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Findings about "Findings About"

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ABSTRACT

Study Data Tabulation Model (SDTM), defines standard structure for study data tabulations for regulatory submissions. This not only saves time and money but also furnishes a choice for sponsors to automate the process of standard data creation.

SDTM defines general observation class which is further divided among three classes Interventions, Events and Findings. The SDTM does not allow the addition of new variable; In addition the supplemental Qualifiers special purpose model is used to capture non-standard variables.

In some situations it is observed that collected data from the case report form can neither be represented within an Event nor in Intervention also it is not always easy to map information in supplemental qualifiers. In such situations findings about domain models are utilized.

This paper discusses advantages of findings about model in certain situations. Case studies from the real life studies will be discussed to get familiar with Findings About.

INTRODUCTION

SDTM (Study Data Tabulation Model) defines a standard structure for human clinical trial data tabulations and SEND (for nonclinical study data tabulations) that are to be submitted as part of a product application to a regulatory authority such as FDA. Observations about subjects are normally collected for all subjects in a series of domains. A domain is defined as a collection of logically related observations with a common topic.

Almost 80% observations collected during the study (other than those represented in special purpose domains) can fit among three general observation classes: Interventions, Events, or Findings.

An intervention captures administration information of therapeutic medications, investigational products, surgical procedures and any other substances that affect physiological changes in the body. Information about planned protocol milestones such as randomization, study completion and occurrences of incidents during the trial or prior to the trial is generally categorized in the event class domains. Findings class addresses the observations resulting from planned evaluations to address specific questions made during the study.

So, what if the information from the study does not fit into events or interventions as a whole but it says something more about them?

Some of the collected data may not directly fit in the specific domain or its supplemental qualifier dataset, but it may impart more information regarding say event or intervention. In such a case, 'Findings about (FA)' domain can be utilized.

FA DOMAIN

FA domain is defined to store findings about Events or Interventions in a vertical structure. FA domain is a specialization of the Findings class with a little addition of a unique variable "--OBJ". FAOBJ provides a description of the Event or Intervention that the measurement/evaluation is about and it is a required variable for FA domain. The value in FAOBJ is required to match the value in the corresponding --TERM or –TRT variables in the event or intervention domain that FA is describing. When the parent domain is dictionary coded or subject to controlled terminology FAOBJ should match the value in –DECOD.

Another important variable is FATESTCD which as the topic variable describes the measurement/evaluation. Both FA and findings domain are exactly same in structure with the exception of "--OBJ".

The following qualifiers are generally not used in FA --BODSYS, --MODIFY, --SEV, --TOXGR. (Refer Section 6.4.5 of SDTMIG 3.1.3)

Some data situations where FA domain can be used are –

- Data that does not describe an event or intervention as a whole
  e.g. If severity of an AE is collected at scheduled time points throughout the duration of the study, the severities have timing information associated that does not fit in SDTM.AE structure.

