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Common Variables in Adverse Event and Exposure analysis datasets specific for Oncology clinical trials

Haridasan Namboodiri, PRA International, Horsham, Pennsylvania

ABSTRACT

Cancer remains the second most common cause of death in the US with approximately 1 million new cases reported every year. According to the American Cancer Society, Cancer accounts for nearly 1 of every 4 deaths in the US. Cancer is also becoming prevalent in the developing world as it is estimated that over 21 million people will have cancer by 2030. Therefore, more and more treatments are entering the market and sponsors are initiating new therapies in their clinical trials to treat the disease.

Since Cancer is the general name for a group of more than 100 diseases, the initiation of a cancer clinical trial can be different based on the type. That is the first level of complexity in the conduct of a trial. As a next level of complexity, a trial can further investigate whether the study drug is for a treatment, or for prevention or for screening and whether they can look at different types of cancers with the same study drug. To make things further complicated, sponsors have added another level of complexity over the last decade or so in their study design to include "Biomarkers".

Although, CDISC, has introduced a Tabulation model (IG 3.1.3), The ADaM IG for oncology is still not available. In this paper, I would present a list of specific variables for Adverse Events and Exposure analysis datasets which are not included in current ADaM Implementation guides but are necessary for all Oncology specific analysis datasets. A brief overview of common Oncology specific analysis variables and their importance in study trials in specific types of cancer therapies is also discussed.

INTRODUCTION

Oncology or the branch of medical science which specifically studies the diagnosis and treatment of cancer disease is the largest therapeutic area in clinical research. According to the Center Watch Monthly Newsletter, one-third of the drugs that entered clinical trials in 2010 were targeted towards Cancer. According to the National Cancer Institute, although the rate of death in the United States from all cancers continued to decline between 2001 and 2010, the estimated new cancer cases and resulting deaths in the US in 2014 is still high: new cases: 1,665,540; deaths: 585,720. Novel cures for cancer therefore, continues to be a major focus of the pharmaceutical industry.

Clinical trials in Oncology are more complicated than those done for other therapeutic areas. For example, Oncology trials are usually conducted to improve and extend a patient's quality of life. Therefore, a placebo is never considered as a comparator in oncology trials. In some cases however, if placebos are used, it is usually used under different scenarios like (a) at a very early stage of the disease or (b) used with a standard treatment regimen or (c) used as an add-on, Drug A and Drug B vs Drug A and placebo or (d) continued use of Drug B after failure of Drug A and placebo. Another complexity in an oncology trial arises because there are several sites which take part in the trial resulting in various associated challenges like site activation, patient recruitment, involving multiple principal investigators etc. Cancer trial also need longer follow-up. These levels of complexity need high level of coordination between different departments at the sponsor/CRO level and the site for successful initiation and running of the trial. Due to all of the above reasons, timely end of the trial may be compromised and in many cases may get extended. The conduct of the clinical trial also varies for the type of cancer under study as choosing appropriate end points, managing data complexity, randomization design, operational challenges, defining safety and efficacy and patient recruitment all vary by the specific cancer type the trial is being conducted.

TABULATION DATASETS

The way clinical data is collected in oncology trials is also different, at least for Adverse Events, Laboratory data, Questionnaires, Medications, Medical History and Tumor Identification, Results and Response assessments. A non-cancer study trial does not have certain criteria defined for the above datasets. But in cancer trials, there are special definitions and criteria defined in the CRF's or in the study protocol. These have to be included in tabulation datasets. Except for laboratory toxicity grading, most of the other derivations are done by the site. Some of the special features which make these oncology specific datasets different from other therapeutic areas are listed in Table 1.

