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Nice SUPPQUAL Variables to Have

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ABSTRACT

A Supplemental Qualifier (SUPPQUAL) data set is a special Study Data Tabulation Model (SDTM) data set that holds non-standard variables which cannot be mapped to any existing standard domain. Although non-standard, some variables can be very useful in data monitoring and standard reporting. This paper discusses some of those variables and the benefits of using them with the perspective of implementing SDTM in a linear fashion and early in the data management process.

Keywords: Supplemental Qualifiers, SUPPQUAL

INTRODUCTION

The Supplemental Qualifiers (SUPPQUAL) special purpose data set model is used to capture non-standard variables and their association to parent records in domains and allows capturing values for variables not presently included in the general-observation-class models. Because the SDTM does not allow the addition of new variables, it is necessary for sponsors to represent the metadata and data for each non-standard variable/value combination in a SUPPQUAL data set.

The SUPPQUAL data set uses a set of key variables, STUDY, RDOMAIN, USUBJIID, IDVAR and IDVARVAL, to identify related records. QNAM holds the name of the supplemental qualifier variable being defined. QLABEL is the long name or label of the qualifier variable. The qualifier variable is used as a column in a domain view with data from the parent domain. Since the value in QNAM and QLABEL represent the column name and label in a data set, the restrictions to the SAS transport file variable name and label are applied to the value of QNAM and QLABEL too, e.g., QNAM value should not be longer than eight characters, QLABEL value should not be longer than 40 characters.

Here is an example that illustrates the SUPPQUAL data structure:

SUPPAE: Supplemental Qualifiers for AE

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1234-005	AE	000600001	AESEQ	1	AETRTEM	Treatment Emergent	N

This row of SUPPAE data adds qualifying information to adverse event data. It applies to the record of STUDYID "1234-005" USUBJID "000600001" where the key IDVAR variable AESEQ is 1 in the parent AE data. The qualifier variable name is AETRTEM with the label as "Treatment Emergent" and the value of AETRTEM is "N".

SUPPQUAL variables can either be CRF collected or derived. The variable usually is displayed with other parent domain variables in an operational data management database. In this example, AETRTEM is displayed in the AE domain in the operational database as follows:

AE: Adverse Events

STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	**AETRTEM**
1234-005	AE	000600001	1	Nausea	**N**

The bolded column in gray shows the SUPPQUAL variable AETRTEM, which further describes the AETERM "Nausea".

Review tools at the FDA or any agencies can tie the SUPPQUAL variables to the records in the parent domain. Reviewers can see the variables along with the original domain as illustrated above.

Besides AETRTEM above, the names of SUPPQUAL variables introduced in this paper are not listed in the SDTM Implementation Guide V3.1.1 as standard names for SUPPQUAL variable names. Standard names for certain expected values for QNAM and QLABEL are included in SDTMIG 3.1.1 Appendix 10.3.4.

In this paper, we will use the gray bolded column format to indicate the SUPPQUAL variable when it is displayed in a domain view.

SUPPQUAL VARIABLES

1. NUMBER OF DAILY DOSES FOR STUDY MEDICATION (EXNUMDOS)

The number of daily doses for study medication is usually CRF collected but is not a qualifier variable defined in EX domain. We can define it as EXNUMDOS in SUPPEX as it can provide clarity to the exposure data collected.

Below is an example where this information is stored in SUPPEX when submitted.

SUPPEX: Supplemental Qualifiers for EX

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1234-005	EX	000600001	EXSEQ	1	EXNUMDOS	Number of Daily Doses	2
1234-005	EX	000600001	EXSEQ	2	EXNUMDOS	Number of Daily Doses	1

These records show USUBJID "000600001" takes 2 daily doses and 1 daily dose for EXSEQ 1 and 2 respectively.

The following table shows the number of daily doses variable in the EX exposure data in the operational database where the EXTRT is usually blinded.

EX: Exposure

STUDYID	DOMAIN	USUBJID	EXSEQ	EXSPID	EXNUMDOS	EXTRT	EXDOSE	EXDOSU	EXDOSTOT
1234-005	EX	000600001	1	A	2	BLINDED	999	BLINDED	999
1234-005	EX	000600001	2	B	1	BLINDED	999	BLINDED	999

EXSPID is sponsor-defined bottle label in this example. We can see that the patient took 2 doses from bottle A and 1 dose from bottle B daily.