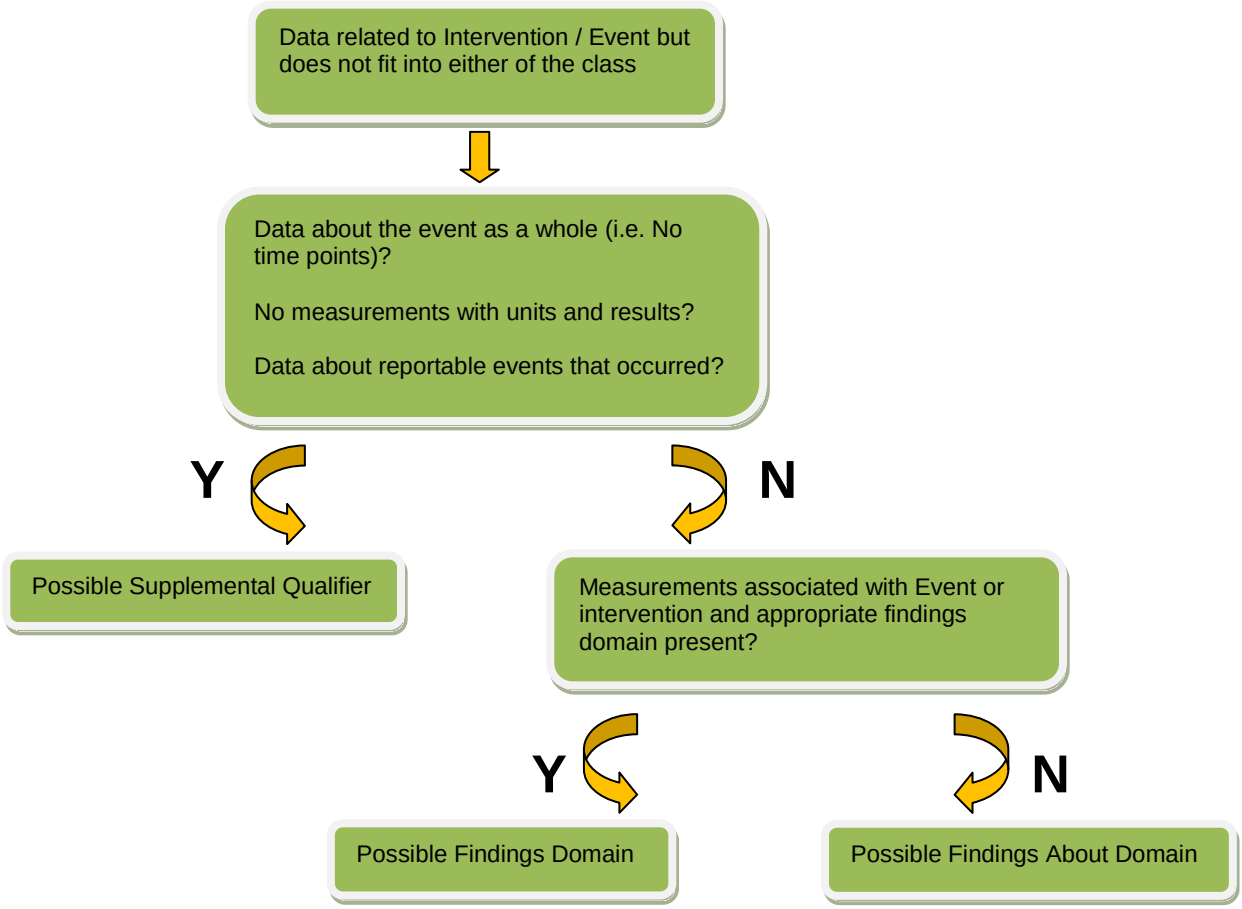
- Data that indicates the occurrence of related symptoms
  e.g. If event is SEIZURE and clinical features related to the event are collected viz. Abnormal Motor Activity and Accidental Injury.

- Data for which no Event or Intervention record has been collected or created
  e.g. Reasons for not taking any concomitant medication are collected but the reasons were not collected as part of Concomitant Medications because it was a prerequisite for study participation.

- Data that indicate the occurrence of pre specified AE's
  e.g. Answers to probing questions about the occurrence of pre-specified adverse events can be stored in the FA domain, and for each positive response there would be a record reflected in the AE domain. The FA and the AE records would then need be linked via RELREC.

- Data having qualifiers that can be represented in Findings variables (units and methods)
  e.g. If the risk of bacterial infection is measured, then the result and measurement unit can be represented in the FA domain in a single record, while other information regarding the high risk of infection (e.g., start and end times), if collected would appear in an Event record.

The following diagram elaborates how the decision of using FA can be made.



The examples discussed in this paper are from phase I/II or phase III studies from different therapeutic areas. For these studies, SDTM datasets were created and validated as per SDTM Implementation Guide. Also snapshot of data is given with essential variables wherever required. These examples describe the scenarios where FA domain had been used. In these cases there may be an alternative approach to mapping and several solutions could be considered valid. Consideration should be about both how the data is collected and linked together on a CRF and how the data will be analyzed.

FINDINGS ABOUT INTERVENTION EXAMPLES

CASE1

DESCRIPTION:

In a study, vitamin D was used as a supplement along with study medication. The eCRF page collects information about reasons why vitamin D was not used at baseline.

Observations about Vitamin D usage such as how many times taken, dose etc. can be represented in interventions class (CM) and the reasons for not taking vitamin D can fit into supplemental qualifiers of CM domain. To utilize this information further in tables or listings data transpose is needed. To avoid this, information can be mapped into findings about intervention domain.

Here FATESTCD describes the evaluation i.e. reason for not taking Vitamin D and FAORRES collects all available reasons. In this case "--OBJ" describes the intervention that the evaluation is about. So FAOBJ is defined as 'Vitamin D'.

The annotated eCRF is given below.

SDTM Data Set Name = FA | FA.DOMAIN = 'FA'

FORM: Reason for no baseline Vitamin D Usage

If not vitamin D, Why?