CRF page	SDTM Dataset	Comments
Adverse Event	AE	Adverse events are usually graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) and is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. The AE Grading (severity) is described as Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening or disabling, Grade 5: Death. Dose Limiting Toxicity(DLT), DLT Evaluable Period: Depending on the design of the trial, DLT could be triggered either in the CRF or if not collected could be additionally derived in analysis datasets
Laboratory Data	LB	The laboratory panels are usually extensive in oncology studies. The CTCAE grading is also applicable to many of the laboratory tests and should be programmed as per NCI CTCAE documentation when available. The grading is usually applicable to higher than normal limit as well as lower than normal limit. Some response criteria may require additional data that may be included in laboratory results. The study of biomarkers have recently become part of many oncology clinical trials as the treatment becomes more and more personalized, e.g., Breast cancer with HER2/ER/PR positive phenotype, Lung Cancer with EGFR positive phenotype etc.
ECOG Status	QS	The Eastern Oncology Cooperation Group provides scales and criteria that are used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis. Grade 0: Fully active, able to carry on all pre-disease performance without restriction, Grade 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work, Grade 2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours, Grade 3: Capable of only limited self-care, confined to bed or chair more than 50% of waking hours, Grade 4: Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair, Grade 5: Dead
Prior therapies	CM	Any major surgical procedures, therapeutic interventions, or diagnostic evaluations performed prior to initial dose of study drug. This may include radiation, surgery, systemic with further details of each applicable treatment and resulting response assessments. The prior treatment response assessments should be linked to the Response Assessment (SDTM.RS) usually through RELREC.
Disease diagnosis	MH	The initial disease diagnosis includes prior cancer history including more details about subtypes, location, involvement of other body organs, WHO classification, clinical onset if hematological cancer, applicable treatments and any other relevant details.
Tumor Identification/ Results	TU/TR	The assessment of the change in tumor burden that includes both tumor reduction and disease progression is an important feature in determining the endpoints during clinical evaluation of cancer therapeutics. The data is collected by identifying tumors or lymph nodes and then repeatedly measuring and assessing at subsequent time points and used in an evaluation of response(s). These assessment criteria include RECIST (Response Evaluation Criteria in Solid Tumors) for solid tumors, Cheson for lymphoma, or, Hallek for chronic lymphocytic leukemia. The tumors are identified by an investigator and/or independent assessor and classified according to the disease assessment criteria. For solid tumors, this equates to the identification of Target (index lesions), Non-Target (non-index lesions) or New (new lesions) tumors. A record in the TU domain contains the following information: a unique tumor ID value; anatomical location of the tumor; method used to identify the tumor; role of the individual identifying the tumor; and timing information The quantitative measurements and/or qualitative assessments of the tumors are also recorded. For each unique tumor ID, the measurements are usually taken at baseline and then at each subsequent assessment to support response evaluations.

CRF page	SDTM Dataset	Comments
Response Assessments	RS	The Response assessments represents the response evaluation determined from the data in TR. Usually the principal investigator provided assessment of each individual tumor identified (target, non-target and new) and summarizes them to give and overall response assessment.

Table 1 The list of CRF pages and the related SDTM datasets in oncology trials which are different from other therapeutic studies.

ANALYSIS DATASETS

The Clinical Data Interchange and Standards Consortium (CDISC) ADaM team have released so far the general data structure and content specific for statistical analysis of Adverse Events and Time to Event analyses. Although the Time to Event ADaM dataset could fit into the BDS structure, the Adverse Event analysis dataset does not fit into the BDS and is therefore considered a log-style or hierarchical data structure. Adverse event dataset is just one example that can use the hierarchical data structure. There are other analysis datasets where a BDS structure would not be applicable. Example datasets may include analysis of exposure, concomitant medications and medical history.

ANALYSIS OF ADVERSE EVENTS

The Analysis Data Model Data Structure for Adverse Event Analysis (V1.0) is based on the ADaM Analysis Data Model V2.1 and the ADaM Analysis Data Model Implementation Guide (ADaMIG, V1.0). The guide represents variables needed to create analysis dataset for any therapeutic area in general. Although, treatment variables already included in the current IG includes DOSEAEON (Study Drug Dose at AE Onset), DOSAEONU (Study Drug Dose at AE Onset Units), DOSECUM (Cumulative Study Drug Dose) and DOSECUMU (Cumulative Study Drug Dose Units), additional variables needed to create analysis datasets for oncology specific studies are listed in Table 2. These variables are generally reported in tables and/or listings and are therefore, needed to be derived in Adverse Events analysis datasets.

