Dataset Integrity Check for the TrialNet(09) Data Files

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1 Standard Disclaimer

The intent of this DSIC is to provide confidence that the data distributed by the NIDDK repository is a true copy of the study data. Our intent is not to assess the integrity of the statistical analyses reported by study investigators. As with all statistical analyses of complex datasets, complete replication of a set of statistical results should not be expected in secondary analysis. This occurs for a number of reasons including differences in the handling of missing data, restrictions on cases included in samples for a particular analysis, software coding used to define complex variables, etc. Experience suggests that most discrepancies can ordinarily be resolved by consultation with the study data coordinating center (DCC), however this process is labor-intensive for both DCC and Repository staff. It is thus not our policy to resolve every discrepancy that is observed in an integrity check. Specifically, we do not attempt to resolve minor or inconsequential discrepancies with published results or discrepancies that involve complex analyses, unless NIDDK Repository staff suspect that the observed discrepancy suggests that the dataset may have been corrupted in storage, transmission, or processing by repository staff. We do, however, document in footnotes to the integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

2 Study Background

The immunopathogenesis of type 1 diabetes mellitus is associated with T-cell autoimmunity. To be fully active, immune T cells need a co-stimulatory signal in addition to the main antigen-driven signal. Abatacept modulates co-stimulation and prevents full T-cell activation. Therefore, this multicenter, double-blind, randomized, controlled trial evaluated the effect of abatacept in subjects with recently diagnosed type 1 diabetes mellitus. Subjects were randomly assigned in a 2:1 ratio to receive either the experimental treatment of 30 minute intravenous infusion of 10 mg/kg of CTLA-4 Ig (abatacept) or an intravenous saline solution (placebo). The treatments were administered on days 1, 14, 28, and then every 28 days for a total of 27 doses over 700 days. All subjects received intensive diabetes management with the goal of achieving excellent glycemic control. 2 hour mixed meal tolerance tests (MMTT) were performed at 3, 6, 12 and 18 months. Four hour MMTTs were performed at baseline and at 24 months. Safety and efficacy were assessed over a two year follow-up period.

3 Archived Datasets

All SAS data files, as provided by the Data Coordinating Center (DCC), are located in the "data" folder in the data package. For this replication, variables were taken from the different analysis datasets created by the DCC.

4 Statistical Methods

Analyses were performed to duplicate results for the data published by Orban, et al [1] in Lancet on 2011, July 30. To verify the integrity of the three datasets, descriptive statistics of baseline characteristics were computed, by treatment group (Table B and Table D).

5 Results

Table 1 in the publication [1], Baseline Demographic and Laboratory Characteristics of Subjects at Entry. Table A lists the variables that were used in the replication and Table B compares the results calculated from the archived data file to the results published in Table 1. The results of the replication are similar to the published results.

Table 2 in the publication [1]: Adverse Events. Table C lists the variables that were used in the replication and Table D compares the results calculated from the archived data file to the results published in Table 2. The results of the replication are similar to the published results.

6 Conclusions

The NIDDK repository is confident that the TrialNet(09) data files to be distributed are a copy of the manuscript data.

7 References

Orban T, Bundy B, Becker DJ, et al.; Type 1 Diabetes TrialNet Abatacept Study Group Co-stimulation modulation with abatacept in patients with recent-onset type 1 diabetes: a randomised, double-blind, placebo-controlled trial. Lancet 2011;378:412–419

Table A: Variables used to replicate Table 1: <u>Baseline Demographic and Laboratory Characteristics of Subjects at Entry.</u>

Table Variable	Variables Used in Replication from the Trialnet(09) Datasets
Age- yr	ctl01_screening.age
Female sex- no. of patients (%)	ctl01_screening.sex
Race - no. of patients* (%)	ctl01_screening.race_white
Ethnicity - no. of patients (%)	ctl01_screening.ethnicity
No. of days from diagnosis to first infusion	ctl02_screening_med_history. DateOfT1DdiagnosisMonth ctl02_screening_med_history. DateOfT1DdiagnosisDay ctl02_screening_med_history. DateOfT1DdiagnosisYear ctl07_study_drug_admin.Date_of_Visit
Weight (kg)	ctl01_screening.WEIGHTKG
Body Mass Index (kg/m2)	ctl01_screening.WEIGHTKG ctl01_screening.HEIGHTCM
Total daily insulin dose at baseline* – (U/kg)	diabetes_management. AverageUnitsOfItermediateInsul diabetes_management .AvgUnitsShortActingInsulin ctl12_visit_form.WEIGHTKG
Ketoacidosis at diagnosis - no. of patients (%)	Screening_medical_history. DKAatDiagnosis
Diabetes associated HLA alleles present - no. of patients* (%) Glycated hemoglobin at baseline (HbA1c -%) AUC Mean for C-peptide (pmol/ml) No. of autoantibodies** - no. of patients (%)	research_labs.VISIT research_labs.SPEC_NAME research_labs.TEST_NAME research_labs.RESULT research_labs.OUTCOME
Treatment Group	treatment_table.treatmentname

