ABSTRACT

Clinical trial sponsors must comply with a wide variety of legal requirements. The focus of this paper is the requirement to publicly register and post clinical trial information, including trial results. Depending on where the trial is conducted, there are different clinical registries that need to be supported. The processes are documented on the corresponding websites where the trials must be registered. While it is possible to manually calculate and enter trial results into the registry, that information must be accurate and manual entry increases the review burden and the risk of human error. Programming support can make the process safer and easier. More specifically, for some content it is possible to directly upload validated content, avoiding the risks associated with manual entry. In other cases, manual entry and review can be facilitated with validated tables that specifically target entry needs. In this paper, we will provide case studies and examples illustrating our current process for creating and validating content designed to support population of clinical trial results in clinical registries.

INTRODUCTION

Many programmers versed in clinical trials will be aware of the Title 21 Code of Federal Regulations, Part 11: Electronic Records and Electronic Signatures. These regulations define the criteria under which electronic data and associated signatures are considered trustworthy and reliable. This paper will be discussing a lesser-known Part 11, of Title 42: Clinical Trials Registration and Results Information Submission. Conduction of a clinical trial includes compliance with legal aspects, specifically providing required information at designated timepoints of the study. Among those requirements is registering and posting clinical information, such as certain, specific trial results. Applicable registry references should be documented in the SDTM Trial Summary domain (TS). More specifically, TS should contain a row for each applicable registry reference in TSVAL where TSPARMCD = ‘REGID’. Different registries are required depending on where the trial is conducted, such as ClinicalTrials.gov (United States), and EudRACCT (Europe). The processes for publicly sharing these results are documented on the respective websites. This paper will discuss our experience supporting entry and upload of clinical trial results on ClinicalTrials.gov.

LEGAL OBLIGATIONS AND REGISTRY RESTRICTIONS

There are two very important deadlines to keep in mind when a trial will need to be registered on ClinicalTrials.gov, and these requirements are fully explained in the text describing Title 42, Part 11, on the Code of Federal Regulations website. The first deadline is regarding the actual registration of the trial, and it is stated that this information must be posted on the clinical trial registry no later than 30 calendar days after the responsible party has submitted information for drug approval. Once the trial is registered, there remains one more important deadline, which is the posting of trial results. It is stated that the clinical trial results will be publicly posted on the registry no later than 1 year from the completion date of the clinical trial. These regulations do fully apply to any trials initiated after September 27, 2007, and additionally to any trials that initiated on or before September 27, 2007, but were ongoing on December 26, 2007.

It could be a costly mistake to not comply with the federal regulations outlined above. In 2021, the FDA issued a Notice of Noncompliance to a pharmaceutical company for failing to submit required trial summary information to a clinical registry. The notice provided a 30-day deadline for submitting these select results, with failure to do so potentially resulting in civil penalties.

Clinical registries require an electronic upload of the information—that is, whether by creating a reference for manual entry of individual terms or a consolidated file designed to be directly uploaded, trial results must be added into this digital registry. There are certain limitations on which results can be uploaded and which require manual entry, which are illustrated in the table below. For example, while both adverse
event and demographic information is required to be included in ClinicalTrials.gov, only the adverse events content can be uploaded in a file at this time. On the other hand, EudRACT allows for a file upload or manual entry for both adverse event and demographic information. While we will not discuss the creation of materials for EudRACT, with slight modifications to the process followed for ClinicalTrials.gov, the XML files for EudRACT can be easily produced.

Table 1 describes the different methods of entry available on EudRACT and ClinicalTrials.gov when electronically uploading the trial results.

<table>
<thead>
<tr>
<th>Registry</th>
<th>Demographic Information</th>
<th>Adverse Event Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>ClinicalTrials.gov</td>
<td>Manual Entry</td>
<td>Manual Entry/Automatic Upload of XLSX file</td>
</tr>
</tbody>
</table>

Table 1. Loading Clinical Trial Results: Digital Upload Options

Considering this information, and the variability of certain efficacy variables to be included in demographics registration data, we prioritized generation of the upload file for the adverse event data and still rely on manual entry of the demographic data (supported by validated outputs that match the format expected in the registry). Since the adverse event related-data comprises the bulk of what is required for the registry, we have successfully mitigated the potential for data-entry issues.

NAVIGATING THE REGISTRY

When navigating the ClinicalTrials.gov website, there are multiple tabs that can be selected for each specific study: Study Details, Tabular View, and Study Results.

Figure 1 is an example of what you may see after selecting a specific study on the registry.

Figure 1. Screenshot of ClinicalTrials.gov Study tabs

The first tab (Study Details) contains Study Description, Arms and Interventions, Outcome Measures, Eligibility Criteria, Contacts and Locations, and More Information. This tab is updated by Corporate Communications, or the otherwise assigned Responsible Party, and our programmers do not enter these results.

The second tab (Tabular View) contains Tracking Information, Descriptive Information, Recruitment Information, and Administrative Information. The information on this tab is updated by the Responsible Party.

The third tab (Study Results) will display as ‘No Results Posted’ if the results have not been uploaded to the registry yet. When populated, this tab contains Participant Flow, Baseline Characteristics, Outcome Measures, Adverse Events, Limitations and Caveats, and More Information. This tab is the focus of our programming support, with validated tables specifically designed to support manual entry of Baseline Characteristics and validated files designed for direct upload for Adverse Events.

ADVANTAGES TO DIRECT UPLOAD

Specifically for the demographics section, as we have discussed above, there is a limitation on how the data can be uploaded. Demographics still requires a manual entry of certain, specific data points. However, the demographics section also requires, where possible, statistics on the primary efficacy parameter. The efficacy parameter is study specific and is summarized separately from demographics in clinical study reports. Thus, if we were not to create a ClinicalTrials.gov-specific demographic output, the Responsible Party may have to search the CSR to source the required values from multiple different tables.

Similarly, other, slight modifications to demographics tables may be required. For example, on some studies, we include all the required statistics by treatment group, but we do not include an overall column.
When this is the case, we do modify the demographics datasets to include this Overall column, since it is required by ClinicalTrials.gov.

Though the data must still be manually entered, we have created a process that will produce a single data-source for all demographic required information. Additionally, if the ability for digital upload ever becomes possible, we need only to adjust the formatting of our demographic output to allow for the upload. We will not need to create the program from scratch at that time.

Regarding the adverse events section, the benefit of programmatic support is even more clear as the validated content can be directly uploaded. The registry requires values that come from 4 very similar tables in our CSR outputs. Rather than individually entering each record of an Adverse Event, it saves time and improves accuracy to upload validated data results for each of the outputs. Additionally, since each of the files requires the same, specific formatting within Excel, it is logical to use a macro as part of the process.

**DEMOGRAPHICS**

<table>
<thead>
<tr>
<th>Arm/Group Title</th>
<th>Arm/Group Description</th>
<th>Number Analyzed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm/Group Title</td>
<td>Participants with autosomal polycystic kidney disease (ADPKD) who received baroxdone methyl capsules at a starting dose of 6 mg and titrate up to a maximal dose of 20 mg (participants with UACR less than or equal to 300 mg/dl) or 30 mg (participants with UACR greater than 300 mg/dl) daily. