**PharmaSUG 2012 - Paper AD20**

# CDISC SDTM CONVERSION IN ISS/ISE STUDIES: TOOLS

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## ABSTRACT:

CDISC SDTM (Study Data Tabulation Model) conversion for Integration Summary of Safety (ISS) and Integrated Summary of Efficacy (ISE) is always a challenging job. The most taxing task is the standardization of different non-CDISC compliant raw datasets to CDISC compliant domains and variables for all the legacy studies involving large amount data and diverse systems of data collection. Having faced this challenge year after year, I have been involved in the development of a set of tools and reports to perform and validate the SDTM conversion for ISS/ISE studies of varying proportion to complete the task in a manner that is efficient and accurate. This paper will describe the functionalities of this utility. The technologies used are SAS, Microsoft Excel, VBA and SAS IOM. Knowledge of VBA and SAS IOM fundamentals is a plus, but not a limiting factor.

## INTRODUCTION:

ISS and ISE analyses are considered as some of the most important components for the FDA NDA submission. When we have tools to check SDTM process implementation at various stages, it makes the process easier and time efficient. This paper will explain the tools and reports generated at various stages of ISS/ISE implementation:

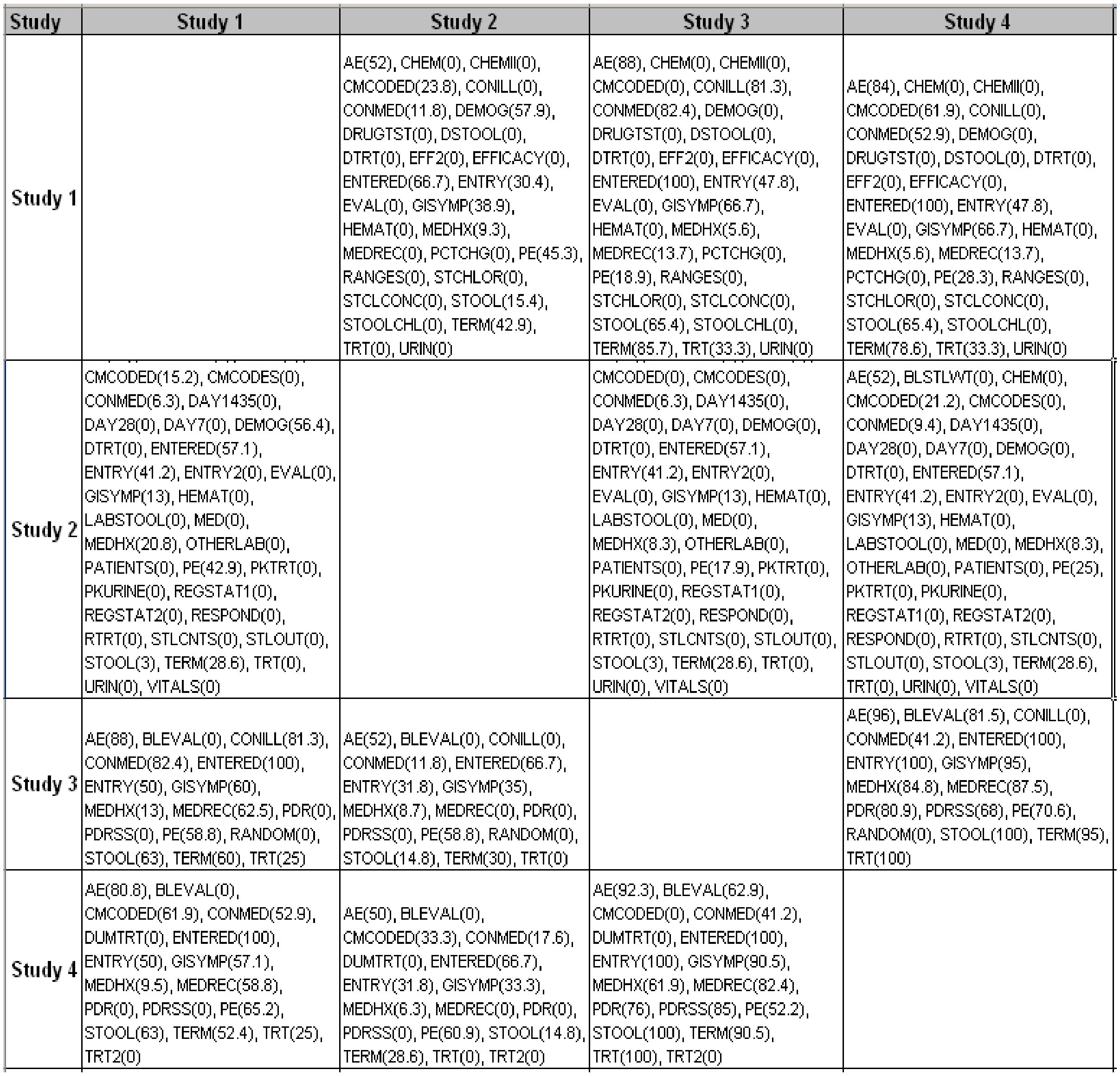
i. Stage I : Pre-processing
ii. Stage II : SDTM Implementation
iii. Stage III: Post-Processing

## STAGE I (PRE-PROCESSING):

In this stage, we will be scrutinizing different scenarios in order to achieve accurate integrated datasets for the ISS/ISE analysis. In the initial stage of the implementation it will be very useful to group the studies with similar data structures.