Table B: Comparison of values computed in integrity check to reference article Table 1 values

Characteristic	Abatacept [Manuscript]	Abatacept [DSIC]	Abatacept [Diff]
Age- yr: Mean	13.9 +- 6.9	14.1 ± 6.9	.2+-0
Age-yr: Median	12	12	0
Age-Yr: Range	6 – 36	6-36	0
Male sex- number of patients (%)	41 (53.2)	40 (52.6)	1(.6)
Race* - number of patients White (%)	71 (93.4)	72 (94.7)	-1(-1.3)
Ethnicity – number of patients (%)Non-Hispanic	67 (87.0)	67 (88.2)	0(-1.2)
Number of autoantibodies** - no. of patients (%) 1	9 (11.7)	8 (10.5)	1(1.2)
Number of autoantibodies** - no. of patients (%) 2	26 (33.8)	24 (31.6)	2(2.2)
Number of autoantibodies** - no. of patients (%) 3	26 (33.8)	27 (35.5)	-1(-1.7)
Number of autoantibodies** - no. of patients (%) 4	16 (20.8)	17 (22.4)	-1(-1.6)
Number of days from diagnosis to first infusion	87.9+- 14.1	87.9 ± 14.2	0+-(0.1)
Range	51 – 108	51-108	0
Weight (kg)	52.6+- 21.9	52.5 ± 22.4	-0.1+--0.5
Body Mass Index (kg/m2)	21.0 +- 4.48	21.11 ± 4.65	-0.1+-0.17
Mean AUC for C-peptide (pmol/ml)	0.743 +- 0.42	0.754 ± 0.413	-0.011+-0.01
Glycated hemoglobin at baseline* (HbA1c -%)	6.31 +-0.80	6.30 ± 0.79	0.01+-0.01
Total daily insulin dose at baseline* – (U/kg)	0.385 +- 0.24	0.380 ± 0.249	0.005+--0.009
Ketoacidosis at diagnosis – number of patients (%)	25 (32.5)	25 (33.3)	0(-0.8)
Diabetes associated HLA alleles present* - number of patients (%) DR3 and DR4	25 (33.8)	25 (33.8)	0
Diabetes associated HLA alleles present* - number of patients (%) DR3 only	11 (14.9)	11 (14.9)	0
Diabetes associated HLA alleles present* - number of patients (%) DR4 Only	30 (40.5)	30 (40.5)	0
Diabetes associated HLA alleles present* - number of patients (%) Neither	8 (10.8)	8 (10.8)	0