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
AEDSLD	Death Day since last dose	Num			Usually defined in the SAP. Example Derivation TRTEDT - AEDTHDT + 1
AEDLTFL	AE Dose Limiting Toxicity Flag	Char	Y	Cond	This variable is conditional on whether the concept of Dose Limiting Toxicity is a feature of the study and whether used for analysis or not
AECYC	AE Cycle	Char		Perm	The Adverse event cycle refers to the cycle during which it occurred. It is populated for all Adverse Events per patient. If the adverse event occurred after dosing of study drug at Cycle 1 Day1 and before the next dosing at Cycle 2 Day 1 then AECYC will be set to Cycle 1. This derivation should be repeated for all adverse events per subject per treatment.
AECYCN	AE Cycle (N)	Num		Perm	Numeric version of AECYC
AEMAXCYC	Maximum Cycle Started	Num		Perm	This will be set to maximum value of AECYCN per patient
AETHRTYP	Therapy Type	Char		Cond	This variable is conditional on whether the study involves a single study drug or a combination of study drugs. Values could be set as ‘SINGLE’, ‘COMBINED’

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
AESTART	Adverse Event Start Period	Char		Perm	The start period when the Adverse event has started relative to the signing of the informed consent and first dose of study drug. Example start period: Started before the signing of consent, Started after consent but before first dose of study drug, Started after first dose of study drug.
AESTARTN	Adverse Event Start Period (N)	Num		Perm	Numeric version of AESTART
AESTRTM	Adverse Event Start Time	Char		Perm	The start time when the Adverse event started. Conditional to study drugs which are administered intravenously. Example start time: Started before first infusion or before infusion on any dosing day, Started during infusion, Started <= 1 hour after infusion completion, Started > 1 hour and <= 24 hours after infusion completion, Started > 24 hours after infusion completion and on a non-dosing day
AESTRTMN	Adverse Event Start Time (N)	Num		Perm	Numeric version of AESTRTM
AERELATE	Related to Protocol Procedure	Char		Perm	Whether adverse event started after signing informed consent and is due to a procedure in the protocol
AEDOSDEL	Adverse Event Leading to Dose Delay	Char		Perm	The adverse event that resulted in dose delay of exposure to study drug
AEDELFL	Adverse Event Leading to Dose Delay Flag	Char	Y	Perm	Whether a particular adverse event led to a dose delay during treatment
AEDOSRED	Adverse Event Leading to Dose Reduction	Char		Perm	The adverse event that resulted in dose reduction of exposure to study drug
AEREDFL	Adverse Event Leading to Dose Reduce Flag	Char	Y	Perm	Whether a particular adverse event led to a dose reduction during treatment
AEDOSADJ	Adverse Event Leading to Dose Adjustment	Char		Perm	The adverse event that resulted in dose adjustment of exposure to study drug
AEADJFL	Adverse Event Leading to Dose Adjustment Flag	Char	Y	Perm	Whether a particular adverse event led to a dose adjustment during treatment
AEINFRN	Infusion Reaction Related AE	Char		Perm	The adverse event that resulted in an infusion related reaction

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
AEINFFL	Infusion Reaction AE Flag	Char	Y	Perm	Whether a particular adverse event was related to any infusion related reaction during treatment
AEINTFL	AE Leading to Infusion Interruption Flag	Char	Y	Perm	Whether a particular adverse event was related to any infusion reaction that led to an infusion interruption during treatment
AEINSTFL	AE Leading to Infusion Stopped Flag	Char	Y	Perm	Whether a particular adverse event was related to any infusion reaction that led the infusion to be stopped during treatment
AEHSR	Hyper sensitivity reaction related AE	Char		Perm	The adverse event that resulted in a hypersensitivity reaction
AEHSRFL	AE Leading to Infusion Stopped Flag	Char	Y	Perm	Whether a particular adverse event was related to any hypersensitivity during treatment