In order to find similar studies or common data structures across the studies, we have developed a macro which takes the metadata information (ie. raw dataset name, variable name, variable attributes like label and format) and checks it to derive the percentage of structural homogeneity. The higher the percentage (number within the parentheses following the dataset name), the higher the similarity. A zero would indicate there is no matching dataset.

For example, if we have a raw AE dataset in study 1, this dataset’s Meta information is compared with all other raw AE datasets. Then another AE dataset is selected and compared against the rest, and so on. This process is followed for all the datasets. At the end, we will have a report with the percentage of similarity for each raw dataset across the studies in an nXn grid, where n is the number of studies. The screen shot below shows a sample report. Percentages are displayed in parenthesis along with each raw dataset.

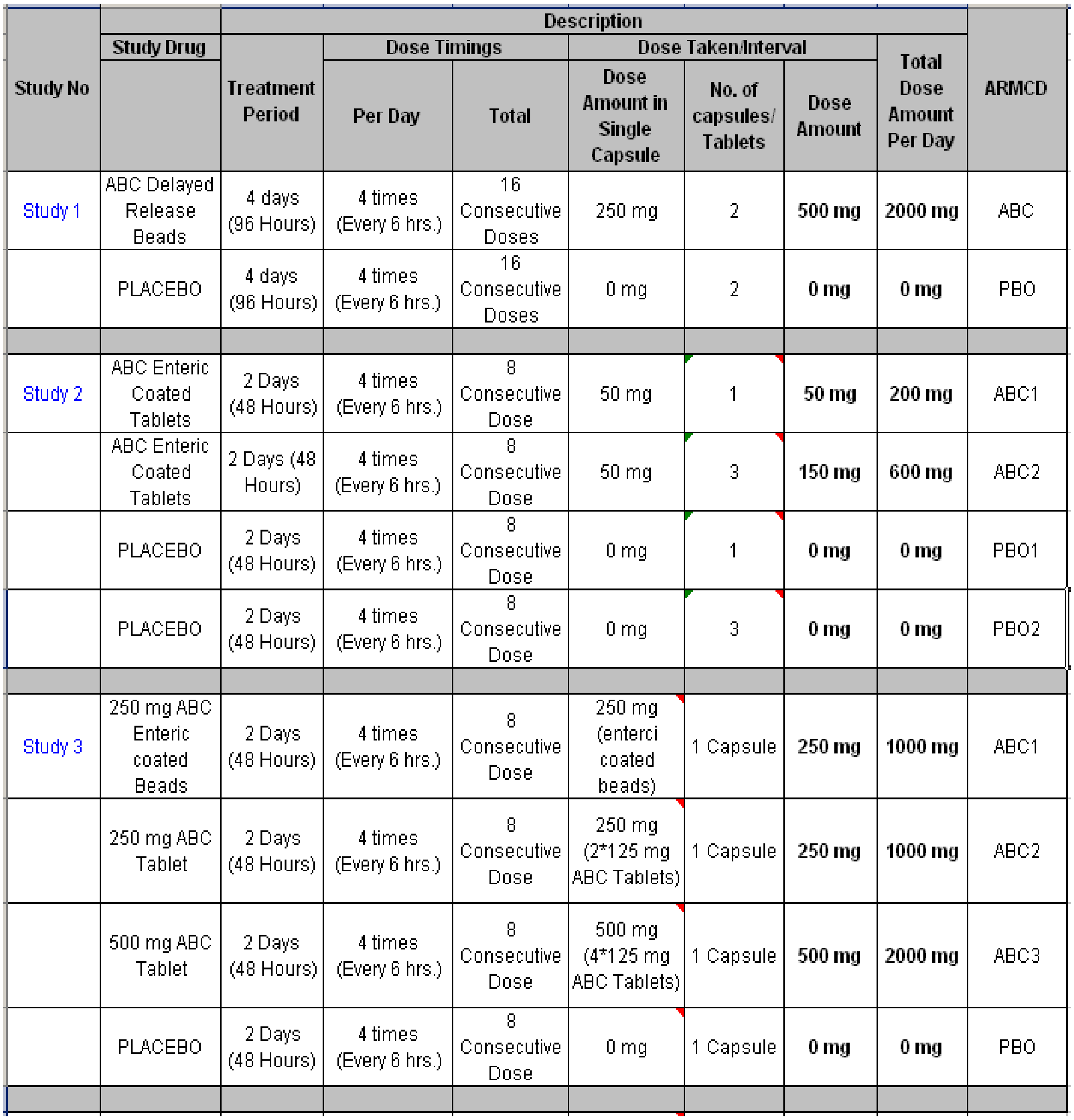


| Study | Study 1 | Study 2 | Study 3 | Study 4 |
|---|---|---|---|---|
| Study 1 | | AE(52), CHEM(0), CHEMII(0), CMCODED(23.8), CONILL(0), CONMED(11.8), DEMOG(57.9), DRUGTST(0), DSTOOL(0), DTRT(0), EFF2(0), EFFICACY(0), ENTERED(66.7), ENTRY(30.4), EVAL(0), GISYMP(38.9), HEMAT(0), MEDHX(9.3), MEDREC(0), PCTCHG(0), PE(45.3), RANGES(0), STCHLOR(0), STCLCONC(0), STOOL(15.4), STOOLCHL(0), TERM(42.9), TRT(0), URIN(0) | AE(88), CHEM(0), CHEMII(0), CMCODED(0), CONILL(81.3), CONMED(82.4), DEMOG(0), DRUGTST(0), DSTOOL(0), DTRT(0), EFF2(0), EFFICACY(0), ENTERED(100), ENTRY(47.8), EVAL(0), GISYMP(66.7), HEMAT(0), MEDHX(5.6), MEDREC(13.7), PCTCHG(0), PE(18.9), RANGES(0), STCHLOR(0), STCLCONC(0), STOOL(65.4), STOOLCHL(0), TERM(85.7), TRT(33.3), URIN(0) | AE(84), CHEM(0), CHEMII(0), CMCODED(61.9), CONILL(0), CONMED(52.9), DEMOG(0), DRUGTST(0), DSTOOL(0), DTRT(0), EFF2(0), EFFICACY(0), ENTERED(100), ENTRY(47.8), EVAL(0), GISYMP(66.7), HEMAT(0), MEDHX(5.6), MEDREC(13.7), PCTCHG(0), PE(28.3), RANGES(0), STCHLOR(0), STCLCONC(0), STOOL(65.4), STOOLCHL(0), TERM(78.6), TRT(33.3), URIN(0) |