FA.FATESTCD = 'REASNTKN'

FA.FAOBJ = 'VITAMIN D'

Elevated Serum Calcium
Elevated Serum Phosphorus
Elevated Calcium X Phosphorous
Not Prescribed
Other

FA.FAORRES

The data snapshot can be viewed below

DOMAIN	USUBJID	FASEQ	FASPID	FATEST	FAORRES	VISIT	FAOBJ	FAPRESP
FA	11112222-111111111	1	W1-000-000	Reason Not Taken	ELEVATED SERUM PHOSPHOROUS	WEEK 1	VITAMIN D	Y
FA	11112222-111111112	1	W1-000-000	Reason Not Taken	OTHER	WEEK 1	VITAMIN D	Y

CASE2

DESCRIPTION:

This example is from an open label, multicenter, phase II oncology study to evaluate efficacy and safety of study drug. Study treatment was administered as a continuous IV infusion at a constant flow rate over four weeks followed by a two-week treatment free interval prior to the next treatment cycle. Also protocol says Infusion bags should be changed in accordance with local pharmacy standards. These bags should be changed every four days for infusion of compounded sterile products at latest and this was done by nursing personnel.

In this study, case report form captures the information such as study medication switched from one lot number to other and when it was switched.

Reason for using FA: This situation is about the change of study medication material but it cannot be considered about the study medication in particular because the standard EX domain describes by subject dose data. Also it cannot fit into SUPPEX since there is no direct link to corresponding EX record as eCRF provided particular lot numbers. Hence FA is utilized.
Following is the snapshot of eCRF.

SDTM Data Set Name = FA | FA.DOMAIN = 'FA'

FA.FACAT = 'CHANGE OF STUDY MATERIAL'

FORM: CHANGE OF STUDY MATERIAL

Was medication switched from lot number 34628 or 34629? — FA.FAORRES | FA.FATESTCD = 'SWITCHED'

Date of Medication Switch — FA.FADTC | FA.FAOBJ = 'MEDICATION TO LOT NUMBER 34628 OR 34629'

CASE3

DESCRIPTION:

This is a multicenter, phase 1/2, open-Label study evaluating the tolerability, safety, pharmacokinetics, and efficacy of study treatment in subjects with cancer. One of the eCRF pages considers prior radio therapy for checking medical condition of subject who is becoming progressively worse.

Radiotherapy uses radiation, such as x-rays, gamma rays, electron beams or protons, to kill or damage cancer cells and stop them from growing and multiplying. It is a localized treatment, which means it generally only affects the part of the body where the radiation is directed. The CRF page collects information such as

a) Location where the radiotherapy was applied, when was it started and ended and type of radiotherapy.
b) Also this page addresses the patient's best response at that time and asks whether chemotherapy was taken and if progression occurred.

The information given in type a) (above) can very well fit into PR (Procedures) domain (Refer Section 6.1 of SDTMIG 3.2) as it is about therapeutic and diagnostic procedures. In order to fit the type of data given in Type b (above) into PR for use of each question supplemental qualifier is needed. So here 3 supplemental qualifier variables were needed for questions.

Although this is a cancer study the questions related to response or progressions are significant for analysis, so dumping this kind of data into supplemental qualifiers can become painful. So to utilize this information effectively FA is used.

The snap shot of annotated eCRF is given below

SDTM Data Set Name = FA | FA.DOMAIN = 'FA'

FA.FACAT = 'HISTORICAL RADIOTHERAPY'

FA.FAOBJ = 'RADIOTHERAPY' | FA.FAPRESP = 'Y'

There are multiple pages being mapped to FA domain in this study which is why FACAT is used to categorize those observations

FORM: Prior Radiotherapy for current malignancy

Best Response	FA.FATESTCD = 'BESTRSP'	Complete Response Partial Response Stable Response Progressive Disease Unable to evaluate Not Done	FA.FAORRES
Was chemotherapy part of a concurrent therapy?	FA.FATESTCD = 'CHEMO'	Yes No	FA.FAORRES
Did progression occur?	FA.FATESTCD = 'PRG'	Yes No	FA.FAORRES
Date of Progression			FA.FADTC

RELREC - In this example a dataset-level relationship between PR and FA is established using an identifier (SPID). The value of SPID was populated with a database generated unique identifier to each iteration of this form.