Characteristic	Placebo [Manuscript]	Placebo [DSIC]	Placebo [Diff]
Age- yr: Mean	13.7 +- 5.3	13.7 ± 5.3	0
Age-yr: Median	14	14	0
Age-Yr: Range	7 – 34	7-34	0
Male sex- number of patients (%)	25 (71.4)	25 (71.4)	0
Race* - number of patients White (%)	32 (91.4)	33 (94.3)	-1(-2.9)
Ethnicity – number of patients (%)Non-Hispanic	31 (88.6)	31 (88.6)	0
Number of autoantibodies** - no. of patients (%) 1	4 (11.4)	4 (11.4)	0
Number of autoantibodies** - no. of patients (%) 2	9 (25.7)	7 (20.0)	2(5.7)
Number of autoantibodies** - no. of patients (%) 3	15 (42.9)	17 (48.6)	-2(-5.7)
Number of autoantibodies** - no. of patients (%) 4	7 (20.0)	7 (20.0)	0
Number of days from diagnosis to first infusion	83.2 +- 17.8	84.9 ± 16.2	-1.7+-1.6
Range	38 – 107	43-107	-5-0
Weight (kg)	53.0 +- 19.7	50.2 ± 18.7	2.8+-1
Body Mass Index (kg/m2)	20.5 +- 3.9	19.86 ± 3.67	.64+-.23
Mean AUC for C-peptide (pmol/ml)	0.745 +- 0.31	0.745 ± 0.315	0+--0.005
Glycated hemoglobin at baseline* (HbA1c -%)	6.74 +-0.94	6.74 ± 0.94	0
Total daily insulin dose at baseline* – (U/kg)	0.339 +- 0.22	0.367 ± 0.249	-0.028+--0.029
Ketoacidosis at diagnosis – number of patients (%)	8 (22.9)	8 (23.5)	1(0.6)
Diabetes associated HLA alleles present* - number of patients (%) DR3 and DR4	16 (48.5)	16 (48.5)	0
Diabetes associated HLA alleles present* - number of patients (%) DR3 only	5 (15.2)	5 (15.2)	0
Diabetes associated HLA alleles present* - number of patients (%) DR4 Only	10 (30.3)	10 (30.3)	0
Diabetes associated HLA alleles present* - number of patients (%) Neither	2 (6.1)	2 (6.1)	0

Table C: Variables used to replicate Table 2: <u>Adverse Events.</u>

Table Variable	Variables Used in Replication
Adverse Effect Category	Adverseevent.Category
Adverse Event Grade	Adverseevent.severity
Treatment Group	treatment_table.treatmentname

Table D: Comparison of values computed in integrity check to reference article Table 2 values

Adverse Effect Grade	Abatacept [Manuscript]	Abatacept [DSIC]	Abatacept [Diff]	Placebo [Manuscript]	Placebo [DSIC]	Placebo [Diff]
0	14 (18.2)	13 (17.1)	1(1.1)	8 (22.9)	8 (22.9)	0
1	1 (1.3)	1 (1.3)	0	1 (2.9)	1 (2.9)	0
2	44 (57.1)	43 (56.6)	1(.5)	17 (48.6)	17 (48.6)	0
3	12 (15.6)	13 (17.1)	-1(-1.5)	7 (20.0)	7 (20.0)	0
4	5 (6.5)	5 (6.6)	0(-0.1)	2 (5.7)	2 (5.7)	0
5**	1 (1.3)	1 (1.3)	0	0 (0.0)	0 (0.0)	0
Total	77	76	1	35	35	0