| Study 2 | CMCODED(15.2), CMCODES(0), CONMED(6.3), DAY1435(0), DAY28(0), DAY7(0), DEMOG(56.4), DTRT(0), ENTERED(57.1), ENTRY(41.2), ENTRY2(0), EVAL(0), GISYMP(13), HEMAT(0), LABSTOOL(0), MED(0), MEDHX(20.8), OTHERLAB(0), PATIENTS(0), PE(42.9), PKTRT(0), PKURINE(0), REGSTAT1(0), REGSTAT2(0), RESPOND(0), RTRT(0), STLCNTS(0), STLOUT(0), STOOL(3), TERM(28.6), TRT(0), URIN(0), VITALS(0) | | CMCODED(0), CMCODES(0), CONMED(6.3), DAY1435(0), DAY28(0), DAY7(0), DEMOG(0), DTRT(0), ENTERED(57.1), ENTRY(41.2), ENTRY2(0), EVAL(0), GISYMP(13), HEMAT(0), LABSTOOL(0), MED(0), MEDHX(8.3), OTHERLAB(0), PATIENTS(0), PE(17.9), PKTRT(0), PKURINE(0), REGSTAT1(0), REGSTAT2(0), RESPOND(0), RTRT(0), STLCNTS(0), STLOUT(0), STOOL(3), TERM(28.6), TRT(0), URIN(0), VITALS(0) | AE(52), BLSTLWT(0), CHEM(0), CMCODED(21.2), CMCODES(0), CONMED(9.4), DAY1435(0), DAY28(0), DAY7(0), DEMOG(0), DTRT(0), ENTERED(57.1), ENTRY(41.2), ENTRY2(0), EVAL(0), GISYMP(13), HEMAT(0), LABSTOOL(0), MED(0), MEDHX(8.3), OTHERLAB(0), PATIENTS(0), PE(25), PKTRT(0), PKURINE(0), REGSTAT1(0), REGSTAT2(0), RESPOND(0), RTRT(0), STLCNTS(0), STLOUT(0), STOOL(3), TERM(28.6), TRT(0), URIN(0), VITALS(0) |
| Study 3 | AE(88), BLEVAL(0), CONILL(81.3), CONMED(82.4), ENTERED(100), ENTRY(50), GISYMP(60), MEDHX(13), MEDREC(62.5), PDR(0), PDRSS(0), PE(58.8), RANDOM(0), STOOL(63), TERM(60), TRT(25) | AE(52), BLEVAL(0), CONILL(0), CONMED(11.8), ENTERED(66.7), ENTRY(31.8), GISYMP(35), MEDHX(8.7), MEDREC(0), PDR(0), PDRSS(0), PE(58.8), RANDOM(0), STOOL(14.8), TERM(30), TRT(0) | | AE(96), BLEVAL(81.5), CONILL(0), CONMED(41.2), ENTERED(100), ENTRY(100), GISYMP(95), MEDHX(84.8), MEDREC(87.5), PDR(80.9), PDRSS(68), PE(70.6), RANDOM(0), STOOL(100), TERM(95), TRT(100) |
| Study 4 | AE(80.8), BLEVAL(0), CMCODED(61.9), CONMED(52.9), DUMTRT(0), ENTERED(100), ENTRY(50), GISYMP(57.1), MEDHX(9.5), MEDREC(58.8), PDR(0), PDRSS(0), PE(65.2), STOOL(63), TERM(52.4), TRT(25), TRT2(0) | AE(50), BLEVAL(0), CMCODED(33.3), CONMED(17.6), DUMTRT(0), ENTERED(66.7), ENTRY(31.8), GISYMP(33.3), MEDHX(6.3), MEDREC(0), PDR(0), PDRSS(0), PE(60.9), STOOL(14.8), TERM(28.6), TRT(0), TRT2(0) | AE(92.3), BLEVAL(62.9), CMCODED(0), CONMED(41.2), DUMTRT(0), ENTERED(100), ENTRY(100), GISYMP(90.5), MEDHX(61.9), MEDREC(82.4), PDR(76), PDRSS(85), PE(52.2), STOOL(100), TERM(90.5), TRT(100), TRT2(0) | |

Before programming, key information about the study design is pooled together in a spread sheet, like study drug, treatment period, frequency dosing information and total dose amount per day.