The Number of Daily Doses is useful to monitor the patient medication status during the study.
In this example, if the protocol is to be followed the patient ought to take 1 tablet from Bottle A and 1 tablet from Bottle B daily. Even with the blind data, we can tell this patient is not compliant. He/she is overdosing.

When the study is unblinded, the number of daily doses can be used to derive the total daily dose EXDOSTOT as follows:
Total daily dose (EXDOSTOT) = Number of daily doses (EXNUMDOS) * Dose per Administration (EXDOSE)

The collected data at unblinding then will be:

EX: Exposure

STUDYID	DOMAIN	USUBJID	EXSEQ	EXSPID	EXNUMDOS	EXTRT	EXDOSE	EXDOSU	EXDOSTOT
1234-005	EX	000600001	1	A	2	Drug A	10	Mg	20
1234-005	EX	000600001	2	B	1	Placebo	0	Mg	0

EXNUMDOS can also be used to identify the non-zero doses. When combined with EXSTDTC, it derives the Reference Start Date RFSTDTC where RFSTDTC is defined as the first non-zero dose of study medication.

2. ACTUAL ARM / ACTUAL ARM CODE (ACTLARM/ACTARMCD)

ARM/ARMCD is the planned arm/arm code variable in DM domain. A patient may take the wrong study medication during the entire study period which makes the patient's planned arm different from the actual arm.

In the example above, the patient's planned arm is "Drug A 10 mg". The patient took 2 doses for "Drug A" as recorded in the exposure form for the entire study period. Therefore, the patient's actual arm became "Drug A 20 mg". It is often not intuitive to tell what actual arm the patient is in from the EX domain, as with the example above, it shows multiple records for each subject in the EX domain. It would be nice to have the actual arm variable in the DM domain at subject level to reflect the patient's actual arm as shown below:

DM: Demographics

STUDYID	DOMAIN	USUBJID	…	ARMCD	ARM	ACTARMCD	ACTLARM
1234-005	DM	000600001	…	1	Drug A 10 mg	5	Drug A 20 mg

The SUPPDM will have two records for this patient:

SUPPDM: Supplemental Qualifiers for DM

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1234-005	DM	000600001			ACTLARM	Actual Arm	Drug A 20 mg
1234-005	DM	000600001			ACTARMCD	Actual Arm Code	5

The two records in SUPPDM for this patient show the patient's actual arm and actual arm code. The IDVAR and IDVARVAL are not populated because the qualifying information is applicable to the subject as a whole and not to any specific record.

When running standard safety reports, counts tables on actual treatment are usually desired. With these two qualifiers in SUPPDM, it can be retrieved easily to generate the reports.

3. DAYS ON TREATMENT (DYSONTRT)

Number of days on treatment is another useful SUPPQUAL variable applied to a subject as a whole. It allows the reviewer to glance at the subject record in DM domain and have an idea of how long the subject is on the study treatment as well as how soon the patient discontinued.

4. STUDY PERIOD FLAG (PRDFLG)

Study period flag can be collected and stored as a SUPPEX variable to filter the EX records for a specific study period to aid the review of exposure records.

EX: Exposure

STUDYID	DOMAIN	USUBJID	EXSEQ	EXSPID	PRDFLG
1234-005	EX	000600002	1	A	Treatment
1234-005	EX	000600002	2	B	Treatment
1234-005	EX	000600002	3	C	Treatment
1234-005	EX	000600002	4	D	Extension
1234-005	EX	000600002	5	E	Extension
1234-005	EX	000600002	6	F	Extension

SUPPEX: Supplemental Qualifiers for EX

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1234-005	EX	000600002	EXSEQ	1	PRDFLG	Study Period Flag	Treatment
1234-005	EX	000600002	EXSEQ	2	PRDFLG	Study Period Flag	Treatment
1234-005	EX	000600002	EXSEQ	3	PRDFLG	Study Period Flag	Treatment
1234-005	EX	000600002	EXSEQ	4	PRDFLG	Study Period Flag	Extension
1234-005	EX	000600002	EXSEQ	5	PRDFLG	Study Period Flag	Extension
1234-005	EX	000600002	EXSEQ	6	PRDFLG	Study Period Flag	Extension

In data management, PRDFLG can be used to filter any data quality issues relating to wrong bottles used in a specific period. In this example, Bottles A, B, and C can only be prescribed in Treatment period; Bottles D, E, and F for Extension period. Any deviation can easily be spotted by filtering PRDFLG.