Adverse Effect Category	Abatacept [Manuscript]	Abatacept [DSIC]	Abatacept [Diff]	Placebo [Manuscript]	Placebo [DSIC]	Placebo [Diff]
Allergy/Immunology	3 2 (2.6)	3 2 (2.6)	0 0 (0.0)	0 0 (0.0)	0 0(0.0)	0 0(0.0)
Auditory/Ear	3 3 (3.9)	4 4 (5.3)	-1 -1 (-1.4)	0 0 (0.0)	0 0(0.0)	0 0(0.0)
Blood/Bone Marrow	16 11 (14.3)	17 11 (14.5)	-1 0 (-0.2)	18 6 (17.1)	19 7 (20.0)	-1 -1(-2.9)
Cardiac Arrhythmia	1 1 (1.3)	1 1(1.3)	0 0 (0.0)	1 1 (2.9)	1 1 (2.9)	0 0(0.0)
Cardiac General	2 2 (2.6)	3 3 (3.9)	-1 -1 (-1.3)	0 0 (0.0)	0 0 (0.0)	0 0(0.0)
Constitutional Symptoms	19 15 (19.5)	19 15 (19.7)	0 0 (-0.2)	2 2 (5.7)	2 2 (5.7)	0 0(0.0)
Death**	1 1 (1.3)	1 1 (1.3)	0 0 (0.0)	0 0 (0.0)	0 0 (0.0)	0 0(0.0)
Dermatology/Skin	15 13 (16.9)	17 14(18.4)	-2 -1 (-1.5)	5 4 (11.4)	8 5 (14.3)	-3 -1(-2.9)
Endocrine	4 4 (5.2)	3 3(3.9)	1 1(1.3)	2 2 (5.7)	2 2 (5.7)	0 0(0.0)
Gastrointestinal	30 18 (23.4)	30 17(22.4)	0 1(1.0)	11 7 (20.0)	12 8 (22.9)	-1 -1(-2.9)
Infection	63 32 (41.6)	65 33 (43.4)	-2 -1(-1.8)	31 15 (42.9)	32 15 (42.9)	-1 0(0.0)
Hypoglycemia	5 3 (3.9)	6 4 (5.3)	-1 -1 (-1.4)	2 1 (2.9)	2 1 (2.9)	0 0(0.0)
Metabolic/Laboratory	8 6 (7.8)	8 6 (7.9)	0 0 (-0.1)	4 2 (5.7)	4 2 (5.7)	0 0(0.0)
Musculoskeletal/Soft Tissue	13 11 (14.3)	15 13 (17.1)	-2 -2 (-2.7)	7 6 (17.1)	7 6 (17.1)	0 0(0.0)
Neurology	13 8 (10.4)	15 9 (11.8)	-2 -1 (-1.4)	3 2 (5.7)	3 2 (5.7)	0 0(0.0)
Ocular/Visual	3 3 (3.9)	3 3 (3.9)	0 0 (0.0)	1 1 (2.9)	1 1 (2.9)	0 0(0.0)
Pain	7 6 (7.8)	7 6 (7.9)	0 0 (-0.1)	5 4 (11.4)	5 4 (11.4)	0 0(0.0)
Pulmonary/Upper Respiratory	20 10 (13.0)	21 10(13.2)	-1 0(-0.2)	7 4 (11.4)	8 5 (14.3)	-1 -1(-2.9)
Renal/Genitourinary	0 0 (0.0)	0 0(0.0)	0 0(0.0)	1 1 (2.9)	1 1 (2.9)	0 0(0.0)
Secondary Malignancy	1 1 (1.3)	1 1 (1.3)	0 0 (0.0)	0 0 (0.0)	0 0 (0.0)	0 0(0.0)
Sexual/Reproductive Function	1 1 (1.3)	1 1 (1.3)	0 0 (0.0)	0 0 (0.0)	0 0 (0.0)	0 0(0.0)
Surgery/Intra-Operative Injury	2 2 (2.6)	2 2 (2.6)	0 0 (0.0)	0 0 (0.0)	0 0 (0.0)	0 0(0.0)
Syndromes	9 9 (11.7)	9 9 (11.8)	0 0 (-0.1)	5 5 (14.3)	5 5 (14.3)	0 0(0.0)
Total	239 --	251	-12	105 --	112	-7

Attachment A: SAS Code

```
*********************************************************************************************************
***Program:
***Programmer: Corey Del Vecchio
***Date Created: 7/8/2013
***Purpose:
***
***
***
***Source of Request:
***Input Files:
***
***Output Files:
***
***History
***Updated by: Michael Spriggs
***Date Modified: 03/05/2015
********************************************************************************************************;

title1 "%sysfunc(getoption(sysin))";
title2 " ";

options nofmterr source2 mprint symbolgen spool;
libname sas_data "/prj/niddk/ims_analysis/TrialNet/private_orig_data/new_data_3_6_15/Data.Extraction.9.Version150305PW/9/sasv9/";
filename sascsv "/prj/niddk/ims_analysis/TrialNet/private_orig_data/Data.Extraction.9.Version110430/9/csv/adverseeventedit.24feb2015.csv";

proc import datafile=sascsv
     out=adversecsv
     dbms=csv
     replace;
     getnames=yes;
run;

data adversecsv;
  set adversecsv;
  length severitynum 8.;
  if (substr(severity,1,1))="1" then severitynum=1;
  else if (substr(severity,1,1))="2" then severitynum=2;
  else if (substr(severity,1,1))="3" then severitynum=3;
  else if (substr(severity,1,1))="4" then severitynum=4;
  else if (substr(severity,1,1))="5" then severitynum=5;
  else delete;

proc sort data=adversecsv;
  by MASKID;

proc format;
  value yesnof
        1="Yes"
        2="No"
        ;
        ;

*** File containing macro for examining each dataset ***;
%include '/prj/niddk/ims_analysis/sas_macros/redaction_data_summary.sas';

%macro freqdata1(order=, invar=, level=, popvar=, totalvl=);
```

