	FM	113670-112321	3	13	FOWT	Fetal Organ Weight	2.45	g	2.45	2.45
14	113670	FM	113670-112321	3	14	CVCOUNT	Caudal Vertebra Count	8		8	8
15	113670	FM	113670-112321	3	15	VOLUME	Volume	0.66	mL	0.66	0.66

Row	FMSTRESU	FMLOC	RPHASE	RPPLDY	FMRPDY
1 (cont)		BODY	GESTATION	21	21
2 (cont)	g	BODY	GESTATION	21	21
3 (cont)	g	PLACENTA	GESTATION	21	21
4 (cont)		CAUDAL VERTEBRA	GESTATION	21	21
5 (cont)	mL	AMNIOTIC FLUID	GESTATION	21	21
6 (cont)		BODY	GESTATION	21	21
7 (cont)	g	BODY	GESTATION	21	21
8 (cont)	g	PLACENTA	GESTATION	21	21
9 (cont)		CAUDAL VERTEBRA	GESTATION	21	21
10 (cont)	mL	AMNIOTIC FLUID	GESTATION	21	21
11 (cont)		BODY	GESTATION	21	21
12 (cont)	g	BODY	GESTATION	21	21
13 (cont)	g	PLACENTA	GESTATION	21	21
14 (cont)		CAUDAL VERTEBRA	GESTATION	21	21
15 (cont)	mL	AMNIOTIC FLUID	GESTATION	21	21

5.4 Fetal Pathology Findings – FX

5.4.1 Specification for Fetal Pathology Findings (FX) Domain Model

fx.xpt, Fetal Pathology Findings – Findings. One record per test per location per finding per fetus per subject, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	FX	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
FETUSID	Unique Fetus Identifier	Char		Identifier	Identifier used to identify a fetus from a maternal subject for prenatal evaluations. Unique per USUBJID across a study.	Req
FXSEQ	Sequence Number	Num		Identifier	Sequence number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
FXGRPID	Group Identifier	Char		Identifier	Optional group identifier, used to link together a block of related records within a subject in a domain. This is not the treatment group number.	Perm
FXREFID	Reference ID	Char		Identifier	Optional internal or external identifier such as lab specimen ID.	Perm
FXTESTCD	Test Short Name	Char	(FXTESTCD)	Topic	Short name of the test described in FXTEST. The value in FXTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g. "1TEST"). FXTESTCD cannot contain characters other than letters, numbers, or underscores.	Req
FXTEST	Fetal Exam Name	Char	(FXTEST)	Synonym Qualifier	Long name for FXTESTCD. The value in FXTEST cannot be longer than 40 characters.	Req
FXORRES	Result or Findings as Collected	Char		Result Qualifier	Result of the finding or measurement as originally received or collected including the morphological change observed and all modifiers.	Exp
FXSTRESC	Standardized Results in Character Format	Char	(FXFINDRS)	Result Qualifier	Contains the morphological change observed from FXORRES in a standard format without modifiers. Or, if the examination was completed and there were no findings, the value must be UNREMARKABLE.	Exp
FXRESCAT	Result Category	Char	(FXRESCAT)	Variable Qualifier	Used to categorize the result or finding of a fetal pathology examination in a standard format. Examples: MALFORMATION, VARIATION.	Exp
FXDISTR	Distribution Pattern of Finding	Char	(DISTR)	Variable Qualifier	Distribution of a particular finding within the tissue or anatomical location affected. Multiple terms are not allowed for this variable. Examples: FOCAL, DIFFUSE, LOCALLY EXTENSIVE.	Perm
FXRESLOC	Result Location of Finding	Char		Result Qualifier	Location where the result was observed (as opposed to the location specified for examination). Should have a higher degree of specificity than FXLOC. Example: if FXLOC is EAR and FXSTRESC is Absent, FXRESLOC may be "Pinna". This field can be a combination of terms where needed. Multiple terms should be separated by a semicolon unless they only make sense together. Example: if FXLOC is SKULL and FXSTRESC is FUSED, FXRESLOC may include (if collected as the base location) "Multiple Skull Bones" or "Parietal; Frontal;	Exp

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
					Supraoccipital"	
FXSTAT	Completion Status	Char	(ND)	Record Qualifier	Used to indicate when a test or examination is not done or a result is missing. Should be null if a result exists in FXORRES.	Perm
FXREASND	Reason Not Done	Char		Record Qualifier	Describes why FXSTAT is NOT DONE. Used only in conjunction with FXSTAT when value is NOT DONE.	Perm
FXANTREG	Anatomical Region	Char		Variable Qualifier	Defines the specific anatomical or biological region of the measurement location (FXLOC), as defined in the protocol. Example: Coronal Sections, when FXLOC is Head for a Visceral Examination.	Perm
FXLOC	Location Used for the Measurement	Char	(LOC)	Record Qualifier	Anatomical location of the fetus relevant to the collection of the measurement. The protocol or procedural location targeted for examination.	Exp
FXLAT	Laterality	Char	(LAT)	Variable Qualifier	Qualifier for anatomical location (FXLOC) further detailing laterality. Examples: RIGHT, LEFT, BILATERAL	Perm
FXMETHOD	Method of Test or Examination	Char		Record Qualifier	Method of the test or examination. This could be type of stain or technique. Examples: Bouin's, Alizarin Red	Perm
FXSEV	Severity	Char	(SEV)	Record Qualifier	Modifier describing the severity or degree of a particular finding. Use only if collected. Examples: MILD, MODERATE, SEVERE	Perm
RPHASE	Reproductive Phase	Char		Timing	Name of the reproductive phase associated with date/time of the observation.	Perm
RPPLDY	Planned Phase Day	Num		Timing	Reproductive phase day the observation was scheduled to occur, relative to RPRFDY in the TP domain. Should be an integer.	Perm
FXDTC	Date/Time	Char	ISO 8601	Timing	Collection date and time of the observation represented in ISO 8601 character format. For post mortem observations, this is the date/time of subject disposition in ISO 8601 format.	Perm
FXDY	Study Day	Num		Timing	Actual study day of the observation expressed in integer days relative to the protocol-defined RFSTDTC.	Perm
FXRPDY	Actual Phase Day	Num		Timing	Reproductive phase day the observation occurred, relative to SJSTDTC for the phase and the start value in RPRFDY (TP). Should be an integer.	Perm

(Parentheses indicate CDISC controlled terminology codelist)

5.4.2 Assumptions for Fetal Pathology Findings (FX) Domain Model

1. FX Definition:
    a. This domain provides a record for each fetal pathology observation. The USUBJID is the maternal subject and the FETUSID is the fetus identifier.
    b. External, Visceral, Skeletal, and Maternal-Fetal are pathology examinations that apply to this domain.
    c. For each test / examination, there should be at least one record per fetus per anatomical location (FXLOC) examined, including locations that were UNREMARKABLE or scheduled but NOT DONE (FXSTAT).
    d. The type of fetal examination is the test when observing tissues for abnormalities. The term "abnormalities" is used to denote changes in the fetal specimen under examination relative to the perceived "norm" of control specimens for a particular species and developmental stage.
    e. Topic specific tests not generally categorized as abnormalities (Variations, Malformations, etc.) or would not be collected as UNREMARKABLE (e.g., Fetal Sex, Caudal Vertebra Count) should be submitted in the FM domain. See FX and FM examples.