Table 2 Variable level metadata for Adverse Event analysis datasets for oncology clinical trials

Example Source code: Derivation of AECYC (AE Cycle) and AETHRTYP (Therapy Type). This example code is for a combination treatment where there are two study drugs, “Study Drug A” dosed once and “Study Drug B” dosed twice.

```
**** Read AE Dataset ****;

data ADAE;
        set CONVERTU.AE;
run;

**** Read EX Dataset, Extract the numeric portion of Visit having format CYCLE X DAY Y ****;

data ADEX;
        set ADEX;
        if input(strip(substr(VISIT,7,2)),best.)>=10 then TEMPCYC = strip(substr(VISIT,7,2));
        else TEMPCYC = strip(substr(VISIT,7,1));
run;

**** Count the number of  EXTRT by STUDYID USUBJID TEMPCYC ****;

proc sql noprint;
        create table ADEX1 as
        select distinct STUDYID, USUBJID, EXSTDT, TEMPCYC
        from ADEX;

        create table EX1 as
        select distinct STUDYID, USUBJID, TEMPCYC, count(EXTRT) as EXTRT1
        from ADEX
        where EXTRT="STUDY DRUG A"
        group STUDYID, USUBJID, TEMPCYC
        ;

        create table EX2 as
        select distinct STUDYID, USUBJID, TEMPCYC, count(EXTRT) as EXTRT2
        from ADEX
```

```
        where EXTRT="STUDY DRUG B"
        group STUDYID, USUBJID, TEMPCYC
        ;
quit;

data ex;
        set ADEX1(where =(EXSTDT ne .)rename=(TEMPCYC=_TEMPCYC));
                EXSTDT1=lag(EXSTDT);
                TEMPCYC=lag(_TEMPCYC);
run;

data excyc;
        set ex;
        by STUDYID USUBJID EXSTDT;
        if FIRST.USUBJID then do;
                EXSTDT1=.;
                TEMPCYC='';
        end;
        output;
        if LAST.USUBJID then do;
                EXSTDT1=EXSTDT;
                TEMPCYC=_TEMPCYC;
                EXSTDT=.;
                output;
        end;
run;

proc sort data=EXCYC;
        by STUDYID USUBJID TEMPCYC;
run;

**** Merge Exposure datasets ****;

data EX1;
        merge EXCYC EX1 EX2;
        by STUDYID USUBJID TEMPCYC;
run;


**** Merge Exposure and Adverse Events datasets ****;
proc sql noprint;
        create table ADAE_EX as
        select distinct ADAE.*, EX.TEMPCYC, EX.EXSTDT, EX.EXTRT1, EX.EXTRT2
        from ADAE_DER ADAE left join EX1 as EX
        on ADAE.USUBJID=EX.USUBJID &
                (.z < EX.EXSTDT1 <= ADAE.ASTDT < EX.EXSTDT or (.z < EX.EXSTDT1 <= ADAE.ASTDT &
                EX.EXSTDT  = .));
quit;


**** Derive AE Cycle and Therapy Type  ****;
data ADAE;
                set ADAE_EX;
                  **** AE Cycle ****;
        if TEMPCYC ne '' then do;
                AECYCN= input(TEMPCYC,BEST.);
                AECYC = "Cycle "||strip(TEMPCYC);
        end;
  **** Therapy Type ****;
        if EXTRT1 >= 1 & EXTRT2 >= 2 then AETHRTYP='COMBINED';
        else if EXTRT1 ne . then AETHRTYP='SINGLE';
run;
```