We can also add ARMCD (planned treatment) and pool column. This sheet will help us provide a quick understanding of each study to the programmers/statistician involved in the analyses and also can be used for Trial Design datasets. This sheet is created manually by going through the protocol/SAP for each study in the analyses.

Please check the screen shot below which gives the key information about the design for all the studies.



| Study No | | Description | | | | | | | ARMCD |
|---|---|---|---|---|---|---|---|---|---|
| | Study Drug | Treatment Period | Dose Timings | | Dose Taken/Interval | | | Total Dose Amount Per Day | |
| | | | Per Day | Total | Dose Amount in Single Capsule | No. of capsules/ Tablets | Dose Amount | | |
| Study 1 | ABC Delayed Release Beads | 4 days (96 Hours) | 4 times (Every 6 hrs.) | 16 Consecutive Doses | 250 mg | 2 | **500 mg** | **2000 mg** | ABC |
| | PLACEBO | 4 days (96 Hours) | 4 times (Every 6 hrs.) | 16 Consecutive Doses | 0 mg | 2 | **0 mg** | **0 mg** | PBO |
| | | | | | | | | | |
| Study 2 | ABC Enteric Coated Tablets | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 50 mg | 1 | **50 mg** | **200 mg** | ABC1 |
| | ABC Enteric Coated Tablets | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 50 mg | 3 | **150 mg** | **600 mg** | ABC2 |
| | PLACEBO | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 0 mg | 1 | **0 mg** | **0 mg** | PBO1 |
| | PLACEBO | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 0 mg | 3 | **0 mg** | **0 mg** | PBO2 |
| | | | | | | | | | |
| Study 3 | 250 mg ABC Enteric coated Beads | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 250 mg (enterci coated beads) | 1 Capsule | **250 mg** | **1000 mg** | ABC1 |
| | 250 mg ABC Tablet | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 250 mg (2*125 mg ABC Tablets) | 1 Capsule | **250 mg** | **1000 mg** | ABC2 |
| | 500 mg ABC Tablet | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 500 mg (4*125 mg ABC Tablets) | 1 Capsule | **500 mg** | **2000 mg** | ABC3 |
| | PLACEBO | 2 Days (48 Hours) | 4 times (Every 6 hrs.) | 8 Consecutive Dose | 0 mg | 1 Capsule | **0 mg** | **0 mg** | PBO |
| | | | | | | | | | |