The data snap shot is given below

SDTM.PR

DOMAIN	USUBJID	PRSEQ	PRSPID	PRTRT	PRSTDTC	VISIT	PRDOSFRM	PRPRESP
PR	88882222-12121211	1	DAY2-000-018	RADIOTHERAPY	2012-08-02	DAY2	EXTERNAL BEAM	Y

SDTM.FA

DOMAIN	USUBJID	FASEQ	FASPID	FATEST	VISIT	FASTRESC	FAOBJ	FAPRESP
FA	88882222-12121211	1	DAY2-000-018	Progression	DAY2	Y	RADIOTHERAPY	Y
FA	88882222-12121211	2	DAY5-000-010	Best Response	DAY5	STABLE DISEASE	RADIOTHERAPY	Y

SDTM.RELREC

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
1	ABC	PR		PRSPID		ONE	1
2	ABC	FA		FASPID		MANY	1

CASE4

DESCRIPTION:
This is a multicenter, randomized, double-blind, placebo-controlled, phase 2 study of IP or placebo with standard of care (SOC) in Postmenopausal Women with Metastatic Breast Cancer.

In this scenario, SOC administration time on PK page was collected. As per protocol Subjects were expected to self-administer the SOC except on PK sample collection days. On PK collection days, SOC would be administered 1 to 2 hours before IP infusion. The CRF page of SOC administration collects details such as date and time of administration and addresses questions like 'did subject eat a meal within 2 hours prior to SOC dose', 'did subject vomit within 1 hour after SOC administration' etc**.**

The collected data meet the following FA criteria:
1) Data that do not describe an Intervention as a whole
2) Data about an Intervention having different timing from the associated intervention as a whole

SDTM Data Set Name = FA | FA.DOMAIN = 'FA' | FA.FACAT = 'PK'

SOC ADMINISTRATION TIME ON PK COLLECTION DAYS

Date and time of SOC administration

FA.FATESTCD = 'OCCUR' | FA.FAOBJ = 'SOC' | FA.FAORRES = 'Y' | FA.FADTC

Did subject eat a meal within 2 hours prior to SOC dose?

FA.FATESTCD = 'OCCUR' | FA.FAOBJ = 'MEAL' | FA.FAORRES | FA.FAEVLINT = '-P2H' | FA.FATPTREF = 'PK SOC'

Did subject vomit within 1 hour after SOC administration?

FA.FATESTCD = 'OCCUR' | FA.FAOBJ = 'VOMIT' | FA.FAORRES | FA.FAEVLINT = 'P1H' | FA.FATPTREF = 'PK SOC'

Example continued from previous page -

Date of previous SOC dose prior to this PK sample collection	FA.FATESTCD = 'OCCUR' FA.FAOBJ = 'SOC' FA.FAORRES = 'Y' FA.FADTC
When was the previous SOC dose approximately taken?	FA.FATPT = 'PRIOR' FA.FATPTREF = 'PK SOC'

FINDINGS ABOUT EVENT EXAMPLES

CASE5

DESCRIPTION:

This is randomized, double-blind and phase 3 Study to assess the efficacy and safety of study treatment in Subjects with Chronic Kidney Disease. The primary objective of this study is to compare efficacy of study treatment with placebo for reducing ionized parathyroid (IPTH) levels. One of the adverse events of interest is seizure.

A seizure is the physical or behavioral changes that occur after an episode of abnormal electrical activity in the brain. So seizure can be considered as event. In this study eCRF collects the information about features of seizure but it does not tell when the seizure had happened. So only creating one record with --TERM as SEIZURE may not make sense to fit it in MH domain. Also as it gives more information about event seizure, it can fit into findings about domain with TESTCD as OCCUR and "--OBJ" as different given features of the seizure. Also PRESP can be mapped here as this is pre-specified event of interest.

The annotated eCRF is given below –

SDTM Data Set Name = FA | FA.DOMAIN = 'FA'

FA.FACAT = 'SEIZURE CLINICAL FEATURES' | FA.FAPRESP = 'Y'

CLINICAL FEATURES OF SEIZURE

Clinical Features associated with Seizure

FA.FATESTCD = 'OCCUR' | FA.FAOBJ

FA.FAORRES = 'Y'

FA.FAEVLINT = 'WITHIN 12 HOURS OF SEIZURE'

- Impairment of Consciousness
- Self-Limited Duration of a Neurological Deficit
- Abnormal Motor Activity
- Incontinence
- Accidental Injury
- Post-Event Weakness
- Hypotension within 12 hours of Seizure
- Arrhythmia within 12 hours of Seizure
- Abnormal laboratory results Within 12 hours of seizure
- CT or MRI findings consistent With a Stroke within 12 hours of Seizure