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```
%if &totalvl.=null %then %do;
   proc freq data=table1 noprint;
         tables &invar*treatmentname/out=data1 outpct;
         format _all_;
         run;

   data data1(keep=LEVEL treatmentname name CHARALL ORDERER);
      set data1(rename=(&invar=LEVEL));
      length name $100 CHARALL $100;
      name=upcase("&invar");
      PCT_DISP=round(PCT_COL,.1);
      CHARALL=compress(put(COUNT,8.))||" ("||compress(put(PCT_DISP,8.1))||")";
      ORDERER=&order;
      if level in &level then output;
%end;
%else %do;
   proc freq data=table1 noprint;
         tables &invar*treatmentname/out=data1 outpct;
         format _all_;
         where &popvar. in &totalvl.;
         run;

   data data1(keep=LEVEL treatmentname name COUNT PCT_DISP ORDERER) total1(keep=accumer1 accumer2);
      set data1(rename=(&invar=LEVEL)) end=end1;
      length name $100;
      retain accumer1 accumer2;
      if _n_=1 then do;
         accumer1=0;
         accumer2=0;
      end;
      if treatmentname=1 then accumer1=accumer1+count;
      else if treatmentname=2 then accumer2=accumer2+count;
      name=upcase("&invar");
      PCT_DISP=round(PCT_COL,.1);
      ORDERER=&order;
      if level in &level then output data1;
      if end1 then output total1;

data total1(drop=accumer:);
   set total1;
   length treatmentname total 8.;
   treatmentname=1;
   total=accumer1;
   output;
   treatmentname=2;
   total=accumer2;
   output;

data data1(drop=COUNT PCT_DISP total);
   merge data1 total1;
   by treatmentname;
   length CHARALL $100;
   CHARALL=compress(put(COUNT,8.))||"/"||compress(put(total,8.))||" ("||compress(put(PCT_DISP,8.1))||")";


%end;
data accumfreq1;
```

```
    set accumfreq1 data1;

%mend freqdata1;

%macro meandata1(order=, invar=, roundvar=, digit=);
proc means data=table1 mean stddev noprint;
        var &invar;
        class treatmentname;
        output out=data1 mean=mean stddev=stddev;
        run;

data data1(drop=_TYPE_ _FREQ_ mean stddev);
   set data1;
   length name CHARALL $100;
   name=upcase("&invar");
   mean=round(mean,&roundvar);
   stddev=round(stddev,&roundvar);
   CHARALL=compress(put(mean,8.&digit))||" ± "||compress(put(stddev,8.&digit));
   ORDERER=&order;

data accummean1;
   set accummean1 data1;

%mend meandata1;

%macro mediandata1(order=, invar=, roundvar=, digit=);
proc means data=table1 median p25 p75 min max noprint;
        var &invar;
        class treatmentname;
        output out=data1 median=median p25=p25 p75=p75 min=min max=max;
        run;

data data1(drop=_TYPE_ _FREQ_ median p25 p75 min max);
   set data1;
   length name CHARALL $100;
   name=upcase("&invar");
   median=round(median,&roundvar);
   min=round(min,&roundvar);
   max=round(max,&roundvar);
   ORDERER=&order;
   CHARALL=compress(put(median,8.&digit));
   output;
   ORDERER=ORDERER+.01;
   CHARALL=compress(put(min,8.&digit)||"-"||put(max,8.&digit));
   output;

data accummedian1;
   set accummedian1 data1;

%mend mediandata1;

