ABSTRACT
Analyzing and reporting data using SAS is only as effective as the data that you are working with. Working with large sets of data requires that the data be uniform and standardized. When working with clinical trials data, this becomes apparent when you are working on an Integrated Safety Summary (ISS) or when you are transforming data into a standard such as CDISC. This paper presents methodologies and tools to automate and optimize the transformation of large sets of data in these scenarios. Some of the topics this paper will address include:

1. Organizing the transformation of data in a specification
2. Expressing the transformation specification in a model
3. Automating the process of applying the transformation model.
4. Methods of validating the transformation

This paper will present some of the challenges presented in transforming large sets of data into one standard format. It will then demonstrate methodologies and automation tools such as Transdata™ and CDISC Builder™ which make the process less prone to errors. The paper will explore approaches that create an abstract of what the transformation is doing. It then captures this in a model that can generate code to implement the transformation.

INTRODUCTION
Transforming data from one structure to another is the most rudimental and oldest database task since the beginning relational database. One of the reasons why data needs to be transformed is that source data is in a non-standard form as compared to a target structure. It would make sense that all data should originally be set up with a standardized target structure so that no transformations are needed. In the ideal world, that would be the case. However, in reality, many scenarios arise that create a plethora of non-standard data structures that need to be transformed.

For example, a small biotech company discovers a potential blockbuster drug and starts clinical trials to gain approval. When they start out, the company does not have a data management or a statistical analysis and reporting department. They start out with Phase I trials outsourcing all of its work to Contract Research Organizations (CROs). The project lead of this project is a Microbiologist and has no background in computer sciences or database design. He place trust upon the expertise of the CROs to setup the data structure to capture the information needed. As the Phase I trials prove to be successful, Phase II trials were added. The original CRO used did not have enough resources, so the new studies were outsourced to other CROs to perform similar tasks. Once these studies prove to be successful, the biotech gained funding to form an internal team. The goal was to bring the data in-house to perform integrated safety summaries (ISS) and also prepare for electronic submission using CDISC Standards. Each CRO had their own quirks and standards. When the data manager and SAS programmer were hired to do the job, they were presented with large sets of data stored in different structures from each CRO. The job now was to transform all the data into a uniform standard to meet the objective of generating summary reports for the electronic submission. This is a common example of how good intentions can still lead to non-standard structures which requires data transformations.

There are two general approaches towards achieving data standards. If you are starting from scratch, it makes sense to use a suggested standard such as CDISC. In this case, the effort will be in ensuring that new data created adheres to this standard. A second approach is when you already have existing data that is structured very different from CDISC standards. In this case, the task is to make sure that all existing data structures follow an internal standard. Any new data created would then need to adhere to this new standard. It is more common for the second scenario to occur.
WHY STANDARDIZE?
Establishing data standards and applying the standards across all studies and projects can be resource intensive. It is reasonable to ask the question whether the effort is worth it. One of the key benefits is that the programs associated with this data become more portable. They can be moved from one study to the next with minor modifications. Not only are the programs more portable, the programmer and statistician working on one study can understand a new study with the same structure relatively quickly compared to learning a new set of programs, macros and data structures. The standard data structure allows for performing analysis across studies that would not be feasible if each study had their own data structure. This is also true for the FDA. If they need to perform aggregate summaries across different submissions from different companies, it would be impossible unless the companies follow an industry standard structure such as CDISC. The benefits of standardized datasets are truly realized when cross studies analysis can be performed where it was not once possible. The productivity gain is sometimes difficult to measure but, in the long run, it will outweigh the efforts invested in standardizing.

IMPLEMENTING CDISC
Applying the data transformation is a pivotal step but it is one among many tasks that need to be performed in order to have a successful CDISC or data standards implementation. This section describes a recommended step by step methodology towards implementing this standards transformation.

STEP 1: Before any code is written or even any specifications are drawn up, it is important to define a transformation plan. This does not have to be formal but a project plan will help the entire team work together cohesively towards a common objective. The project plan should include the list of tasks and an estimated time line for the tasks at hand. An example of an abbreviated test plan is shown here:
The test plan contains high level tasks which would then be placed on the projected schedule. These milestones are target dates for projected completion.