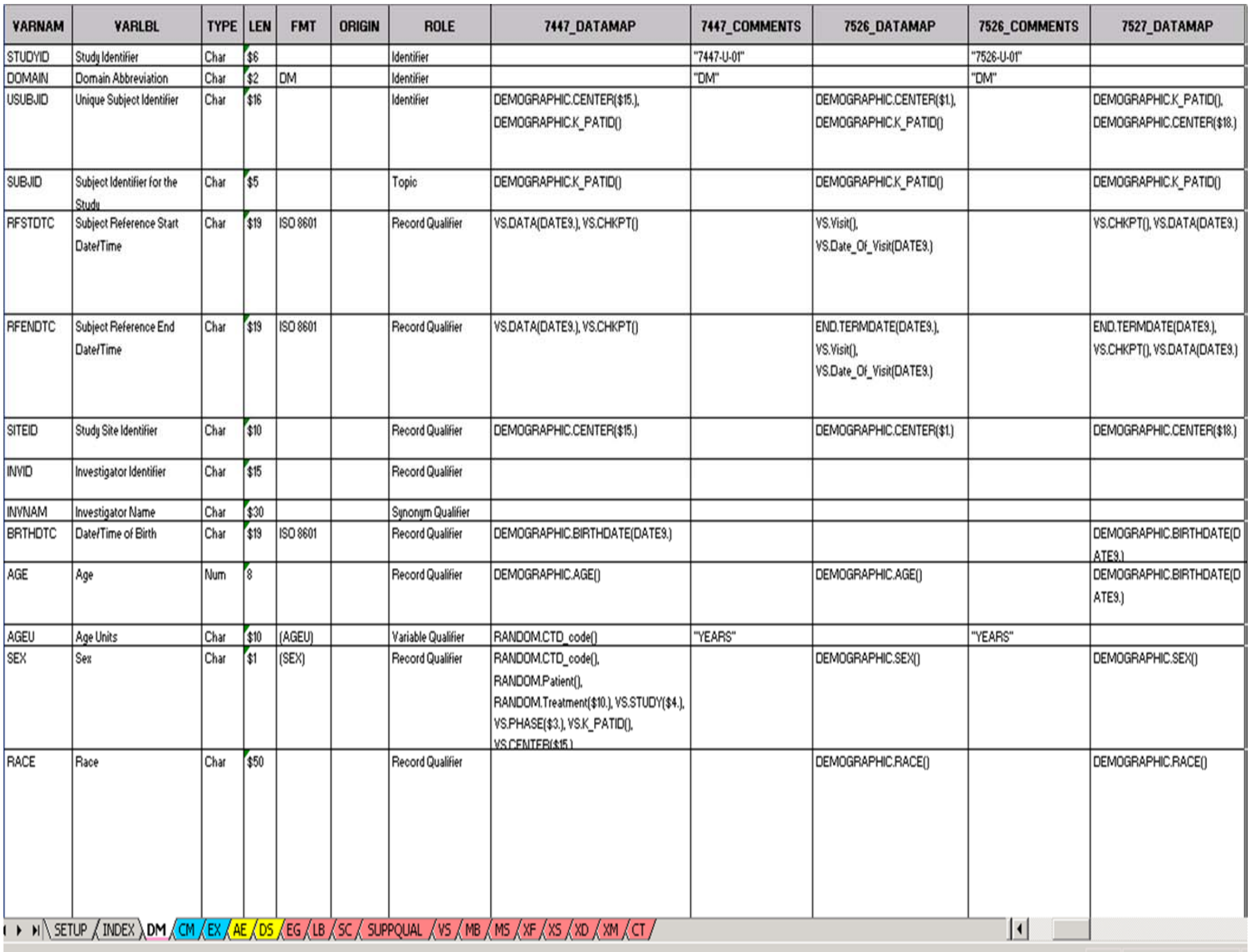
When we have a good understanding about the design of each study and knowledge about similar studies, it will make it easier for the team to accurately integrate the datasets for the ISS/ISE analyses. It is advisable to collect all the unique raw dataset values for key variables to which control terminologies are to be applied. For example, collect all the unique DSTERM values in the spreadsheet for which control terminology is applied. DSDECOD is derived. The same is true for AEACN, AEOUT, LBTEST, etc.. The sheet can then be used for creating the SAS formats while implementing SDTM conversion across the study.

## STAGE II (SDTM IMPLEMENTATION):

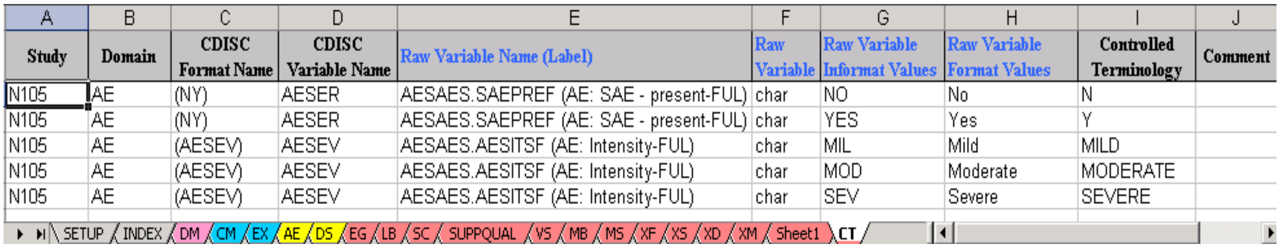
During the programming stage for SDTM conversion across the studies, the tool is used to create a CDISC Variable mapping and a Control Terminology document. This describes, at study level, how the CDISC variables are mapped to the raw dataset variable(s) for each domain across the studies. Standardizing the unique values for certain variables in standard CDISC domains is documented in Control Terminology (CT).

The ISS CDISC variable mapping document will have sheets to contain the Project Directory paths (Directories like: Raw Dataset, CDISC Dataset, SAS Program, etc.) and mapping information of Raw dataset(s) for each domain. Sheets for each Domain, which are to be mapped, will be present in this spreadsheet. There are pre-defined columns, like CDISC variable name, label, type, length, CT format, if applicable. For more details about CDISC variable mapping and CT document tool, please refer to "CDISC Variable Mapping and Control Terminology Implementation Made Easy" (PharmaSUG2011 - Paper CD11, http://www.lexjansen.com/pharmasug/2011/cd/pharmasug-2011-cd11.pdf)

The main advantage of this document is that we know how each raw variable is mapped to a CDISC variable for the corresponding domain across the studies. It helps us to avoid mistakes while mapping the raw dataset variables. Please check the screen shot of the variable mapping document for ISS studies below.



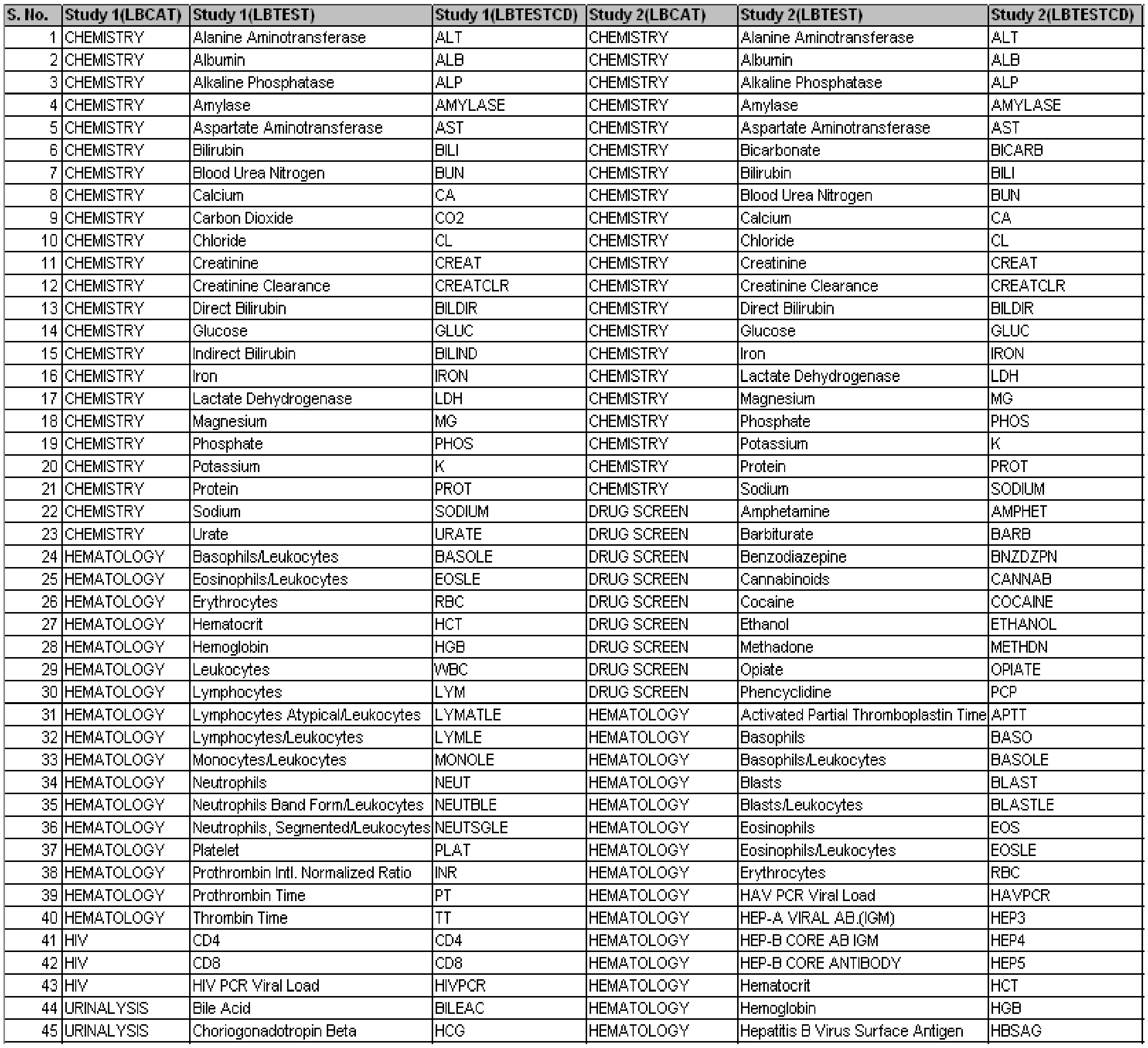
| VARNAM | VARLBL | TYPE | LEN | FMT | ORIGIN | ROLE | 7447_DATAMAP | 7447_COMMENTS | 7526_DATAMAP | 7526_COMMENTS | 7527_DATAMAP |
|---|---|---|---|---|---|---|---|---|---|---|---|
| STUDYID | Study Identifier | Char | $6 | | | Identifier | | "7447-U-01" | | "7526-U-01" | |
| DOMAIN | Domain Abbreviation | Char | $2 | DM | | Identifier | | "DM" | | "DM" | |
| USUBJID | Unique Subject Identifier | Char | $16 | | | Identifier | DEMOGRAPHIC.CENTER($15.),<br>DEMOGRAPHIC.K_PATID() | | DEMOGRAPHIC.CENTER($1.),<br>DEMOGRAPHIC.K_PATID() | | DEMOGRAPHIC.K_PATID(),<br>DEMOGRAPHIC.CENTER($18.) |
| SUBJID | Subject Identifier for the Study | Char | $5 | | | Topic | DEMOGRAPHIC.K_PATID() | | DEMOGRAPHIC.K_PATID() | | DEMOGRAPHIC.K_PATID() |
| RFSTDTC | Subject Reference Start Date/Time | Char | $19 | ISO 8601 | | Record Qualifier | VS.DATA(DATE9.), VS.CHKPT() | | VS.Visit(),<br>VS.Date_Of_Visit(DATE9.) | | VS.CHKPT(), VS.DATA(DATE9.) |
| RFENDTC | Subject Reference End Date/Time | Char | $19 | ISO 8601 | | Record Qualifier | VS.DATA(DATE9.), VS.CHKPT() | | END.TERMDATE(DATE9.),<br>VS.Visit(),<br>VS.Date_Of_Visit(DATE9.) | | END.TERMDATE(DATE9.),<br>VS.CHKPT(), VS.DATA(DATE9.) |
| SITEID | Study Site Identifier | Char | $10 | | | Record Qualifier | DEMOGRAPHIC.CENTER($15.) | | DEMOGRAPHIC.CENTER($1.) | | DEMOGRAPHIC.CENTER($18.) |
| INVID | Investigator Identifier | Char | $15 | | | Record Qualifier | | | | | |
| INVNAM | Investigator Name | Char | $30 | | | Synonym Qualifier | | | | | |
| BRTHDTC | Date/Time of Birth | Char | $19 | ISO 8601 | | Record Qualifier | DEMOGRAPHIC.BIRTHDATE(DATE9.) | | | | DEMOGRAPHIC.BIRTHDATE(DATE9.) |
| AGE | Age | Num | 8 | | | Record Qualifier | DEMOGRAPHIC.AGE() | | DEMOGRAPHIC.AGE() | | DEMOGRAPHIC.BIRTHDATE(DATE9.) |
| AGEU | Age Units | Char | $10 | (AGEU) | | Variable Qualifier | RANDOM.CTD_code() | "YEARS" | | "YEARS" | |
| SEX | Sex | Char | $1 | (SEX) | | Record Qualifier | RANDOM.CTD_code(),<br>RANDOM.Patient(),<br>RANDOM.Treatment($10.), VS.STUDY($4.),<br>VS.PHASE($3.), VS.K_PATID(),<br>VS.CENTER($15.) | | DEMOGRAPHIC.SEX() | | DEMOGRAPHIC.SEX() |
| RACE | Race | Char | $50 | | | Record Qualifier | | | DEMOGRAPHIC.RACE() | | DEMOGRAPHIC.RACE() |