%macro rangedata1(order=, invar=, roundvar=, digit=);
proc means data=table1 median p25 p75 min max noprint;
        var &invar;
        class treatmentname;
        output out=data1 min=min max=max;
        run;
```

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```
data data1(drop=_TYPE_ _FREQ_ min max);
   set data1;
   length name CHARALL $100;
   name=upcase("&invar");
   min=round(min,&roundvar);
   max=round(max,&roundvar);
   ORDERER=&order;
   CHARALL=compress(put(min,8.&digit)||"-"||put(max,8.&digit));
   output;

data accummedian1;
   set accummedian1 data1;

%mend rangedata1;

data accumfreq1 accummean1 accummedian1;
   set _null_;

data research_labs;
   set sas_data.research_labs;

proc sort data=research_labs;
   by maskid;


data research_aa(drop=test_name result rename=(s_test_name=test_name s_result=result));
   set research_labs;
   length s_test_name s_result $10. result_n 8.;
   s_test_name=strip(test_name);
   s_result=strip(result);
   if test_name in("GAD65" "ICA512" "ICA" "MIAA") and strip(visit)="Screening" then do;
     if s_result='<.05' then result_n=0.025;
     else if s_result ne " " then result_n=put(s_result,8.2);
     output;
   end;

data research_peptide(drop=test_name result rename=(s_test_name=test_name s_result=result));
   set research_labs;
   length s_test_name s_result $10. result_n 8.;
   s_test_name=strip(test_name);
   s_result=strip(result);
   if index(spec_name,"peptide")>0 then do;
     if s_result='<.05' then result_n=0.025;
     else if s_result ne " " then result_n=put(s_result,8.2);
     output;
   end;

data research_hemo(drop=test_name result rename=(s_test_name=test_name s_result=result));
   set research_labs;
   length s_test_name s_result $10. Glyc_HEMO 8.;
   s_test_name=strip(test_name);
   s_result=strip(result);
   if index(spec_name,"HbA1c")>0 and Visit="Baseline" then do;
     if s_result ne " " then Glyc_HEMO =put(s_result,8.2);
     output;
   end;

data research_DR(drop=test_name result rename=(s_test_name=test_name s_result=result));
```

```
    set research_labs;
    length s_test_name s_result $10.;
    s_test_name=strip(test_name);
    s_result=strip(result);
    if index(test_name,"DR")>0 then  output;

data research_DR_short(keep=MaskID DR_NET);
    set research_DR;
    by MaskID;
    length DR_N 8. DR_NET $10;
    retain DR_N;
    if first.MASKID then DR_N=0;
    if strip(test_name)="DR3" and strip(result)="ABSENT" then DR_N=DR_N+2;
    if strip(test_name)="DR4" and strip(result)="ABSENT" then DR_N=DR_N+1;
    if last.MASKID then do;
      DR_NET=strip(put(DR_N,8.));
      output;
    end;

data research_short(keep=MASKID ANTIBODY_CHAR);
    set research_aa;
    by MASKID;
    length ANTIBODY_COUNT 8. ANTIBODY_CHAR $8.;
    retain ANTIBODY_COUNT;
    if first.MASKID then ANTIBODY_COUNT=0;
    if test_name="GAD65" and result_n>.032 then ANTIBODY_COUNT=ANTIBODY_COUNT+1;
    if test_name="ICA512" and result_n>.049 then ANTIBODY_COUNT=ANTIBODY_COUNT+1;
    if test_name="ICA" and result_n>=10 then ANTIBODY_COUNT=ANTIBODY_COUNT+1;
    if test_name="MIAA" and result_n>.01 then ANTIBODY_COUNT=ANTIBODY_COUNT+1;
    if last.MASKID then do;
      ANTIBODY_CHAR=strip(put(ANTIBODY_COUNT,8.));
      output;
    end;

data screen;
    set sas_data.ctl01_screening;
    screen_date=date_of_visit;

data cvis;
    set sas_data.ctl12_visit_form;
    where visit="Baseline";

data diab;
    set SAS_DATA.diabetes_management;
    where visit="Baseline";


data treatment_table;
    set sas_data.treatment_table;
    where MASKID ne .;

data cscrmedhist;
    set sas_data.ctl02_screening_med_history;
        if DateOfT1DMonth="Jan" then DateOfT1DMonthn=1;
    else if DateOfT1DMonth="Feb" then DateOfT1DMonthn=2;
    else if DateOfT1DMonth="Mar" then DateOfT1DMonthn=3;
    else if DateOfT1DMonth="Apr" then DateOfT1DMonthn=4;
    else if DateOfT1DMonth="May" then DateOfT1DMonthn=5;
```

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```
    else if DateOfT1DMonth="Jun" then DateOfT1DMonthn=6;
    else if DateOfT1DMonth="Jul" then DateOfT1DMonthn=7;
    else if DateOfT1DMonth="Aug" then DateOfT1DMonthn=8;
    else if DateOfT1DMonth="Sep" then DateOfT1DMonthn=9;
    else if DateOfT1DMonth="Oct" then DateOfT1DMonthn=10;
    else if DateOfT1DMonth="Nov" then DateOfT1DMonthn=11;
    else if DateOfT1DMonth="Dec" then DateOfT1DMonthn=12;
    DXDATE=MDY(DateOfT1DMonthn,DATEOFT1DDay,DATEOFT1DYear);


data celig;
    set sas_data.ctl05_eligibility;

data cdrugadmin;
    set sas_data.ctl07_study_drug_admin;
    DA_DATE=DATE_OF_VISIT;
    if visit="Baseline" then output;


data research_auc(drop=test_name result rename=(s_test_name=test_name s_result=result));
    set research_labs;
    length s_test_name s_result $10.;
    s_test_name=strip(test_name);
    s_result=strip(result);
    if visit="Screening" and index(test_name,"PEP")>0 then output;

data research_auc_proc(keep=MaskID result_:);
    set research_auc;
        by MaskID;
    length resultn
            result_m10
            result_0
            result_15
            result_30
            result_60
            result_90
            result_120
            result_150
            result_180
            result_210
            result_240
8.;
    retain result_m10
            result_0
            result_15
            result_30
            result_60
            result_90
            result_120
            result_150
            result_180
            result_210
            result_240
            ;

    if result="<.05" then resultn=.025;
    else resultn=input(result,8.);
    resultn=resultn*.33;
```

```
   if first.maskid then do;
     result_m10=.;
     result_0  =.;
     result_15 =.;
     result_30 =.;
     result_60 =.;
     result_90 =.;
     result_120=.;
     result_150=.;
     result_180=.;
     result_210=.;
     result_240=.;
   end;

   if test_name="PEP-10" then result_m10  =resultn;
   if test_name="PEP0"   then result_0    =resultn;
   if test_name="PEP120" then result_120  =resultn;
   if test_name="PEP15"  then result_15   =resultn;
   if test_name="PEP150" then result_150  =resultn;
   if test_name="PEP180" then result_180  =resultn;
   if test_name="PEP210" then result_210  =resultn;
   if test_name="PEP240" then result_240  =resultn;
   if test_name="PEP30"  then result_30   =resultn;
   if test_name="PEP60"  then result_60   =resultn;
   if test_name="PEP90"  then result_90   =resultn;

   if last.maskid then output;

data research_auc_proc_b;
   set research_auc_proc;
   length result_string $50;
   if result_m10>. then result_string=strip(result_string)||"-10,";
   if result_0  >. then result_string=strip(result_string)||"0,"  ;
   if result_15 >. then result_string=strip(result_string)||"15," ;
   if result_30 >. then result_string=strip(result_string)||"30," ;
   if result_60 >. then result_string=strip(result_string)||"60," ;
   if result_90 >. then result_string=strip(result_string)||"90," ;
   if result_120>. then result_string=strip(result_string)||"120,";
   if result_150>. then result_string=strip(result_string)||"150,";
   if result_180>. then result_string=strip(result_string)||"180,";
   if result_210>. then result_string=strip(result_string)||"210,";
   if result_240>. then result_string=strip(result_string)||"240,";

   if index(result_string,'-10,15,30,60,90,120,')>0 then do;
     AUC_RESULT=(7.5*result_m10+15*result_15+22.5*result_30+30*result_60+30*result_90+15*result_120)/120;
   end;
   *** Has to be looked at after the first because it is a substring of it ***;
   else if index(result_string,'0,15,30,60,90,120,')>0 then do;
     AUC_RESULT=(7.5*result_0+15*result_15+22.5*result_30+30*result_60+30*result_90+15*result_120)/120;
   end;
   else if index(result_string,'0,15,30,60,90,180,')>0 then do;
     AUC_RESULT=(7.5*result_0+15*result_15+22.5*result_30+30*result_60+37.5*result_90+7.5*result_180)/120;
   end;