2. The FXREFID may be used as a substitute ID for a subject's FETUSID/FXLOC for comments that apply to multiple findings records for a subject's fetal specimen (FETUSID) and fetal anatomical location (FXLOC). The comment then can get into the CO domain using FXREFID as the IDVAR.
3. FXLOC describes where the protocol said to look. FXRESLOC, FXDISTR, FXSEV, and supplemental qualifier FXRESMOD, if applicable, are qualifiers of the morphological change seen in FXSTRESC.
4. FXRESLOC specifies the base location where the finding was seen within the test location (FXLOC), if specified or collected separate from the test location. This is the location relevant to FXSTRESC, in particular if different or more granular than FXLOC. Sublocation information for FXLOC or FXRESLOC collected as modifiers / descriptors as opposed to the base location of the finding should be populated in the FXRESMOD supplemental qualifier. Generally, the data provider should determine if sublocations of FXLOC and/or FXRESLOC are considered part of the standardized result (base finding) or modifiers. For Example, specifying the specific ribs that are fused in a Fused Rib finding.
5. Results Definition
    a. FXORRES is the original result including the morphological change observed (base finding) and all descriptors.
    b. FXSTRESC and FXRESLOC are important for standardizing the value in FXORRES. From FXORRES, the base finding and base location, if applicable, should be populated in FXSTRESC and FXRESLOC, respectively.
    c. FXSTRESC and FXRESLOC can further be described by FXDISTR and FXSEV.
    d. The Supplemental Qualifier FXRESMOD can be used to further qualify the base morphological finding recorded when terms in FXORRES are not otherwise represented by other variables (e.g. FXSTRESC, FXRESLOC FXDISTR, FXSEV).
        - QNAM = "--RESMOD"
        - QLABEL = "Result Modifiers"
        - QVAL = "concatenated modifiers of the morphological finding separated by semicolons (e.g., Left; Tan) unless they only make sense together (e.g., well defined area)". Key modifiers may include result laterality, sublocations, directionality, color, or shape. Modifiers captured in other variables should not be repeated in this variable.

    Note: The use of FXRESMOD does not preclude data providers from creating other Supplemental Qualifiers containing specifically defined modifiers.
    e. FXRESCAT should be populated with the following exceptions: If the Test is 'Fetal Pathology Examination' and FXSTRESC is UNREMARKABLE or FXSTAT is NOT DONE.

5.4.3 Examples for Fetal Pathology Findings (FX) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1
This example represents fetal examinations for fetuses 3 and 4 from female subject F014. In the data provider's system the finding and the result location are collected as a string in FXORRES separated from descriptors by commas. The result location in the provider's base result, if different than FXLOC, is submitted in FXRESLOC. The descriptors after the comma are submitted as Supplemental Qualifiers in the SUPPFX domain.

Row 1: Illustrates an external finding for fetus 3 during the external examination of the Tail. The tail was the location targeted for examination (FXLOC). Misdirected Tail is the result as collected in FXORRES. FXRESLOC is null.

Rows 2-3: Illustrate visceral examination results for fetus 3. In Row 2, Heart is the location targeted for examination. There is a SEND standardized term

for Ventricular Septum Defect captured in FXSTRESC. A separate result location is not recorded for the finding. Row 3 shows that the coronal sectioned tissues of the Head (FXLOC) were "Unremarkable". The fixative, Bouin's solution, is captured in FXMETHOD.

Rows 4-5: Illustrate skeletal examination results for fetus 3. In Row 4, Rib is the location targeted for examination (FXLOC) and Supernumerary is the finding. The result location is equivalent to the test location of Rib. "T14" is a modifier (sublocation) submitted as a Supplemental Qualifier (FXRESMOD). See the SUPPFX as per Example 1 below.
In Row 5 Sternebra is the location targeted for examination (FXLOC) and Incomplete Ossification is the finding. The result location is equivalent to the test location of Sternebra. "5th" is a modifier submitted as a Supplemental Qualifier (FXRESMOD). See the SUPPFX for Example 1 below.

Row 6: Illustrates a finding for fetus 4 during the External examination of the Eye.
Eye Bulge is the finding location specified in FXRESLOC, collected by the sponsor.

Row 7: Illustrates an UNREMARKABLE finding for fetus 4 for the visceral examination. Since only the trunk region was specified in the protocol for this fetus, the sponsor included a single UNREMARKABLE record for Trunk (FXLOC).

Row 8: Illustrates findings for fetus 4 during the skeletal examination of the skull bone. 'Naris' is the result location within the skull for the finding (Fused).

Row 9: Illustrates findings for fetus 4 during the skeletal examination of the Vertebra. 'Vertebral Arch(es)' is the result location within the Vertebra for the finding (Incomplete Ossification). Since there are multiple values for result laterality (Left, Right), and severity (Severe, Moderate) for the "S-4" descriptor, these were all captured together as a Supplemental Qualifier (FXRESMOD), each descriptor separated by a semicolon. See SUPPFX for Example 1 below.

fx.xpt

Row	STUDYID	DOMAIN	USUBJID	FETUSID	FXSEQ	FXTESTCD	FXTEST	FXORRES
1	TST01	FX	TST01-F014	3	1	EXTREXAM	External Examination	Misdirected Tail
2	TST01	FX	TST01-F014	3	2	VISCEXAM	Visceral Examination	Ventricular Septum Defect
3	TST01	FX	TST01-F014	3	3	VISCEXAM	Visceral Examination	Not Remarkable
4	TST01	FX	TST01-F014	3	4	SKELEXAM	Skeletal Examination	Supernumerary Rib, T14
5	TST01	FX	TST01-F014	3	5	SKELEXAM	Skeletal Examination	Incomp. Oss. Sternebra, 5th
6	TST01	FX	TST01-F014	4	6	EXTREXAM	External Examination	Absent Eye Bulge
7	TST01	FX	TST01-F014	4	7	VISCEXAM	Visceral Examination	Not Remarkable
8	TST01	FX	TST01-F014	4	8	SKELEXAM	Skeletal Examination	Fused Naris
9	TST01	FX	TST01-F014	4	9	SKELEXAM	Skeletal Examination	Incomplete Ossification of Vertebral Arch(es), S-4 Right Severe, S-4 Left Moderate

Row	FXSTRESC	FXRESCAT	FXRESLOC	FXANTREG	FXLOC	FXMETHOD
1 (cont)	MALPOSITIONED	MALFORMATION			TAIL	
2 (cont)	MUSCULAR VENTRICULAR SEPTAL DEFECT	MALFORMATION			HEART	
3 (cont)	UNREMARKABLE			Coronal Sections	HEAD	Bouins fixative
4 (cont)	SUPERNUMERARY	VARIATION			RIB	
5 (cont)	INCOMPLETE OSSIFICATION	OSSIFICATION			STERNEBRA	Alizarin Red
6 (cont)	ABSENT	VARIATION	Eye Bulge		EYE	
7 (cont)	UNREMARKABLE				TRUNK	
8 (cont)	FUSED	MALFORMATION	Naris		SKULL	Alizarin Red
9 (cont)	INCOMPLETE OSSIFICATION	OSSIFICATION	Vertebral Arch(es)		VERTEBRA	Alizarin Red

Row 1: Shows the Supplemental Qualifier record for the modifiers associated with FXSEQ 4 (Row 4) findings in fx.xpt above.
Row 2: Shows the Supplemental Qualifier record for the modifiers associated with FXSEQ 5 (Row 5) findings in fx.xpt above.
Row 3: Shows the Supplemental Qualifier record for the modifiers associated with FXSEQ 9 (Row 9) findings in fx.xpt above.

suppfx.xpt

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1	TST01	FX	TST01-F014	FXSEQ	4	FXRESMOD	Result Modifiers	T14	COLLECTED	Toxicologist
2	TST01	FX	TST01-F014	FXSEQ	5	FXRESMOD	Result Modifiers	5th	COLLECTED	Toxicologist
3	TST01	FX	TST01-F014	FXSEQ	9	FXRESMOD	Result Modifiers	S-4 Right Severe; S-4 Left Moderate	COLLECTED	Toxicologist

FX Example 2

This example represents fetal examinations for fetuses 1 and 2 from USUBJID TST04-4 in a rabbit EFD study. The dash "-" in FXORRES separates the protocol location (FXLOC) from the finding in the data provider's collection system.

Rows 1-3: Represent external examinations of the Head, Limb, and Paw with the results collected of 'no abnormalities detected' and the SEND standardized result of UNREMARKABLE.