| A | B | C | D | E | F | G | H | I | J |
|---|---|---|---|---|---|---|---|---|---|
| Study | Domain | CDISC Format Name | CDISC Variable Name | Raw Variable Name (Label) | Raw Variable | Raw Variable Informat Values | Raw Variable Format Values | Controlled Terminology | Comment |
| N105 | AE | (NY) | AESER | AESAES.SAEPREF (AE: SAE - present-FUL) | char | NO | No | N | |
| N105 | AE | (NY) | AESER | AESAES.SAEPREF (AE: SAE - present-FUL) | char | YES | Yes | Y | |
| N105 | AE | (AESEV) | AESEV | AESAES.AESITSF (AE: Intensity-FUL) | char | MIL | Mild | MILD | |
| N105 | AE | (AESEV) | AESEV | AESAES.AESITSF (AE: Intensity-FUL) | char | MOD | Moderate | MODERATE | |
| N105 | AE | (AESEV) | AESEV | AESAES.AESITSF (AE: Intensity-FUL) | char | SEV | Severe | SEVERE | |

## STAGE III(POST-PROCESSING):

After completing SDTM conversions for all the studies, it is a good practice to do some post-processing checks to make sure integrated datasets are accurate. The report created will show unique SDTM dataset values with respect to the individual study (a.k.a "Study Wise") and also for integrated datasets. For example, if we want to check the values of LBCAT, LBTEST & LBTESTCD when we pass these variables in the macro, we will have the following report.