**STEP 2:** Perform data review of the existing source structure. This will capture deviations which will be resolved before any transformation occurs. It also highlights findings between differences and similarities between the source and the target CDISC structures. These findings will help identify what needs to be transformed. Some of the recommended review tasks
include:

<table>
<thead>
<tr>
<th>Tasks</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source Data Review</td>
<td>Evaluate variable attributes differences within internal data and Source Data.</td>
</tr>
<tr>
<td>Source Data and Internal Standards</td>
<td>Evaluate variable attributes between Source Data as compared to Internal Standards.</td>
</tr>
<tr>
<td>Source Data and CDISC SDS 3.1</td>
<td>Evaluate Source Data differences and similarities with CDISC SDS v3.1.</td>
</tr>
<tr>
<td>Source Data and CDISC SDS 3.1</td>
<td>Evaluate potential matches of Source Data variable names and labels against CDISC SDS v3.1.</td>
</tr>
<tr>
<td>CDISC Evaluation</td>
<td>Evaluate Source Data against CDISC evaluation from a set of specified rules.</td>
</tr>
<tr>
<td>Source Data Attributes</td>
<td>Review PROC CONTENTS and PROC PRINT of Source Data.</td>
</tr>
</tbody>
</table>

The review can be performed manually with the use of PROC REPORT. Considerable attention has to be paid to the details of the attributes in order to capture the discrepancies through visual inspection. Some example findings are shown here:

1. The most significant finding is that there are 125 incidences of variable labels being inconsistent for the same variable name. Some of these were how the subject was labeled. For example, the variable PATNUM has these two different labels across different datasets:
   - Data name: ae  Variable: patnum  Label: PROTOCOL CASE NO.
   - Data name: pat  Variable: patnum  Label: Subject ID (Num)

2. There were three incidences where the variable lengths differ for the same variable.
   - Data name: death  Variable: comment  Type: C  Length: 300*  Label: Death comment*
   - Data name: txsumm  Variable: tythmod  Type: C  Length: 200*  Label: Comments*
   - Data name: txsumm  Variable: tythmod  Type: C  Length: 25*  Label: Type of Dose Mod to Protocol Therapy*

3. When compared with CDISC SDS v.31, the findings were revealing. For example, there were 120 instances found of variable lengths that were different between MXI213 and the CDISC data model yet they share the same variable name. There were multiple occurrences of the same variables such as SEX, RACE and VISIT.
   - Data name: undocfu  Variable: visit  Type: N*  Length: 8*  Label: PROG BASED PHYS EXAM*
   - Data name: tv  Variable: visit  Type: C*  Length: 100*  Label: Visit Name*

4. Other findings between CDISC and the source data includes 14 instances where there were the same variables defined as CDISC but the variable types were different.
   - Variable: undocfu  Type: N*  Length: 8*  Label: PROG BASED PHYS EXAM*
   - Variable: tv  Type: C*  Length: 100*  Label: Visit Name*

These examples are representative of a review that was done on a study. These results are useful to help identify ways of
making the data structure more consistent. They can also help identify attributes that may need to be changed to meet target CDISC standards.

**STEP 3:** Define the transformation specification. This is the result of the review of the source data compared with the destination CDISC data structure. It is also a result of careful review of each variable and how it would fit into the data structure of CDISC. Note that the related records, supplemental qualification and comments are treated separately. This will be described in the next step.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Label</th>
<th>Transformation Type</th>
<th>Update_To</th>
</tr>
</thead>
<tbody>
<tr>
<td>aestctc</td>
<td>Action Taken with Study Treatment</td>
<td>aeactx label=&quot;Action Taken with Study Treatment&quot; length=$100</td>
<td></td>
</tr>
<tr>
<td>aeodt</td>
<td>AE Onset Date</td>
<td>aeodtc label=&quot;Start Date/Time of Adverse Event&quot; format=yymmdd10. length=10</td>
<td></td>
</tr>
<tr>
<td>aeodtc</td>
<td>NCI-CRC Adverse Event Term</td>
<td>aeodt label=&quot;Reported Term for the Adverse Event&quot; length=$100</td>
<td></td>
</tr>
<tr>
<td>aeodt</td>
<td>AE Reporting Period Begin Date</td>
<td>aeodt label=&quot;Study Day of Start of Event&quot; length=5 format=yymmdd10.</td>
<td></td>
</tr>
<tr>
<td>aeodt</td>
<td>AE Reporting Period End Date</td>
<td>aeodt label=&quot;Study Day of End of Event&quot; length=8 format=yymmdd10.</td>
<td></td>
</tr>
<tr>
<td>aecsrc</td>
<td>AE Collection Source</td>
<td>aecsrc label=&quot;Adverse Event Collection Source&quot; length=$100</td>
<td></td>
</tr>
<tr>
<td>aecnum</td>
<td>PROTOCOL CASE NO.</td>
<td>aecnum label=&quot;Unique Subject Identifier&quot; length=$100</td>
<td></td>
</tr>
<tr>
<td>aecsn</td>
<td>Sex</td>
<td>aecsn label=&quot;Sex&quot; length=$4/0</td>
<td></td>
</tr>
<tr>
<td>aecstudy</td>
<td>Clinical Study</td>
<td>aecstudy label=&quot;Study Identifier&quot; length=$10</td>
<td></td>
</tr>
<tr>
<td>inlib</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>outlib</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The transformation model is captured in a SAS dataset. The variable and label columns identify the source data. The transformation type indicates what attributes are to be transformed. The “Update_to” column is the actual code example of the actual transformation. There are other types of transformations such as transpose and value change that are beyond the scope of this paper. The subset of transformation types described here demonstrates how transformations can be expressed in a series of columns which is referred to as a transformation model.