Rows 4-12: Represent the data provider's terms in FXORRES into SEND standard format and the categorizations as malformations and variations in FXRESCAT. Specific details are as follows:

In Rows 4, 5, 6, 8, and 11, the term following the "-" in FXORRES is the location of the result (FXRESLOC) within the location of FXLOC, the next term after the comma is the finding (FXSTRESC). Row 11 also has a result laterality (left) captured as a Supplemental Qualifier (FXRESMOD) in the SUPPFX for Example 2 below.

In Rows 7, 9, and 10, the term following the "-" in FXORRES is the finding (FXSTRESC) for the location of FXLOC. The result descriptors collected after the finding, separated by a comma, are captured as a Supplemental Qualifier (FXRESMOD) in the SUPPFX for Example 2 below.

fx.xpt

Row	STUDYID	DOMAIN	USUBJID	FETUSID	FXSEQ	FXTESTCD	FXTEST	FXORRES
1	TST04	FX	TST04-4	1	1	EXTREXAM	External Examination	No abnormalities detected
2	TST04	FX	TST04-4	1	2	EXTREXAM	External Examination	No abnormalities detected
3	TST04	FX	TST04-4	1	3	EXTREXAM	External Examination	No abnormalities detected
4	TST04	FX	TST04-4	1	4	VISCEXAM	Visceral Examination	Ear – inner ear, hemorrhagic
5	TST04	FX	TST04-4	1	5	VISCEXAM	Visceral Examination	Lung – all lobes, misshapen
6	TST04	FX	TST04-4	1	6	SKELEXAM	Skeletal Examination	Sternum - 5th sternebra, not ossified
7	TST04	FX	TST04-4	1	7	SKELEXAM	Skeletal Examination	Caudal vertebra - number of centra: <=14
8	TST04	FX	TST04-4	2	8	EXTREXAM	External Examination	Trunk – Spinal Cord, Spina Bifida
9	TST04	FX	TST04-4	2	9	MTFTEXAM	Maternal - Fetal Examination	Placenta – red material, around umbilical cord
10	TST04	FX	TST04-4	2	10	VISCEXAM	Visceral Examination	Kidney – absent, right
11	TST04	FX	TST04-4	2	11	SKELEXAM	Skeletal Examination	Forelimb - distal end of humerus, not ossified, left
12	TST04	FX	TST04-4	2	12	SKELEXAM	Skeletal Examination	Rib - 5th to 6th, fused, left

Row	FXSTRESC	FXRESCAT	FXRESLOC	FXLOC
1 (cont)	UNREMARKABLE			HEAD

Row	FXSTRESC	FXRESCAT	FXRESLOC	FXLOC
2 (cont)	UNREMARKABLE			LIMB
3 (cont)	UNREMARKABLE			PAW
4 (cont)	RED MATERIAL	MALFORMATION	inner ear	EAR
5 (cont)	MISSHAPEN	VARIATION	all lobes	LUNG
6 (cont)	UNOSSIFIED	VARIATION	5th sternebra	STERNUM
7 (cont)	number of centra: <=14	VARIATION		CAUDAL VERTEBRA
8 (cont)	SPINA BIFIDA	MALFORMATION	Spinal Cord	TRUNK
9 (cont)	RED MATERIAL	VARIATION		PLACENTA
10 (cont)	ABSENT	MALFORMATION		KIDNEY
11 (cont)	UNOSSIFIED	VARIATION	distal end of humerus	FORELIMB
12 (cont)	FUSED	MALFORMATION	5th To 6th	RIB

Rows 1-4: Show the Supplemental Qualifier records for the modifiers associated with the findings in Example 2. These records are linked to the FXSEQ with the values 9, 10, 11, 12 respectively.

fx.xpt

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1	TST01	FX	TST04-4	FXSEQ	9	FXRESMOD	Result Modifiers	around umbilical cord	COLLECTED	PATHOLOGIST
2	TST01	FX	TST04-4	FXSEQ	10	FXRESMOD	Result Modifiers	right	COLLECTED	PATHOLOGIST
3	TST01	FX	TST04-4	FXSEQ	11	FXRESMOD	Result Modifiers	left	COLLECTED	PATHOLOGIST
4	TST01	FX	TST04-4	FXSEQ	12	FXRESMOD	Result Modifiers	left	COLLECTED	PATHOLOGIST

6 Trial Design

6.1 Additions to the Trial Design Model

6.1.1 Reproductive (Repro) Stages, Paths, and Phases

The concepts of reproductive Stages, Paths, and Phases within the Trial Design Model provide a standard way to define reproductive segments of a study that subjects will experience, and when planned assessments will occur. These segments are important time periods of a study for which subjects are planned (or assigned) to experience and are evaluated based on the day within a particular segment (i.e., Repro Phase) rather than the study day (per RFSTDTC).

The concepts are modeled with two new domains, Trial Repro Stages (TT) and Trial Repro Paths (TP), and Repro Phase timing variables. Repro Phase (RPHASE) is defined in the TP domain. The Repro Phase timing variables are described in Section 3 and listed in Appendix C for your reference. Repro Stages, Repro Paths, and Repro Phases are also referred to as Stages, Paths, and Phases in this document.

Trial Repro Stages are the building blocks of Trial Repro Paths. The TP domain provides a record of the planned sequence of Stages within Phases for each Path. Paths consisting of Stages are Paths that subjects are planned to follow throughout a study regardless of when treatment occurs. The Phase is a period of time consisting of one or more Stages, consistent across all Paths within a Trial.

See figures for TP examples in Section 6.3.3. Examples are based on the study type(s) for the SENDIG-DART version. See Appendix E for supplemental study design diagrams.

6.2 Trial Repro Stages – TT

6.2.1 Specification for Trial Repro Stages (TT) Domain Model

tt.xpt, Trial Repro Stages - Trial Design. One record per planned Stage, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	TT	Identifier	Two-character abbreviation for the domain.	Req
RSTGCD	Repro Stage Code	Char		Topic	RSTGCD (the short form of RSTAGE) is limited to 8 characters and does not have special character restrictions.	Req
RSTAGE	Description of Repro Stage	Char		Synonym Qualifier	Name of the Repro Stage.	Req
TTSTRL	Rule for Start of Repro Stage	Char		Rule	Expresses rule for beginning Repro Stage.	Req
TTENRL	Rule for End of Repro Stage	Char		Rule	Expresses rule for ending Repro Stage. Either TTENRL or TTDUR must be present for each Stage.	Exp
TTDUR	Planned Duration of Repro Stage	Char	ISO 8601	Timing	Planned duration of Repro Stage in ISO 8601 character format. Use when a Stage represents a fixed duration. TTENRL or TTDUR must be present for each Element; both may be present.	Perm

6.2.2 Assumptions for Trial Repro Stages (TT) Domain Model

1. TT Definition: Repro Stages are the building blocks of Trial Repro Paths (TP). Stages are segments / intervals of a study that are independent of treatment (or lack of treatment). Stages may overlap treatment Elements, or more than one treatment Element may exist within a Stage. Therefore, Paths consisting of Stages (i.e., reproductive segments) are Paths that subjects will follow throughout a study in addition to the treatment plan.
2. A Repro Stage is uniquely defined by the start rule and the end rule or duration. The start and end rules for Stages are represented as unique values in TTSTRL and TTENRL. A Stage cannot span more than one Repro Phase (RPHASE).
3. Repro Stages that have different planned durations are different Stages. Treatment (or lack of treatment) does not distinguish separate Stages.
4. There are no gaps between Stages. The instant one Stage ends, the next Stage begins. A subject spends no time between Stages.
5. The RSTAGE variable contains the name of the Stage and often indicates the condition, event, or activity occurring during a Stage. However, Stages that have different planned durations are different Stages (e.g., Gestation_TK, Gestation_NonTK).
6. TTSTRL identifies the event that marks the transition into a Stage. The start of the study for a particular Repro Path is defined by the value of TTSTRL for the first Stage within that Path. Note that the actual date/time of the event that starts a Stage for a subject, which is described in TTSTRL, will be used to populate the SJSTDTC date/times in the SJ dataset. Therefore, the TTSTRL should refer to an event which will be captured during the course of the study.
7. TTENRL describes the circumstances under which a Stage ends, causing subjects to enter into another Stage. The TP dataset, not the TT dataset, describes where the subject moves next; therefore, TTENRL values must be expressed independently of Repro Paths.