ANALYSIS OF EXPOSURE

In oncology trials, the patient is usually given different categories of study drugs like targeted drugs (those that attack cancer cells more specifically than normal cells by attacking the mutant genes of the cancer cell and could be used as a main treatment or to maintain remission), differentiating drugs (those that change cancer cells mature to normal cells), hormone drugs (drugs that are hormones) or immune drugs (antibodies that destroy cancer cells only). Because of the aggressive nature of the disease, cancer treatment provides some flexibility when the investigative study drug is given. Since the quality of life of the patient is never supposed to be compromised, the patient is usually given the option of taking chemotherapy/alternative surgical procedures etc., at any particular point of taking the study drug. Therefore, combination therapy is widely used in oncology trials together with mono-therapy. Another important concept when dealing with Exposure data in oncology trials is the concept of Cycle which is the number of days after which the study drug will be administered. A cycle may run for as short as few days to 28 days or even in some cases longer. In combination therapy, Drug A may be given on Cycle 1 Day 1 and Drug B may be given on Cycle 1 Day 2 and again on Cycle 1 Day 3. Usually the trial runs for a fixed number of cycles with the same repetitive order of exposure. Like Adverse event analysis datasets, the variables usually needed to be derived in Exposure datasets are given in Table 3. Many of the dosing variables have ------xx suffix and these could usually be defined to point to the cycle numbers and could be a summation for Cycle 1 through 2, summation of Cycles 1 through 4 etc.

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
AVISIT	Analysis visit	Char		Perm	Usually the cycle number concatenated with “Cycle”
AVISITN	Analysis visit (N)	Num		Perm	The numeric portion of AVISIT.
EXADJ	Reason for Dose Adjustment	Char		Cond	This variable is conditional on whether the study drug is intravenously administered and captures the reason for any dose adjustments. The dose may have to be adjusted due to infusion related adverse event or due to some other reason.
EXADJN	Reason for Dose Adjustment (N)	Num		Cond	Numeric version of EXADJ
EXADJNUM	Number of dose adjustments per cycle	Num		Perm	The number of dose adjustments which have taken place per subject per study drug per cycle
EXDELAY	Dose delayed per protocol reasons	Char		Perm	This variable is conditional on whether the study drug is intravenously administered and if there was any dose delay. The dose may be delayed due to adverse event or due to some other reason.
EXDELAYN	Dose delayed per protocol reasons (N)	Num		Perm	Numeric version of EXDELAY
EXDELNUM	Number of dose delays per cycle	Num		Cond	The number of dose delay which have taken place per subject per study drug per cycle
EXDELAE	AE causing dose delay	Char		Cond	The adverse event that resulted in the delay of exposure of study drug
EXREDUCE	Dose Reduced per protocol reasons	Char		Cond	This variable is conditional on whether the study drug is intravenously administered and if there was any reduction in the administered dose. The dose may be reduced due to adverse event or due to any other reason.
EXREDUCN	Dose Reduced per protocol reasons (N)	Num		Cond	Numeric version of REDUCE

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
EXREDNUM	Number of dose reductions per cycle	Num		Cond	The number of dose reduced which have taken place per subject per study drug per cycle
EXREDAE	Primary AE causing dose reduction	Char		Cond	The adverse event that resulted in the reduction of exposure of study drug
EXADJAE	Primary AE causing dose adjustment	Char		Cond	The adverse event that resulted in the adjustment of exposure of study drug
EXDOSLVL	Intended dose (unit)	Num		Cond	The intended dose (with the unit) of the study drug which has been planned to be administered
EXDOSADJ	Adjusted actual dose administered	Num		Cond	The actual dose (with the unit) of the study drug which has been administered. May or may not be equal to DOSLEVEL.
EXINFR	Any infusion-related reactions	Char		Cond	This variable is conditional on whether the study drug is intravenously administered and will specify if there were any infusion related reactions.
EXINFNUM	Number of infusion reactions per cycle	Num		Cond	The number infusion related reactions which have taken place per subject per study drug per cycle
EXINFAE	AE for infusion related reactions	Char		Perm	The adverse event that resulted in a infusion related reaction
EXHSR	Any Hypersensitivity reactions	Char		Cond	This variable is conditional on whether the study drug is intravenously administered and will specify if there were any hypersensitivity reactions.
EXHSNUM	Number of Hypersensitivity reactions	Num		Cond	The number of hypersensitivity reactions which have taken place per subject per study drug per cycle
EXHSRAE	AE for hypersensitivity reactions	Char		Perm	The adverse event that resulted in a hypersensitivity reaction
EXTHRTYP	Therapy Type	Char		Perm	This variable is conditional on whether the study involves a single study drug or a combination of study drugs
TRTDURxx	Duration of Treatment	Num		Perm	The duration of treatment as defined in the SAP. May be expressed in days, weeks or months. The xx refers to the start or end of a cycle if needed. Duration of treatment for example for cycles 1-2 will be represented as TRTDUR12, for cycles 3-4 as TRTDUR34 overall treatment duration of treatment as TRTDUR. Example derivation: last dose date – first dose date + 1
EXDOSCNT	Total number of doses	Num		Perm	Count of total number of doses.