CASE6

DESCRIPTION:

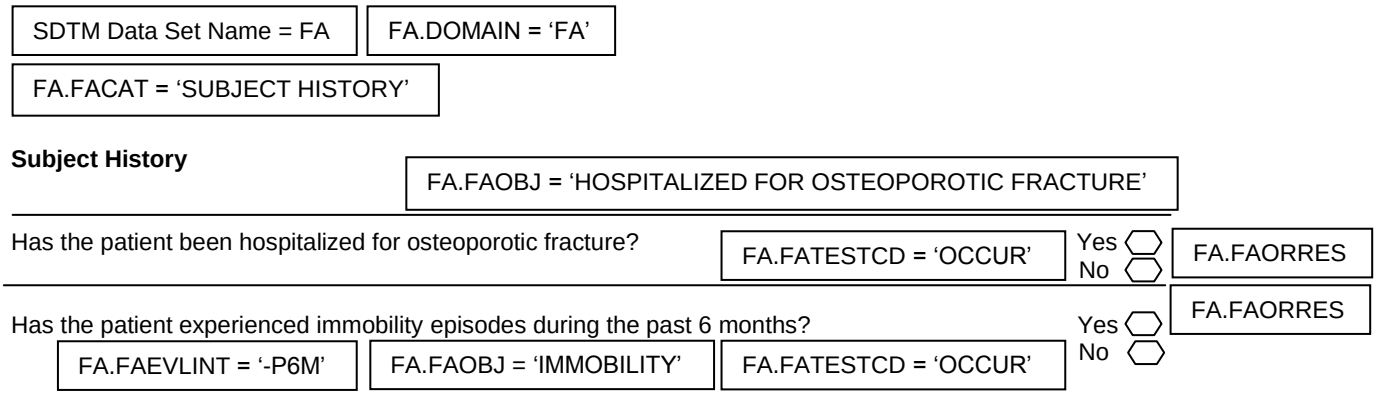
This case is from observational study of postmenopausal osteoporosis treated with study treatment. The objective of this observational study is to describe characteristics of postmenopausal women treated with study treatment in routine clinical practice.

The routine clinical practice includes collecting data of osteoporotic fractures suffered by patient.

This data is about medical history and it is reportable event occurred and the questions addressed here are as follows

1) Has the patient been hospitalized for osteoporotic fracture?
2) Has the patient experienced immobility episodes during the past 6 months?

So here 2 supplemental qualifier variables were needed in order to fit this data into MH. Since these questions are directly related to study objective so putting such information into supplemental qualifier variables may not be fruitful In order to represent this data in right and meaningful way FA is considered here. The aCRF is given below



SPECIAL CASE FROM A COSMETIC PRODUCT TRIAL

The objective of this study is to determine if the topical use of product preparation can stimulate the skin to result in clinically visible differences, as far as whiteness is concerned. The various spots on face or chin are measured by instrument. The objective is to check increased whiteness after applying the investigated cosmetic product.

Skin fairness is measured using Chroma meter and one of its parameters is L* intensity. For this parameter increase in value as compared to baseline shows efficacy.

As this study is about skin and its response is collected, the data can fit into SR domain as subject is typically exposed to many cosmetic products at the same time. SROBJ needs to represent cosmetic product for each response is being recorded. SR domain is used here to submit dermal responses. The SR (skin response) domain was recently added to SDTMIG version 3.2.

The data snap shot is given below

DOMAIN	USUBJID	SRSEQ	SRTESTCD	SRTEST	SROBJ	SRORRES	SRLOC	VISITNUM
SR	33444-101010	1	LINTN	LSTAR INTENSITY	CP1	56.71	FORE HEAD	1

Above mentioned domain SR has been added to SDTM model version 3.1.4 and its details can be referred to in section 6.4 of SDTMIG version 3.2.

CONCLUSION

Data collected about events or interventions that cannot fit into standard domain or if the importance of information is considered it may also not fit into supplemental qualifiers then FA domain can be utilized. So FA is a solution to map data that cannot be handled by supplemental qualifiers.

The use of FA domain class is rare but its importance is prodigious. The questions which are not related exactly to event and interventions but discussing more about these can be well represented in FA domain.

REFERENCES

1. CDISC SDTM Implementation Guide Version 3.1.3 and 3.2
2. http://www.cdisc.org/

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CONTACT INFORMATION

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