| S. No. | Study 1(LBCAT) | Study 1(LBTEST) | Study 1(LBTESTCD) | Study 2(LBCAT) | Study 2(LBTEST) | Study 2(LBTESTCD) |
|---|---|---|---|---|---|---|
| 1 | CHEMISTRY | Alanine Aminotransferase | ALT | CHEMISTRY | Alanine Aminotransferase | ALT |
| 2 | CHEMISTRY | Albumin | ALB | CHEMISTRY | Albumin | ALB |
| 3 | CHEMISTRY | Alkaline Phosphatase | ALP | CHEMISTRY | Alkaline Phosphatase | ALP |
| 4 | CHEMISTRY | Amylase | AMYLASE | CHEMISTRY | Amylase | AMYLASE |
| 5 | CHEMISTRY | Aspartate Aminotransferase | AST | CHEMISTRY | Aspartate Aminotransferase | AST |
| 6 | CHEMISTRY | Bilirubin | BILI | CHEMISTRY | Bicarbonate | BICARB |
| 7 | CHEMISTRY | Blood Urea Nitrogen | BUN | CHEMISTRY | Bilirubin | BILI |
| 8 | CHEMISTRY | Calcium | CA | CHEMISTRY | Blood Urea Nitrogen | BUN |
| 9 | CHEMISTRY | Carbon Dioxide | CO2 | CHEMISTRY | Calcium | CA |
| 10 | CHEMISTRY | Chloride | CL | CHEMISTRY | Chloride | CL |
| 11 | CHEMISTRY | Creatinine | CREAT | CHEMISTRY | Creatinine | CREAT |
| 12 | CHEMISTRY | Creatinine Clearance | CREATCLR | CHEMISTRY | Creatinine Clearance | CREATCLR |
| 13 | CHEMISTRY | Direct Bilirubin | BILDIR | CHEMISTRY | Direct Bilirubin | BILDIR |
| 14 | CHEMISTRY | Glucose | GLUC | CHEMISTRY | Glucose | GLUC |
| 15 | CHEMISTRY | Indirect Bilirubin | BILIND | CHEMISTRY | Iron | IRON |
| 16 | CHEMISTRY | Iron | IRON | CHEMISTRY | Lactate Dehydrogenase | LDH |
| 17 | CHEMISTRY | Lactate Dehydrogenase | LDH | CHEMISTRY | Magnesium | MG |
| 18 | CHEMISTRY | Magnesium | MG | CHEMISTRY | Phosphate | PHOS |
| 19 | CHEMISTRY | Phosphate | PHOS | CHEMISTRY | Potassium | K |
| 20 | CHEMISTRY | Potassium | K | CHEMISTRY | Protein | PROT |
| 21 | CHEMISTRY | Protein | PROT | CHEMISTRY | Sodium | SODIUM |
| 22 | CHEMISTRY | Sodium | SODIUM | DRUG SCREEN | Amphetamine | AMPHET |
| 23 | CHEMISTRY | Urate | URATE | DRUG SCREEN | Barbiturate | BARB |
| 24 | HEMATOLOGY | Basophils/Leukocytes | BASOLE | DRUG SCREEN | Benzodiazepine | BNZDZPN |
| 25 | HEMATOLOGY | Eosinophils/Leukocytes | EOSLE | DRUG SCREEN | Cannabinoids | CANNAB |
| 26 | HEMATOLOGY | Erythrocytes | RBC | DRUG SCREEN | Cocaine | COCAINE |
| 27 | HEMATOLOGY | Hematocrit | HCT | DRUG SCREEN | Ethanol | ETHANOL |
| 28 | HEMATOLOGY | Hemoglobin | HGB | DRUG SCREEN | Methadone | METHDN |
| 29 | HEMATOLOGY | Leukocytes | WBC | DRUG SCREEN | Opiate | OPIATE |
| 30 | HEMATOLOGY | Lymphocytes | LYM | DRUG SCREEN | Phencyclidine | PCP |
| 31 | HEMATOLOGY | Lymphocytes Atypical/Leukocytes | LYMATLE | HEMATOLOGY | Activated Partial Thromboplastin Time | APTT |
| 32 | HEMATOLOGY | Lymphocytes/Leukocytes | LYMLE | HEMATOLOGY | Basophils | BASO |
| 33 | HEMATOLOGY | Monocytes/Leukocytes | MONOLE | HEMATOLOGY | Basophils/Leukocytes | BASOLE |
| 34 | HEMATOLOGY | Neutrophils | NEUT | HEMATOLOGY | Blasts | BLAST |
| 35 | HEMATOLOGY | Neutrophils Band Form/Leukocytes | NEUTBLE | HEMATOLOGY | Blasts/Leukocytes | BLASTLE |
| 36 | HEMATOLOGY | Neutrophils, Segmented/Leukocytes | NEUTSGLE | HEMATOLOGY | Eosinophils | EOS |
| 37 | HEMATOLOGY | Platelet | PLAT | HEMATOLOGY | Eosinophils/Leukocytes | EOSLE |
| 38 | HEMATOLOGY | Prothrombin Intl. Normalized Ratio | INR | HEMATOLOGY | Erythrocytes | RBC |
| 39 | HEMATOLOGY | Prothrombin Time | PT | HEMATOLOGY | HAV PCR Viral Load | HAVPCR |
| 40 | HEMATOLOGY | Thrombin Time | TT | HEMATOLOGY | HEP-A VIRAL AB.(IGM) | HEP3 |
| 41 | HIV | CD4 | CD4 | HEMATOLOGY | HEP-B CORE AB IGM | HEP4 |
| 42 | HIV | CD8 | CD8 | HEMATOLOGY | HEP-B CORE ANTIBODY | HEP5 |
| 43 | HIV | HIV PCR Viral Load | HIVPCR | HEMATOLOGY | Hematocrit | HCT |
| 44 | URINALYSIS | Bile Acid | BILEAC | HEMATOLOGY | Hemoglobin | HGB |
| 45 | URINALYSIS | Choriogonadotropin Beta | HCG | HEMATOLOGY | Hepatitis B Virus Surface Antigen | HBSAG |

The Study Wise sheet in the report will show us the unique values of LBCAT, LBTEST, and LBTESTCD and ensures control terminology is applied appropriately across the studies. The Unique Value sheet will provide information for the integrated ISS dataset. This post-process will allow us to check and make sure all variables are standardized and compliant.

## CONCLUSION:

These different tools are used at various stages of implementation to achieve the accuracy of the integrated datasets in a time efficient manner. It is useful for creating CDISC variable and CT mappings with no typing errors. These tools will drastically reduce the time for preparing documentation. These documents can also be used as a source for creating the DEFINE.XML file.

## REFERENCES:

Using VBA and BASE SAS to Get Data from SAS to Excel without Data Integrity Issues
http://www.lexjansen.com/phuse/2005/as/as11.pdf

CDISC Variable Mapping and Control Terminology Implementation made easy
http://www.lexjansen.com/pharmasug/2011/cd/pharmasug-2011-cd11.pdf

## ACKNOWLEDGEMENTS:

I would like to thank Paul Ragland and Shridhar Patel for providing excellent ideas and helping to implement this paper.

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