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
EXDSCNTC	Total number of doses per cycle	Num		Perm	Count of total number of doses per cycle.
EXCYC	Total number of cycles	Num		Perm	Count of total number of cycles.
EXCYCxx	Total number of cycles, range	Num		Perm	Count of total number of cycles during a range of cycles, xx represent the range of cycle numbers
EXCUMDOS	Cumulative dose	Num		Perm	Sum of actual dose administered for each subject per EXTRT
EXCMDOSC	Cumulative dose per cycle	Num		Perm	Sum of actual dose administered for each subject per EXTRT per cycle
EXCMDSxx	Cumulative dose per cycle range	Num		Perm	Sum of actual dose administered for each subject per cycle range
EXADOSI	Absolute dose intensity	Num		Perm	Sum of absolute dose intensity for each subject per EXTRT
EXADOSIC	Absolute dose intensity per cycle	Num		Perm	Sum of absolute dose intensity for each subject per EXTRT per cycle
EXADSIxx	Absolute dose intensity per cycle range	Num		Perm	Sum of absolute dose intensity for each subject per EXTRT per cycle range
EXIDOSI	Intended Dose Intensity per cycle	Num		Perm	Sum of intended dose level for each subject per EXTRT
EXIDOSIC	Intended dose intensity per cycle	Num		Perm	Sum of intended dose level for each subject per EXTRT per cycle
EXIDSIxx	Intended Dose Intensity per cycle range	Num		Perm	Sum of intended dose level for each subject per EXTRT per cycle range
EXRDOSI	Relative Dose Intensity	Num		Perm	Usually defined in the SAP. Example derivation: (EXADOSI) / (EXIDOSI) * 100
EXRDOSIC	Relative Dose Intensity per cycle	Num		Perm	Usually defined in the SAP. Example derivation: (EXADOSIC) / (EXIDOSIC) * 100
EXRDSIxx	Relative Dose Intensity per cycle range	Num		Perm	Usually defined in the SAP. Example derivation: (EXADSIxx) / (EXIDSIxx) * 100

Table 3 Variable level metadata for Exposure analysis datasets for oncology clinical trials