6.2.3 Examples for Trial Repro Stages (TT) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (Available at http://www.cancer.gov/research/resources/terminology/cdisc).

TT Example 1
EFD Toxicity and TK Study in Mice

This is a basic study design example illustrating that Gestation for non-TK and TK are different Stages because the planned duration of Gestation is different for each group. The start rule (TTSTRL) is the same for both Stages, but the end rule (TTENRL) and planned duration (TTDUR) are different.

tt.xpt

Row	STUDYID	DOMAIN	RSTGCD	RSTAGE	TTSTRL	TTENRL	TTDUR
1	111209	TT	GEST	GESTATION18D	Confirmation of Mating	Scheduled C-section Sacrifice	P19D
2	111209	TT	GESTTK	GESTATION12D	Confirmation of Mating	Scheduled TK Sacrifice	P13D

The Trial Paths and Phase information and diagram for this example are illustrated in Example 1 of the TP domain, Section 6.3.3.

TE (Trial Elements) domain for TT Example 1 (the TE domain is defined in the SENDIG)
This is an example of the planned treatment Elements that may exist for the TT example above. If the planned duration of treatment (or lack of treatment) is different for a particular group of subjects within the same protocol-defined group code, it should be a different Element.

Since dosing begins on GD 6, there is a Pre-treatment Element from GDs 0-6 for all subjects. There is a Post-treatment Element for the non-TK subjects, since in-life observations for this study (e.g., body weights, clinical signs) are collected after dosing ends.

te.xpt

Row	STUDYID	DOMAIN	ETCD	ELEMENT	TESTRL	TEENRL	TEDUR
1	111209	TE	PRETXT	Pre-treatment	Confirmation of Mating	First Day of Dosing	P7D
2	111209	TE	TXT1	Control Vehicle	Start of dosing control vehicle	Last day of dosing control vehicle	P10D
3	111209	TE	TXT1TK	Control Vehicle - TK	Start of dosing control vehicle	Scheduled sacrifice for TK sampling	P7D
4	111209	TE	TXT2	10 mg/kg/day A123	Start of dosing 10 mg/kg/day	Last day of dosing 10 mg/kg/day	P10D
5	111209	TE	TXT2TK	10 mg/kg/day A123 - TK	Start of dosing 10 mg/kg/day	Scheduled sacrifice for TK sampling	P7D
6	111209	TE	TXT3	50 mg/kg/day A123	Start of dosing 50 mg/kg/day	Last day of dosing 50 mg/kg/day	P10D
7	111209	TE	TXT3TK	50 mg/kg/day A123 - TK	Start of dosing 50 mg/kg/day	Scheduled sacrifice for TK sampling	P7D
8	111209	TE	POSTTXT	Post-treatment	Day after last dose	Sacrifice C-section	P2D

6.3 Trial Repro Paths Domain – TP

6.3.1 Specification for Trial Repro Paths (TP) Domain Model

tp.xpt, Trial Repro Paths - Trial Design. One record per planned Stage per Path, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	TP	Identifier	Two-character abbreviation for the domain.	Req
RPATHCD	Planned Repro Path Code	Char		Topic	Short name for the planned Repro Path (may be up to 20 characters) used for sorting and programming. Should be populated in Demographics when Repro Paths have been defined in this domain.	Req
RPATH	Description of Planned Repro Path	Char		Synonym Qualifier	Name of the planned Repro Path.	Req
TPSTGORD	Order of Repro Stage within Repro Path	Num		Timing	Number that gives the planned order of the Repro Stage within the Repro Path. This value should be an integer.	Req
RSTGCD	Repro Stage Code	Char		Topic	RSTGCD (the companion to RSTAGE) is limited to 8 characters and does not have special character restrictions. . The values of RSTGCD used in the Trial Repro Paths dataset must match values for the same Repro Stage in the Trial Stages dataset.	Req
RSTAGE	Description of Repro Stage	Char		Synonym Qualifier	Name of the Repro Stage.	Perm
TPBRANCH	Branch	Char		Rule	Conditions subjects meet, occurring at the end of a Repro Stage, which cause a Repro Path to branch off from another Repro Path.	Perm
RPHASE	Repro Phase	Char	(NCDPHASE)	Timing	Name of the Repro Phase with which this Repro Stage of the Repro Path is associated.	Req
RPRFDY	Repro Phase Start Reference Day	Num		Timing	Protocol-defined first day of Repro Phase. Should be 0 or 1. Data Providers should refer to scientific conventions to designate the Repro Phase Start Reference Day.	Req

6.3.2 Assumptions for Trial Repro Paths (TP) Domain Model

1. TP Definition: The Trial Repro Paths dataset provides a record of the planned sequence of Repro Stages for each Repro Path. Paths are independent of treatment Arms. Subject groupings based on treatments are defined in the TA, TE, and TX domains. It is not necessary to define separate Paths for each treatment Element if each Arm is planned to experience the same sequence of Stages in the same order.
2. RPATH and RPATHCD are defined in TP, then RPATHCD is applied to subjects in DM. RPATHCD values in DM and TP must coincide.
3. TPSTGORD is an integer and is used to order the Stages within a Path. In general the value of TPSTGORD is "1" for the first Stage in each Path, "2" for the second Stage in each Path, etc. Although the values of TPSTGORD need not always be consecutive, the values must always be populated according to the correct order of the Stages within a Path, with the first Stage equivalent to the lowest value of TPSTGORD and the last Stage equivalent to the highest value of TPSTGORD.

4. The Stages in each Path must be consecutive in time; it is not correct to leave any gaps in time between Stages. If there is a multi-day pause between Stages, either it should be reflected within one of the existing Stage definitions, or a new Stage representing the block of time between Stages should be included.
5. Stages in different Paths with the same value of TPSTGORD may or may not happen at the same time, depending on the design of the study.
6. TPBRANCH describes the outcome of a branch decision point in the trial design for subjects in the Path. A branch decision point takes place between Phases and is associated with the Stage end, at which point the branching decision is made.
7. The values of RPHASE provide a description of a time period that is independent of the value of RPATH. RPHASE should be assigned in such a way that Stages from different Paths with the same value of RPHASE are comparable in some sense.

6.3.3 Examples for Trial Repro Paths (TP) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

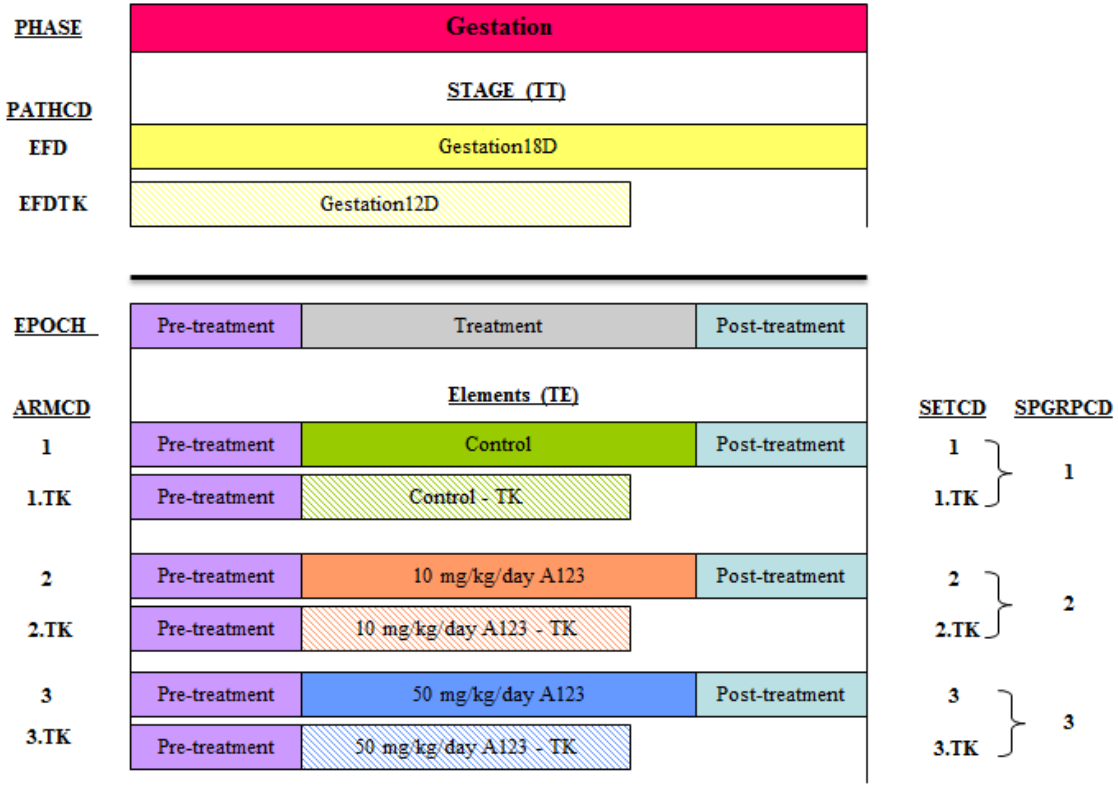
Example 1
(EFD Toxicity and TK Study in Mice)