You can choose to capture the transformation model in an Excel spreadsheet but in this example, the Transdata utility expects the transformation model to be captured in a SAS dataset format.

**STEP 4:** Identify supplemental qualifiers, relational records and comment fields. The CDISC data model is restrictive in what variables can be included. However, it has structures which can capture information from your source data in separate datasets. The definition of these three structures mentioned in the SDTM definition document found at the website: cdisc.org. Once you have identified these variables, you can then transform your source dataset into these structures.

**STEP 5:** Develop SAS programs to apply the transformation. This is based on the transformation model which functions as specifications to your transformation. A simple transformation program is shown below:

```
*** Program: trans_ae.sas
*** Description: Transform Adverse Events data
*** from inlib.ae to outlib.ae
*** By: %trans, 06/16/2005, 8:11:57 pm
******************************************************************************;
libname inlib "C:\sample\location\source\data";
libname outlib "C:\sample\location\cdisc\data";
data outlib.ae (label="Adverse Events");
attrib aecsrc label = "Adverse Event Collection Source" length=$100;
set inlib.ae;
*** Define a new variable aecn to replace old variable: aeactx ***;
attrib aecn label="Action Taken with Study Treatment" length=$100;
aecn = left(trim(aeactx));
drop aegn;

*** Define a new variable aestdtc to replace old variable: aeodt ***;
attrib aestdtc label="Start Date/Time of Adverse Event" length=$100;
aestdtc = put(aeodt,yymmdd10.);
drop aeodt;

*** Define a new variable aeterm to replace old variable: aepctc ***;
attrib aeterm label="Reported Term for the Adverse Event" length=$100;
```
aeterm = left(trim(aepctc));
*** Define a new variable studyid to replace old variable: study ***;
attrib studyid label="Study Identifier" length=80;
studyid = left(trim(study));
drop study;
drop toxcat;
drop toxcd;
run;

**STEP 6:** Verify the transformation. Depending on your SOP, this can be formally applied with requirements, functional specifications and test plan. Or it can be a series of SAS programs which confirms the results. Some of the verification tasks include:

<table>
<thead>
<tr>
<th>Code Review</th>
<th>Systematic review of SAS programs according to a predetermined checklist of verification criteria.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Code Testing</td>
<td>Perform testing on SAS programs or macros supplying valid and invalid inputs and verify expected output.</td>
</tr>
<tr>
<td>Log Evaluation</td>
<td>Evaluate the SAS log for error, warning and other unexpected messages.</td>
</tr>
<tr>
<td>Output Review</td>
<td>Visual or programmatic review of report outputs as compared to expected results.</td>
</tr>
<tr>
<td>Data Review</td>
<td>Review attributes and contents of output data for accuracy and integrity.</td>
</tr>
<tr>
<td>Duplicate Programming</td>
<td>Independent programming to produce the same output for comparison.</td>
</tr>
</tbody>
</table>

**STEP 7:** Document the metadata of the transformed data. Metadata is information about the data. This can be attributes of the variables such as variable label and type. It can also include the origin of the variable such as whether it is a source or a derived variable. This is commonly referred to as the DEFINE.PDF file or domain documentation. There are two sections to this documentation. The first lists all the datasets and the second details all the variables for each dataset.