The PRDFLG can also be used to break the tie scenario. For example, if a specific record having EXSTDTC equals to both the end date of treatment period and the start date of the extension period, then PRDFLG can help us to put the record into the correct period.

5. CLINICAL INTEREST AE FLAG (AECLINT)

Usually a study has some pre-specified AE of clinical interest. During the course of the study, the clinical staff monitors these AEs closely along with serious AEs. With a checkbox in the AE CRF form to indicate these AEs, clinical can easily spot any AEs of clinical interest without digging into every AE record.

In collected AE data, the record might look like this:

STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	AECLINT
1234-005	AE	000600001	1	Nausea	Y

For submission purposes, AECLINT will be mapped to SUPPAE:

SUPPAE: Supplemental Qualifiers for AE

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1234-005	AE	000600001	AESEQ	1	AECLINT	Clinical Interest	Y

6. NUMERIC CODING OF AESEV, AEREL, AEACN (AESEVCD, AERELCD, AEACNCD)

Adding numerical codes to these AE variables can help to sort the data in a desired way for easy reviewing.

For example, a severe drug related AE that leads to the discontinuation of study medication can have the following SUPPQUAL variables in SUPPAE:

SUPPAE: Supplemental Qualifiers for AE

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1234-005	AE	000600001	AESEQ	1	AESEVCD	AE Intensity Code	3
1234-005	AE	000600001	AESEQ	1	AERELCD	AE Causality Code	2
1234-005	AE	000600001	AESEQ	1	AEACNCD	AE Action Code	4

Where AESEVCD=3 represents severe, AEACNCD = 4 means "Drug Withdrawn" and AERELCD= 2 means "Related".

7. AE DURATION (AEDURDD, AEDURDDU)

AE duration AEDUR holds only collected AE duration. When AE duration is not collected, AEDUR will be null. It is possible in some studies to choose to only collect AE duration if the duration is less than 1 day or 24 hours. Durations greater than or equal to1 day would then require an AE Stop Date to be collected. In this case, AEDUR column will only populate for the durations less than 1 day. AEDURDD is derived to provide AE durations not only for durations less than 1 day, but also for those greater than or equal to 1 day. It is convenient to have all the durations in one column for data review.

8. TIME SINCE LAST DOSE (AEDOSDUR)

When a reviewer is interested in further investigation of some specific AE records, it would be convenient to know immediately how much time elapsed from the last dose to the AE start date/time. This information can be stored in the variable AEDOSDUR in SUPPAE.

9. PROTOCOL VERSION (IEPROTV)

During a study, there are times when protocol is amended due to different reasons. When the amendment involves changes to the collection of data, it is helpful to have a protocol version variable to associate with the changes. For example, when the protocol amendment changes the Inclusion/Exclusion criteria during the course of the study, patients enrolled into the study before the change may have different criteria than patients enrolled after the change.

IE: Inclusion/Exclusion:

STUDYID	DOMAIN	USUBJID	IESEQ	IETEST	IETESTCD	IEPROTV
1234-005	IE	000600001	1	Patient has serum triglycerides less than 350 mg/dL	INA	00
1234-005	IE	000600001	2	Patient has mean trough SiBP < 140/92 mmHg.	INB	00
1234-005	IE	000600002	3	Patient has serum triglycerides less than 350 mg/dL	INAA	01
1234-005	IE	000600002	4	Patient has mean trough SiBP < 170/105 mmHg.	INBB	01

In this example, the inclusion criterion INB has changed due to the protocol amendment 01. The TESTCD is changed to INBB. Although INA criterion is not changed, the TESTCD is also changed to reflect the protocol amendment.

Patient 000600001 was enrolled before the change; Patient 000600002 was enrolled after the change. The IEPROTV variable can make that distinction and help clarify the data.

CONCLUSION

Although non-standard, SUPPQUAL variables are important because they provide additional information to parent domain topics. They can enable easier review and provide clarity to the collected data. Either collected or derived, they can also be used to monitor the operational data base in data management activities as well as assist in the generation of standard reports.

REFERENCES

CDISC Study Data Tabulation Model Implementation Guide: Human Clinical Trials
Version 3.1.1

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