In this example, subjects were time-mated and Study Day 1 is Gestation Day (GD) 0. Non-TK females were dosed from GD 6 through 16 then C-sectioned on GD 18. TK females were dosed from GD 6 through 12 then terminated for TK sampling.

Dose Groups:

Test/Control Article	Dose Level	Dose Group #	No. of Females	
			Non TK	TK
Vehicle	Control	1	20	4
A123	10 mg/kg/day	2	24	8
A123	50 mg/kg/day	3	24	8

Figure 6.3.3 Trial Repro Paths Domain Example 1



In this routine EFD toxicity and TK study in mice, there are two planned Paths for the female subjects (EFD and EFDTK). There is one Phase (Gestation), and the Repro Phase Start Reference Day (RPRFDY) is 0. The planned start and end rules for stages are defined in the tt.xpt (Section 6.2.3).

tp.xpt

Row	STUDYID	DOMAIN	RPATHCD	RPATH	TPSTGORD	RSTGCD	RSTAGE	RPHASE	RPRFDY
1	EFD111	TP	EFD	Embryo-Fetal Development	1	GEST	Gestation18D	GESTATION	0
2	EFD111	TP	EFDTK	Embryo-Fetal Development with TK	1	GESTTK	Gestation12D	GESTATION	0

TA (Trial Arms) domain for TP Example 1 (the TA domain is defined in the SENDIG)
The females in the same dose group have two separate Trial Arms (non-TK and TK) because they experience different Elements and/or Elements of different durations. Subjects scheduled for TK bleeds do not experience the Post-treatment Element that the non-TK subjects experience.

ta.xpt

Row	STUDYID	DOMAIN	ARMCD	ARM	TAETORD	ETCD	ELEMENT	EPOCH
1	EFD111	TA	1	Control	1	PRETXT	Pre-treatment	Pre-treatment
2	EFD111	TA	1	Control	2	TXT1	Control Vehicle	Treatment
3	EFD111	TA	1	Control	3	POSTTXT	Post-treatment	Post-treatment
4	EFD111	TA	1.TK	Control - TK	1	PRETXT	Pre-treatment	Pre-treatment
5	EFD111	TA	1.TK	Control - TK	2	TXT1TK	Control Vehicle - TK	Treatment
6	EFD111	TA	2	10 mg/kg/day	1	PRETXT	Pre-treatment	Pre-treatment
7	EFD111	TA	2	10 mg/kg/day	2	TXT2	10 mg/kg/day A123	Treatment
8	EFD111	TA	2	10 mg/kg/day	3	POSTTXT	Post-treatment	Post-treatment
9	EFD111	TA	2.TK	10 mg/kg/day - TK	1	PRETXT	Pre-treatment	Pre-treatment
10	EFD111	TA	2.TK	10 mg/kg/day - TK	2	TXT2TK	10 mg/kg/day A123 - TK	Treatment
11	EFD111	TA	3	50 mg/kg/day	1	PRETXT	Pre-treatment	Pre-treatment
12	EFD111	TA	3	50 mg/kg/day	2	TXT3	50 mg/kg/day A123	Treatment
13	EFD111	TA	3	50 mg/kg/day	3	POSTTXT	Post-treatment	Post-treatment
14	EFD111	TA	3.TK	50 mg/kg/day - TK	1	PRETXT	Pre-treatment	Pre-treatment
15	EFD111	TA	3.TK	50 mg/kg/day - TK	2	TXT3TK	50 mg/kg/day A123 - TK	Treatment

7 Changes to Existing Domains

7.1 Effects on Existing Domains When Submitted for DART Studies

Table 7.1a: Changes to Existing Domains in the SENDIG

Domain Code	Domain	Domain Class	Metadata (SENDIG) and CT Changes	SENDIG-DART Variables *(Variables must be implemented in the order shown in the SDTM v1.6)*
*DM	Demographics	Special-Purpose	RFXSTDTC (Exp), RFXENDTC (Exp)	RPATHCD (Exp)
*EX	Exposure	Interventions		RPHASE (Exp), RPPLSTDY (Perm), RPPLENDY (Perm), EXRPSTDY (Exp), EXRPENDY (Perm)
*DS	Disposition	Events	DSNOMDY (Perm)	RPHASE (Exp), RPPLSTDY (Perm), DSRPSTDY (Exp)
CO	Comments	Special-Purpose		RPHASE, CORPDY (Perm)
SC	Subject Characteristics	Findings		RPHASE, SCRPDY (Perm)
BW	Body Weight	Findings	BWNOMDY (Perm), BWBLFL (Perm) TEST and TESTCD CT	RPHASE, RPPLDY, BWRPDY (Exp)
BG	Body Weight Gain	Findings	TEST and TESTCD CT	RPHASE (Exp), RPPLDY (Perm), RPPLENDY (Perm), BGRPDY (Exp), BGRPENDY (Exp)
FW	Food and Water Consumption	Findings		RPHASE (Exp), RPPLDY (Perm), RPPLENDY (Perm), FWRPDY (Exp), FWRPENDY (Exp)
CL	Clinical Observations	Findings	CLNOMDY (Perm)	RPHASE (Exp), RPPLDY (Exp), RPPLENDY (Perm), CLRPDY (Exp), CLRPENDY (Perm)
LB	Laboratory Test Results	Findings	LBNOMDY (Perm)	RPHASE (Exp), RPPLDY (Exp), RPPLENDY (Perm), LBRPDY (Exp), LBRPENDY (Perm)
PC	Pharmacokinetics Concentrations	Findings	PCNOMDY (Perm)	RPHASE (Exp), RPPLDY (Exp), RPPLENDY (Perm), PCRPDY (Exp), PCRPENDY (Perm)
PP	Pharmacokinetics Parameters	Findings	PPNOMDY (Perm)	RPHASE, RPPLDY, PPRPDY (Exp)
DD	Death Diagnosis	Findings		RPHASE, DDRPDY (Exp)
MA	Macroscopic Findings	Findings		RPHASE, RPPLDY, MARPDY (Perm)
OM	Organ Measurements	Findings	OMNOMDY (Perm)	RPHASE, RPPLDY, OMRPDY (Exp)
MI	Microscopic Findings	Findings		RPHASE, MIRPDY (Perm)

** Required Domains*

( ) Unless otherwise specified, the Core expectancy indicated in parenthesis applies to all the Variables listed for the Domain Code.