<table>
<thead>
<tr>
<th>Dataset Name</th>
<th>Location</th>
<th>Keys</th>
<th>Number of Variables</th>
<th>Number of Records</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ae</td>
<td>ae.xpt</td>
<td>usubjid</td>
<td>9</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>cm</td>
<td>cm.xpt</td>
<td>usubjid</td>
<td>4</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>co</td>
<td>co.xpt</td>
<td>usubjid</td>
<td>15</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>dm</td>
<td>dm.xpt</td>
<td>usubjid</td>
<td>7</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>ds</td>
<td>ds.xpt</td>
<td>usubjid</td>
<td>5</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

**ae (ae.xpt)**

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Type</th>
<th>Length</th>
<th>Variable Label</th>
<th>Format</th>
<th>Decode Formats</th>
<th>Origins</th>
<th>Role</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aeacn</td>
<td>Character</td>
<td>100</td>
<td>Action Taken with Study Treatment</td>
<td>actfmt.</td>
<td>1 = None 2 = Dose Increase 3 = Dose Decrease</td>
<td>Derived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aeendy</td>
<td>Numeric</td>
<td>8</td>
<td>Study Day of End of Event</td>
<td></td>
<td></td>
<td>Derived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variable Name</td>
<td>Type</td>
<td>Length</td>
<td>Variable Label</td>
<td>Format</td>
<td>Decode Formats</td>
<td>Origins</td>
<td>Role</td>
<td>Comment</td>
</tr>
<tr>
<td>---------------</td>
<td>------------</td>
<td>--------</td>
<td>---------------------------------------------</td>
<td>--------</td>
<td>----------------</td>
<td>---------</td>
<td>--------</td>
<td>---------------</td>
</tr>
<tr>
<td>Aesrc</td>
<td>Character</td>
<td>100</td>
<td>Adverse Event Collection Source</td>
<td></td>
<td></td>
<td>Derived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aestdtc</td>
<td>Character</td>
<td>100</td>
<td>Start Date/Time of Adverse Event</td>
<td></td>
<td></td>
<td>Derived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aestdy</td>
<td>Numeric</td>
<td>8</td>
<td>Study Day of Start of Event</td>
<td></td>
<td></td>
<td>Derived</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**STEP 8:** Make the data available for users as a standard for future uses. The domain documentation can be published to users. In addition to the domain documentation, a full PROC CONTENTS of the transformed data and template code can also be included to give users a starting point if they need to create the same data standards for their next study.

### Sample Code Templates

```plaintext
/*----------------------------------------
Program: attribcode.sas
Description: Sample code segment including attributes for standards.
By: metadata, 07/15/2005, 11:43:58 am
----------------------------------------*/

*** Define sample data SOTHEL.AF ***;
data work.AF [label="Adverse Events"]
set SOTHEL.AF;
attrib aescrc length=100. label="Adverse Event Collection Source" ;
attrib aedtst length=100. label="Action Taken with Study Treatment" ;
attrib aestdtc length=100. label="Start Date/Time of Adverse Event" ;
attrib aestdy length=8. label="Study Day of Start of Event" ;
attrib aesscc length=8. label="Study Day of End of Event" ;
attrib aessubj length=100. label="Unique Subject Identifier" ;
attrib aessite length=100. label="Study Site Identifier" ;
attrib aessid length=100. label="Study Identifier" ;
run;

*** Define sample data SOTHEL.CN ***;
data work.CN [label="Concurrent Medications"]
set SOTHEL.CN;
attrib aesubj length=100. label="Unique Subject Identifier" ;
attrib asite length=100. label="Study Site Identifier" ;
attrib aetime length=100. label="Start Date/Time of Medication" ;
attrib amdrug length=100. label="Reported Name of Drug, Med, or Therapy" ;
run;
```
As seen in the eight steps, the actual data transformation portion is only one step. The other accompanying steps are essential in making the transformation accurate and useful.

AUTOMATING TRANSFORMATION

The eight steps described above can be very labor intensive if they are done manually. Some of the tasks are tedious and require great attention to detail since there are many variables and attributes related to a data transformation. Each step will once again be described with the aid of tools such as the CDISC Builder and Transdata to automate certain tasks.

STEP 1: The test plan has to be manually edited. In the example used, an HTML version was created using FrontPage as a tool.

STEP 2: This step included a data review of the existing source structure. The findings in step 2 utilizes %difftest which is a tool provided within CDISC Builder. It evaluates each variable and the associated attributes to determine if there are any differences. This automation captures detailed attributes which would otherwise be missed through visual inspection. In addition, the %cdisc macro within CDISC Builder was used to generate the following report. This helps identify deviations from rules established by CDISC.