Source code: Derivation of EXCUMDOS, EXADOSI, EXIDOS, EXDOSCNT EXDELNUM, EXREDNUM, EXADJUST, EXINFNUM, EXHSRNUM

```
**** Read EX Dataset ****;
data ADEX2;
        set CONVERTU.EX;
run;
```

```
proc sql noprint;

**** Calculate Cumulative Dose ****;
      create table CUMDOS as
 select USUBJID, EXTRT, AVISIT, sum(EXDOSE) as EXCUMDOS
 from ADEX2 (where=(EXDOSE > 0))
 group by USUBJID, EXTRT, AVISIT;

**** Calculate Actual dose Intensity ****;
      create table ADOSI as
 select USUBJID, EXTRT, AVISIT, sum(EXDOSADJ)/21 as EXADOSI
 from ADEX2 (where=(EXDOSADJ > 0))
 group by USUBJID, EXTRT, AVISIT;

**** Calculate Intended dose Intensity ****;
      create table idosi as
 select USUBJID, EXTRT, AVISIT, sum(EXDOSLVL)/21 as EXIDOSI
 from ADEX2 (where=(EXDOSE > 0))
 group by USUBJID, EXTRT, AVISIT;

**** Calculate Dose Count ****;
      create table DOSCNT as
 select USUBJID, EXTRT, AVISIT, count(EXDOSE) as EXDOSCNT
 from ADEX2 (where=(EXDOSE>0))
 group by USUBJID, EXTRT, AVISIT;

**** Calculate Cycle ****;
      create table EXCYC as
 select distinct USUBJID, EXTRT, count(AVISIT) as EXCYC, CYCNUM
 from ADEX2 (where=(EXDOSE>0))
 group by USUBJID, EXTRT, CYCNUM
 order by USUBJID, EXTRT, CYCNUM;

 **** Calculate number of Dose Delay ****;
      create table EXDEL1 as
 select USUBJID, EXTRT, AVISIT,  count(EXDELAY) as EXDELNUM
 from ADEX2 (where=(EXDOSE>0 and EXDELAY='Yes'))
 group by USUBJID, EXTRT, AVISIT;

   create table EXDEL as
   select distinct * from EXDEL1
 order by USUBJID, EXTRT, AVISIT;

 **** Calculate number of Dose Reduction ****;
      create table exred1 as
 select USUBJID, EXTRT, AVISIT, count(EXREDUCE) as EXREDNUM
 from ADEX2 (where=(EXDOSE>0 and EXREDUCE='Yes'))
 group by USUBJID, EXTRT, AVISIT;

  create table EXRED as
   select distinct * from EXRED1
 order by USUBJID, EXTRT, AVISIT;

 create table EXADJ1 as
 select USUBJID, EXTRT, AVISIT, count(EXADJ) as EXADJNUM
 from ADEX2 (where=(EXDOSE>0 and EXADJ ne ''))
 group by USUBJID, EXTRT, AVISIT;

 **** Calculate number of Dose Adjustment ****;
 create table EXADJ as
   select distinct * from EXADJ1
 order by USUBJID, EXTRT, AVISIT;
```

```
   **** Calculate number of Infusion related reaction ****;
 create table EXINF1 as
  select USUBJID, EXTRT, AVISIT, count(EXINF) as EXINFNUM
  from ADEX2 (where=(EXDOSE>0 and EXINF ='Yes'))
  group by USUBJID, EXTRT, AVISIT;

 create table EXINF as
  select distinct * from EXINF1
  order by USUBJID, EXTRT, AVISIT;

   **** Calculate number of Hypersensitvity reactions ****;
 create table HSR1 as
  select USUBJID, EXTRT, AVISIT, count(EXHSR) as EXHSRNUM
  from ADEX2 (where=(EXDOSE>0 and EXHSR ='Yes'))
  group by USUBJID, EXTRT, AVISIT;

 create table EXHSR as
  select distinct * from HSR11
  order by USUBJID, EXTRT, AVISIT;
quit;
```

CONCLUSION

The need for standardization of clinical data for regulatory filing has been recognized as an immediate need for streamlining, providing transparency as well as faster review from regulatory authorities. The Coalition for Accelerating Standards and Therapies (CFAST), is implementing these efforts by providing standards specifically for tabulation datasets. Therapeutic areas which have been approved by CFAST as of March 2014 include Alzheimer Disease, Asthma, Breast Cancer, COPD, Cardiovascular disease, Diabetes, Traumatic Brain Injury, Hepatitis C. Schizophrenia, Influenza and Metabolic diseases. Standardization could be extrapolated for analysis datasets also based on therapeutic area. Oncology is one area where standardization could be easily applied. This paper describes the first step towards this approach by selecting commonly derived variables used in analysis datasets for adverse events and exposure.

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CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Name: Haridasan Namboodiri
PRA International
630 Dresher Road
Horsham, PA 18902
Work Phone: 215-444-8569
E-mail: namboodirihari@praintl.com