Table 7.1b: Existing Domains in the SENDIG with No Changes

Domain Code	Domain	Domain Class	Description
*TS	Trial Summary	Trial Design	Domains have no specific changes to domain structure or controlled terminology.
*TA	Trial Arms	Trial Design	
*TE	Trial Elements	Trial Design	
*TX	Trial Sets	Trial Design	
SE	Subject Elements	Special-Purpose	

7.2 Demographics – DM

Two SDTM variables, RFXSTDTC and RFXENDTC, have been added to DM for the DART implementation to provide the start and end of treatment dates in DM, since these may be different from the reference study start date (RFSTDTC) and end date (RFENDTC) defined in Demographics. The former variables were introduced in the SDTM v1.3 (July 2012), and do not appear in the published SEND Implementation Guide.

RPATHCD is a variable in the DM domain for DART studies. RPATHCD is defined in the Trial Paths (TP) domain.

These variables must be implemented in the order shown in the SDTM v1.6.

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core	SEND Variable Order
RFXSTDTC	Date/Time of First Study Treatment	Char	ISO 8601	Timing	First date of exposure to any protocol-specified treatment in ISO 8601 character format. Equal to the earliest value of EXSTDTC.	Exp	After RFENDTC, before RFXENDTC
RFXENDTC	Date/Time of Last Study Treatment	Char	ISO 8601	Timing	Last date of exposure to any protocol-specified treatment in ISO 8601 character format. Equal to the latest value of EXENDTC (or the latest value of EXSTDTC if EXENDTC was not collected).	Exp	After RFXENDTC, before SITEID
RPATHCD	Planned Repro Path Code	Char		Record Qualifier	Short name for the Repro Path (RPATH) to which the subject was assigned in the TP domain. Limited to 20 characters.	Exp	After SETCD

7.2.1 Assumptions for Demographics (DM) Domain Model

1. When submitting study design information, the values for RPATHCD should be identical to the values defined for that subject in the Trial Repro Paths (TP) domain. When TP is submitted, RPATHCD is required in DM structure; likewise, when RPATHCD is populated in DM, the TP domain is required. The assignment of values should be consistent, if possible, within a submission.
2. RFSTDTC is a study day variable only, and is equivalent to the protocol-defined Study Day 1 for a subject. This date/time variable may or may not be equivalent to the start of treatment (RFXSTDTC) in a DART study.

7.2.2 Examples for Demographics (DM) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1
(EFD Toxicity and TK Study in Rabbits)

Exact birth dates are unknown; however, the age range at study start is available (AGETXT, AGEU). The planned Repro Path (RPATHCD) is different for non-TK (GEST) and TK (GESTTK) subjects.

Row 1: Illustrates the demographic record for F0 female 01. The RFSTDTC is GD (GD) 0 and the RFENDTC is GD 28 via scheduled C-section. Treatment was administered daily from GD 7 (RFXSTDTC) through GD 20 (RFXENDTC).

Rows 2-3: F0 females 05 and 06 were terminated for TK sampling on GD 15 (RFENDTC). TK assigned females are in a different Trial Set (SETCD) than non-TK females. Females 05 and 06 have a different ARMCD and RPATHCD than female 01.

Rows 4-6: Illustrates a subject in a different treatment group (ARMCD and/or SETCD) from subjects in Rows 1-3, but have the same PATHCD.

Row	STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	AGETXT	AGEU	SEX	ARMCD	SETCD	RPATHCD
1	XYZ	DM	XYZ-01	01	2005-07-05	2005-08-02	2005-07-12	2005-07-25	5-6	MONTHS	F	1	1	EFD
2	XYZ	DM	XYZ-05	05	2005-07-05	2005-07-20	2005-07-12	2005-07-19	5-6	MONTHS	F	1TK	1TK	EFDTK
3	XYZ	DM	XYZ-06	06	2005-07-05	2005-07-20	2005-07-12	2005-07-19	5-6	MONTHS	F	1TK	1TK	EFDTK
4	XYZ	DM	XYZ-20	20	2005-07-05	2005-08-02	2005-07-12	2005-07-25	5-6	MONTHS	F	2	2	EFD
5	XYZ	DM	XYZ-25	25	2005-07-05	2005-07-20	2005-07-12	2005-07-19	5-6	MONTHS	F	2TK	2TK	EFDTK
6	XYZ	DM	XYZ-26	26	2005-07-05	2005-07-20	2005-07-12	2005-07-19	5-6	MONTHS	F	2TK	2TK	EFDTK

7.3 Body Weight – BW

A test for the gestation body weight adjusted for the gravid uterus weight on the day of C-section was added to the BWTESTCD and BWTEST CT lists. The gravid uterus weight, if collected, is submitted in the Organ Measurements (OM) domain.

The BWBLFL variable is Permissible for DART studies (Table 7.1a) and therefore the column is not expected in the dataset unless it was collected.

Timing variables, RPHASE, RPPLDY, and BWRPDY are Expected per Table 7.1a. The Study Day variable (BWDY), Permissible per the SENDIG, may be included in examples for demonstration purposes.

The timing variables must be implemented in the order shown in the SDTM v1.6. As a convenience the Repro Phase Day variable order is also shown in Appendix C.

7.3.1 Examples for Body Weight (BW) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1
This example represents maternal body weights in an EFD toxicity and TK study in rabbits. Gestation Day (GD) 0 is 2010-09-13.

Rows 1-4: Illustrate body weights collected for female 01 on GD 0, 7, 14, and 28.

Row 5: Illustrates the adjusted body weight on GD 28 for female 01 that was adjusted for the gravid uterus weight (OM domain) recorded at C-section.

Rows 6-8: Illustrate body weights collected for female 02 on GD 0, 7, and 14. Female 02 was terminated on GD 15 for TK sampling.

Row	STUDYID	DOMAIN	USUBJID	BWSEQ	BWTESTCD	BWTEST	BWORRES	BWORRESU	BWSTRESC	BWSTRESN
1	10020	BW	10020-01	1	BW	Body Weight	2202	g	2202	2202
2	10020	BW	10020-01	2	BW	Body Weight	2070	g	2070	2070
3	10020	BW	10020-01	3	BW	Body Weight	2000	g	2000	2000
4	10020	BW	10020-01	4	BW	Body Weight	2182	g	2182	2182
5	10020	BW	10020-01	5	BWADJGU	Gravid Uterus Adjusted Body Weight	2030	g	2030	2030
6	10020	BW	10020-02	6	BW	Body Weight	2195	g	2195	2195
7	10020	BW	10020-02	7	BW	Body Weight	1905	g	1905	1905
8	10020	BW	10020-02	8	BW	Body Weight	2010	g	2010	2010

Row	BWSTRESU	RPHASE	RPPLDY	BWDTC	BWDY	BWRPDY
1 (cont)	g	GESTATION	0	2010-09-13T09:11	1	0
2 (cont)	g	GESTATION	7	2010-09-20T08:53	8	7
3 (cont)	g	GESTATION	14	2010-09-27T08:56	15	14
4 (cont)	g	GESTATION	28	2010-10-11T09:11	29	28
5 (cont)	g	GESTATION	28	2010-10-11T09:11	29	28
6 (cont)	g	GESTATION	0	2010-09-13T09:11	1	0
7 (cont)	g	GESTATION	7	2010-09-20T08:53	8	7
8 (cont)	g	GESTATION	14	2010-09-27T08:56	15	14

Example 2

This example represents maternal body weights in an EFD toxicity study in rats. GD 0 is 2010-03-01.

Rows 1-5: Illustrate body weights collected for female (dam) 05 on GD 0, 6, 12, 13, and 21. The GD 13 body weight was unscheduled and is excluded from the summary data, BWEXCLFL = Y. Since GD 13 weight was not planned RPPLDY is null.

Row 6: Illustrates the GD 21 body weight adjusted for the gravid uterus weight.

Rows 7-10: Illustrate gestation body weights collected for female (dam) 06 on GD 0, 6, 12, and 21. This female had all resorptions and the sponsor elected to exclude GD 21 from the maternal body weight summary data, BWEXCLFL = Y.