### Data Table Name=AE
### Data Table Label=AE Data Set

<table>
<thead>
<tr>
<th>Library Name</th>
<th>Dataset and Variable</th>
<th>Variable Label</th>
<th>Variable Type</th>
<th>Variable Length</th>
<th>Case Number</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>cutib</td>
<td>ae</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Data Missing Variable USUBID</td>
</tr>
<tr>
<td>cutib</td>
<td>ae</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Data Missing Variable STUDYID</td>
</tr>
<tr>
<td>cutib</td>
<td>ae</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Data Missing Variable --SEQ</td>
</tr>
<tr>
<td>cutib</td>
<td>ae.aeactx</td>
<td>Action Taken with Study Drug due to AE</td>
<td>C</td>
<td>20</td>
<td>3</td>
<td>Variable Label &gt; 40 Characters</td>
</tr>
<tr>
<td>cutib</td>
<td>ae.aeactx</td>
<td>Action Taken with Study Drug due to AE</td>
<td>C</td>
<td>20</td>
<td>14</td>
<td>The word &quot;with&quot; within the label has casing irregularities</td>
</tr>
<tr>
<td>cutib</td>
<td>ae.aeactc</td>
<td>MZH-CTC Adverse Event Category</td>
<td>C</td>
<td>40</td>
<td>12</td>
<td>Variable label matches the text CATEGORY, but variable does not contain abbreviation CAT</td>
</tr>
<tr>
<td>cutib</td>
<td>ae.aeactc</td>
<td>MZH-CTC Adverse Event Category</td>
<td>C</td>
<td>40</td>
<td>14</td>
<td>The word &quot;MZH&quot; within the label has casing irregularities</td>
</tr>
</tbody>
</table>

STEP 3: This step defines the transformation specification. The Transdata tool is used to automate the transformation model definition. It captures the variables from the source and then provides a mechanism to populate the transformed attributes through recommendations. The recommendations are derived from the CDISC SDS v3.1 structure.
**STEP 4:** This step identifies supplemental qualifiers, relational records and comment fields and then imports them into the new structure defined by CDISC. The CDISC Builder tools automate this process by helping you identify which fields pertain to related records. Once identified, it would transpose your source data into the specified relational record data structure as defined by CDISC. It also has similar tools for the supplemental qualifier and comment fields.

**STEP 5:** This step generates the SAS programs used to apply the transformation. The Transdata automates this step by reading the transformation model and applying these rules to generate the transformation code.
This handles most of the transformation needs. However, for more customized transformations, the code can be saved and edited to fulfill the requirements of any specific transformation requirements.

**STEP 6:** This step verifies the transformation. The Transdata tool assists in the verification task by generating reports to help verify the source against the transformed data. The verification report is an HTML report which has a dual frame screen with a subset of three subjects for fast review.

This allows visual inspection of the “before” and “after” to verify if the transformation is being performed correctly. In addition to this PROC PRINT report, there is also a PROC FREQ for categorical variables. The frequency report helps to verify values in a summarized manner to help identify potential discrepancies in the transformation.

**STEP 7:** This step makes the data available for users as a standard for future uses. The CDISC builder captures all the metadata using PROC CONTENTS and stores this in a centralized database. It then generates a report in HTML format along with template code. This can be published on an intranet or emailed to users so that they can use the same standard on their next study. The metadata database also has search capabilities for users to easily find attributes among the large set of metadata that has been transformed.

There are many efforts that are needed to perform data transformation such as the CDISC example described in this section. Automating each step can help ensure that the transformation is done with accuracy. It also saves time since it elevates the tedium of many small but labor intensive tasks.
CONCLUSION

Data transformation is an essential and unavoidable task when working with clinical trials data. It can be used to move towards a new data standard such as CDISC or an internal standard used for an integrated safety summary. Accomplishing standards leads to portability of data between studies, while also increasing the mobility of team members between projects. It also gives you capabilities of performing analysis across studies that would not be available otherwise. Performing a successful transformation of data from one structure to another is not limited to just programming the transposition. There are other steps in managing and verifying the transformation to ensure the integrity and accuracy of the transformed data. These tasks can be resource intensive and time consuming if done manually. Automation tools can add value in removing the tedium while increasing efficiency and accuracy of the work. This can ultimately be the difference between a time consuming failed project and one of accuracy and success.

REFERENCES

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