proc freq data=research_auc_proc_b;
   tables result_string/missing list;
```

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```
data adverseevent;
   set sas_data.adverseevent;

proc sort data=screen;
   by MASKID;

proc sort data=cvis;
   by MASKID;

proc sort data=diab;
   by MASKID;

proc sort data=treatment_table;
   by MASKID;

proc sort data=cscrmedhist;
   by MASKID;

proc sort data=celig;
   by MASKID;

proc sort data=cdrugadmin;
   by MASKID;

proc sort data=adverseevent;
   by MASKID;

data table1;
   merge screen(in=in_screen)
         diab
         cvis
         treatment_table
         cscrmedhist
         celig
         cdrugadmin
         research_hemo
         research_short
         research_dr_short
         research_auc_proc_b
         ;
   by maskid;
   length c_race_white $8.;
   c_race_white=strip(put(race_white,8.));
   total_insulin_kg=(AverageUnitsOfItermediateInsul+AvgUnitsShortActingInsulin)/weightkg;
   bmi=PhysicalWEIGHTKG/(PhysicalHeightCM*PhysicalHeightCM/10000);
   INFUSE_DAYS=DA_DATE-DXDATE;
   if in_screen then output;

%meandata1(order=1,   invar=age              , roundvar=.1, digit=1);
%mediandata1(order=1.5,  invar=age             , roundvar=1, digit=0);
%freqdata1(order=2,   invar=sex             , level=("Male"),popvar=, totalvl=null);
%freqdata1(order=3,   invar=c_race_white    , level=("1"),popvar=, totalvl=null);
%freqdata1(order=4,   invar=ethnicity       , level=("Not Hispanic or Latino"),popvar=, totalvl=null);
%freqdata1(order=7,   invar=ANTIBODY_CHAR   , level=("1"),popvar=, totalvl=null);
%freqdata1(order=8,   invar=ANTIBODY_CHAR   , level=("2"),popvar=, totalvl=null);
%freqdata1(order=9,   invar=ANTIBODY_CHAR   , level=("3"),popvar=, totalvl=null);
%freqdata1(order=10,  invar=ANTIBODY_CHAR   , level=("4"),popvar=, totalvl=null);
%meandata1(order=11,  invar=INFUSE_DAYS     , roundvar=.1, digit=1);
```

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```
%rangedata1(order=11.5, invar=INFUSE_DAYS, roundvar=1, digit=0);
%meandata1(order=12,  invar=PhysicalWEIGHTKG         , roundvar=.1, digit=1);
%meandata1(order=13,  invar=bmi                , roundvar=.01, digit=2);
%meandata1(order=13.5, invar=AUC_RESULT     , roundvar=.001, digit=3);
%meandata1(order=14,  invar=GLYC_HEMO , roundvar=.01, digit=2);
%meandata1(order=15,  invar=total_insulin_kg       , roundvar=.001, digit=3);
%freqdata1(order=17,  invar=DKAAtTimeOfDiagnosis , level=("Yes"),popvar=, totalvl=null);
%freqdata1(order=18,  invar=DR_NET  , level=("0"),popvar=, totalvl=null);
%freqdata1(order=19,  invar=DR_NET  , level=("1"),popvar=, totalvl=null);
%freqdata1(order=20,  invar=DR_NET  , level=("2"),popvar=, totalvl=null);
%freqdata1(order=21,  invar=DR_NET  , level=("3"),popvar=, totalvl=null);


data accumtab1;
   set accumfreq1 accummean1 accummedian1;
   if treatmentname=" " then delete;

proc sort data=accumtab1;
   by treatmentname orderer;

proc print data=accumtab1 noobs;
   by treatmentname;
   title3 'Table 1 stats (list)';

data adversecsv;
   set adversecsv;
   if ReportType="Initial" and maskid ne . then output;

proc sort data=adversecsv;
   by MASKID severitynum;

data adversecsv_short;
   set adversecsv;
   by MASKID severitynum;
   if last.MASKID then output;


data table2_1;
   merge table1(drop=other in=in_tab1)
         adversecsv_short
         ;
   by MASKID;
   if in_tab1;
   if treatmentname=' ' then delete;
   if severitynum=. then severitynum=0;

data table2_2a;
   merge table1(drop=other in=in_tab1)
         adversecsv
         ;
   by MASKID;
   if in_tab1;
   if treatmentname=' ' then delete;
   if severitynum=. then delete;
   length old_category $40;
   OLD_CATEGORY=CATEGORY;
   if index(supraordinateterm,"hypoglycemia")>1 then CATEGORY="Hypoglycemia";
```

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```
proc freq data=table2_2a;
   tables OLD_CATEGORY*CATEGORY/missing list;
   where category ne old_category;

proc sort data=table2_2a out=table2_2b nodupkeys;
   by MASKID CATEGORY;

proc freq data=table2_1;
   tables Severitynum*treatmentname/missing nopercent norow;
   title3 'Table 2 part 1';

proc freq data=table2_2a;
   tables Category*treatmentname/missing norow nopercent nocol;
   title3 'Table 2 part 2a (No of events)';
   where category ne " ";

proc freq data=table2_2b;
   tables Category*treatmentname/missing norow nopercent nocol;
   title3 'Table 2 part 2b (No of subjects)';
   where category ne " ";
```