Row	STUDYID	DOMAIN	USUBJID	BWSEQ	BWTESTCD	BWTEST	BWORRES	BWORRESU	BWSTRESC	BWSTRESN	BWSTRESU
1	99001	BW	99001-05	1	BW	Body Weight	217	g	217	217	g
2	99001	BW	99001-05	2	BW	Body Weight	243	g	243	243	g
3	99001	BW	99001-05	3	BW	Body Weight	240	g	240	240	g
4	99001	BW	99001-05	4	BW	Body Weight	242	g	242	242	g
5	99001	BW	99001-05	5	BW	Body Weight	365	g	365	365	g
6	99001	BW	99001-05	6	BWADJGU	Gravid Uterus Adjusted Body Weight	306	g	306	306	g
7	99001	BW	99001-06	7	BW	Body Weight	215	g	215	215	g
8	99001	BW	99001-06	8	BW	Body Weight	260	g	260	260	g
9	99001	BW	99001-06	9	BW	Body Weight	290	g	290	290	g
10	99001	BW	99001-06	10	BW	Body Weight	390	g	390	390	g

Row	BWEXCLFL	BWREASEX	BWUSCHFL	RPHASE	RPPLDY	BWDTC	BWDY	BWRPDY
1 (cont)				GESTATION	0	2010-03-01T08:30	1	0
2 (cont)				GESTATION	6	2010-03-07T08:39	7	6
3 (cont)				GESTATION	12	2010-03-13T08:58	13	12

Row	BWEXCLFL	BWREASEX	BWUSCHFL	RPHASE	RPPLDY	BWDTC	BWDY	BWRPDY
4 (cont)	Y	Inadvertently weighed on GD 13	Y	GESTATION		2010-03-14T08:20	14	13
5 (cont)				GESTATION	21	2010-03-22T06:57	22	21
6 (cont)				GESTATION	21	2010-03-22T07:18	22	21
7 (cont)				GESTATION	0	2010-03-01T08:31	1	0
8 (cont)				GESTATION	6	2010-03-07T08:40	7	6
9 (cont)				GESTATION	12	2010-03-13T08:59	13	12
10 (cont)	Y	Female had all resorptions.		GESTATION	21	2010-03-22T07:30	22	21

7.4 Body Weight Gain – BG

A test for body weight gains adjusted for the gravid uterus weight on the day C-section was added to the BGTESTCD and BGTEST CT lists. The gravid uterus weight is submitted in the Organ Measurements (OM) domain.

Timing variables RPHASE, BGRPDY, and BGRPENDY are Expected per Table 7.1a. RPLDY and RPPLENDY, Permissible per Table 7.1a, may be included in examples for illustration purposes. Study Day timing variables BGDY and BGENDY, Permissible per the SENDIG, may be included in examples for illustration purposes.

7.4.1 Repro Examples for Body Weight Gain (BG) Domain Model

The terminology used in some examples is for illustration purposes only, and may not represent CDISC Controlled Terminology. Controlled terminology may be published for use at a later time. Data providers should check for the latest version of CDISC Controlled Terminology (available at http://www.cancer.gov/research/resources/terminology/cdisc).

Example 1
This example represents body weight changes for maternal subject 11 in an EFD toxicity (EFD) study in rats. The scheduled C-section occurred on GD 20.

Row 1: Illustrates the maternal body weight change between GD 0-6.
Rows 2-3: Illustrate BGSTAT / BGREASND. The maternal body weight changes could not be derived for planned intervals GD 6-8 and GD 8-14 due to the missing GD 8 body weight. Since the intervals could not be generated, BGDY, BGENDY, BGRPDY, and BGRPENDY (actual study and phase day variables) are null.
Rows 4-5: Illustrate the maternal body weight change between GD 6-14 and GD 6-20.
Row 6: Illustrates the adjusted maternal body weight gain between GD 6 and adjusted GD 20. The GD 20 maternal body weight was adjusted for the gravid uterus weight.

Row	STUDYID	DOMAIN	USUBJID	BGSEQ	BGTESTCD	BGTEST	BGORRES	BGORRESU	BGSTRESC	BGSTRESN	BGSTRESU
1	10333	BG	10333-11	1	BWGAIN	Body Weight Gain	43.4	g	43.4	43.4	g
2	10333	BG	10333-11	2	BWGAIN	Body Weight Gain					
3	10333	BG	10333-11	3	BWGAIN	Body Weight Gain					
4	10333	BG	10333-11	4	BWGAIN	Body Weight Gain	45.8	g	45.8	45.8	g
5	10333	BG	10333-11	5	BWGAIN	Body Weight Gain	153.0	g	153.0	153	g
6	10333	BG	10333-11	6	BWGAINGU	Gravid Uterus Adjusted	75.1	g	75.1	75.1	g

Row	STUDYID	DOMAIN	USUBJID	BGSEQ	BGTESTCD	BGTEST	BGORRES	BGORRESU	BGSTRESC	BGSTRESN	BGSTRESU
						Body Weight Gain					

Row	BGSTAT	BGREASND	RPHASE	RPPLDY	RPPLENDY	BGDTC	BGENDTC	BGDY	BGENDY	BGRPDY	BGRPENDY
1 (cont)			GESTATION	0	6	2008-08-01T07:20	2008-08-07T07:15	1	7	0	6
2 (cont)	NOT DONE	Missing GD 8 body weight	GESTATION	6	8	2008-08-07T07:15					
3 (cont)	NOT DONE	Missing GD 8 body weight	GESTATION	8	14		2008-08-15T07:03				
4 (cont)			GESTATION	6	14	2008-08-07T07:15	2008-08-15T07:03	7	15	6	14
5 (cont)			GESTATION	6	20	2008-08-07T07:15	2008-08-21T07:42	7	21	6	20
6 (cont)			GESTATION	6	20	2008-08-07T07:15	2008-08-21T07:42	7	21	6	20

Appendices

Appendix A: CDISC SEND Development and Reproductive Toxicology (DART) Subteam*

DART Subteam Contributors	
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** Individuals having met membership criteria throughout the development of the version.*
*** Individuals are members of the DART Subteam and DART Controlled Terminology Workstream.*

Appendix B: Glossary and Acronyms

The following abbreviations and terms are used in this document. Additional definitions can be found in the CDISC Glossary (http://www.cdisc.org/cdisc-glossary).

CDISC	Clinical Data Interchange Standards Consortium
CT	Controlled Terminology
C-section	Cesarean Section
DART	Developmental and Reproductive Toxicology
Dataset	A collection of structured data in a single file
Domain	A collection of observations with a topic-specific commonality.
EFD	Embryo-Fetal Development
GD	Gestation Day
ISO	International Organization for Standardization
ISO 8601	ISO character representation of dates, date/times, intervals, and durations of time. The SDTM uses the extended format.
SDTM	Study Data Tabulation Model
Repro	Reproductive
SDTMIG	Study Data Tabulation Model Implementation Guide
SEND	Standard for Exchange of Nonclinical Data
SENDIG	Standard for Exchange of Nonclinical Data Implementation Guide
SENDIG-DART	Standard for Exchange of Nonclinical Data Implementation Guide for Developmental and Reproductive Toxicology Studies
TK	Toxicokinetic

Appendix C: Repro Phase Day Timing Variable Order

Variable Name	Variable Label	Type	Role	Description	SDTM v1.6 Variable Order
RPHASE	Repro Phase	Char	Timing	Name of the Repro Phase which this Repro Stage of the Repro Path is associated. Defined in Trial Repro Paths (TP) domain. The RPHASE variable is Required when any Phase Day variable is used.	After EPOCH, before RPPLDY
RPPLDY	Planned Repro Phase Day of Observation	Num	Timing	The planned Repro Phase day in which the observation was scheduled to occur. Expressed as an integer.	After RPHASE, before RPPLSTDY
RPPLSTDY	Planned Repro Phase Day of Obs Start	Num	Timing	The planned Repro Phase day of the start of the observation. Expressed as an integer.	After RPPLDY, before RPPLENDY
RPPLENDY	Planned Repro Phase Day of Obs End	Num	Timing	The planned Repro Phase day of the end of the observation. Expressed as an integer.	After RPPLSTDY, before --DTC
--RPDY	Actual Repro Phase Day of Observation	Num	Timing	The actual Repro Phase day in which the observation occurred. Expressed as an integer.	After --NOMLBL, before --RPSTDY
--RPSTDY	Actual Repro Phase Day of Obs Start	Num	Timing	The actual Repro Phase day of the start of the observation. Expressed as an integer.	After –RPDY, before --RPENDY
--RPENDY	Actual Repro Phase Day of Obs End	Num	Timing	The actual Repro Phase day of the end of the observation. Expressed as an integer.	After --RPSTDY, before --DUR

Appendix D: Dataset Metadata Definition

"Using the SEND Domain Models in Regulatory Submissions – METADATA" is covered in Section 3 of the SENDIG.

The dataset definition below is an example for an EFD Toxicity Study. Contents may vary depending on the domains submitted for a particular study and how keys for each domain are defined.

Dataset	Description	Class	Structure	Purpose	Keys	Location
TS	Trial Summary	Special-Purpose Domain	One record per Trial Summary parameter value	Tabulation	STUDYID, TSPARMCD, TSSEQ	ts.xpt
TE	Trial Elements	Special-Purpose Domain	One record per planned Element	Tabulation	STUDYID, ETCD	te.xpt
TA	Trial Arms	Special-Purpose Domain	One record per planned Element per Arm	Tabulation	STUDYID, ARMCD, TAETORD	ta.xpt
TX	Trial Sets	Special-Purpose Domain	One record per Trial Set parameter per Trial Set	Tabulation	STUDYID, SETCD, TXPARMCD	tx.xpt
TT	Trial Stages	Special-Purpose Domain	One record per planned Stage	Tabulation	STUDYID, RSTGCD	tt.xpt
TP	Trial Paths	Special-Purpose Domain	One record per planned Stage per Path	Tabulation	STUDYID, RPATHCD, TPSTGORD	tp.xpt
DM	Demographics	Special-Purpose Domain	One record per subject	Tabulation	STUDYID, USUBJID	dm.xpt
EX	Exposure	Interventions	One record per constant dosing interval per treatment per subject or pool	Tabulation	STUDYID, USUBJID or POOLID, EXTRT, EXSTDTC	ex.xpt
SE	Subject Elements	Special-Purpose Domain	One record per element experienced per subject	Tabulation	STUDYID, USUBJID, ETCD, SESTDTC	se.xpt
SJ	Subject Stages	Special-Purpose Domain	One record per Actual Stage	Tabulation	STUDYID, USUBJID, RSTGCD	sj.xpt
BW	Body Weights	Findings	One record per test per observation time per subject	Tabulation	STUDYID, USUBJID, BWTESTCD, BWDTC	bw.xpt
BG	Body Weight Gains	Findings	One record per test per interval per subject	Tabulation	STUDYID, USUBJID, BGTESTCD, BGDTC, BGENDTC	bg.xpt
FW	Food and Water Consumption	Findings	One record per test per interval per subject or pool	Tabulation	STUDYID, USUBJID or POOLID, FWTESTCD, FWDTC, FWENDTC	fw.xpt
CL	Clinical Observations	Findings	One record per finding per observation time per subject or pool	Tabulation	STUDYID, USUBJID or POOLID, CLTESTCD, CLCAT, CLORRES, CLLOC, CLDTC	cl.xpt
PC	Pharmacokinetics Concentrations	Findings	One record per test per specimen per observation time per subject or pool	Tabulation	STUDYID, USUBJID or POOLID, PCTESTCD, PCSPEC, PCDTC	pc.xpt
DS	Disposition	Events	One record per subject	Tabulation	STUDYID, USUBJID	ds.xpt
DD	Death Diagnosis	Findings	One record per diagnosis per subject (for unscheduled deaths only)	Tabulation	STUDYID, USUBJID	dd.xpt
MA	Macroscopic	Findings	One record per	Tabulation	STUDYID, USUBJID,	ma.xpt

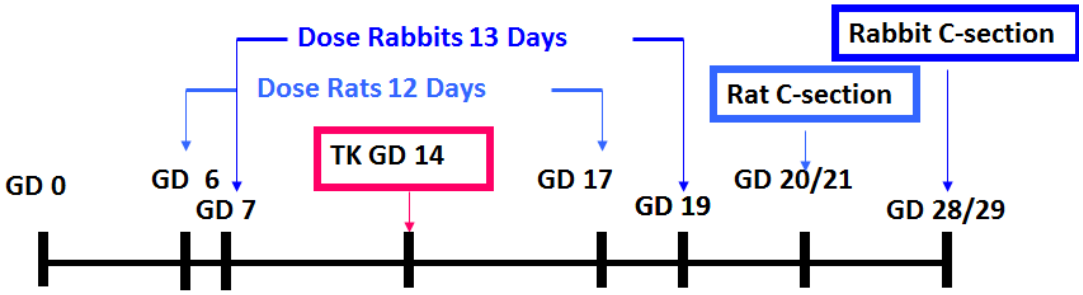
Dataset	Description	Class	Structure	Purpose	Keys	Location
	Findings		finding per specimen per subject		MATESTCD, MAORRES, MASPEC, MAANTREG, MALAT, MADIR	
OM	Organ Measurements	Findings	One record per test per specimen per subject	Tabulation	STUDYID, USUBJID, OMTESTCD, OMSPEC, OMANTREG, OMLAT, OMDIR	om.xpt
IC	Implantation Classification	Findings	One record per implantation site per fetus per subject	Tabulation	STUDYID, USUBJID, FETUSID, ICTESTCD, ICIMPLBL, ICRESLOC	ic.xpt
FX	Fetal Pathology Findings	Findings	One record per category per finding per specimen per fetus per subject	Tabulation	STUDYID, USUBJID, FETUSID, FXTESTCD, FXLOC, FXSTRESC, FXRESLOC	fx.xpt
FM	Fetal Measurements	Findings	One record per finding per fetus per subject	Tabulation	STUDYID, USUBJID, FETUSID, FMTESTCD, FXLOC	fm.xpt
PY	Nonclinical Pregnancy Results	Findings	One record per test per subject	Tabulation	STUDYID, USUBJID, PYTESTCD	py.xpt
CO	Comments	Special-Purpose Domain	One record per comment	Tabulation	STUDYID, COSEQ	co.xpt

Appendix E: Supplemental Information – Study Design Diagrams

Appendix E1: EFD Toxicity Example Diagram 1

This diagram is an example of what the study timeline may be for a Rat or Rabbit EFD Toxicity study. Exact endpoints may vary between species / strains and data providers.

Embryo-fetal Developmental Toxicity and Toxicokinetic Study in Rats



Standard Parameters

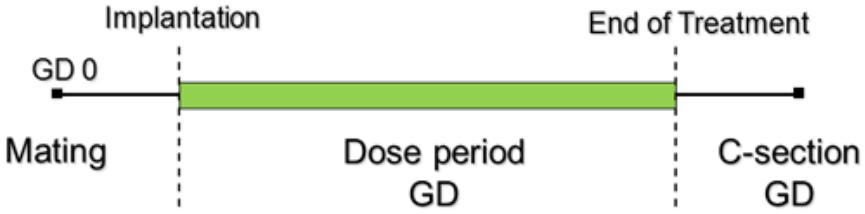
Clinical Signs, Body Weights, Food Consumption, Toxicokinetic (TK), Gross Pathology

Cesarean Section

Pregnancy, Corpora Lutea, Implantations, Resorptions, Fetal viability, Fetal Gender & Weight, Fetal Morphology

Appendix E2: EFD Toxicity Example Diagram 2

This diagram is an example of what the study timeline may be for a different species. Exact endpoints may vary between data providers.



Rat	6-17	20/21
Mouse	6-15	18
Rabbit	6-19	28/29
Monkey	20-50	100

= Dose Period

Appendix F: Representations and Warranties, Limitations of Liability, and Disclaimers

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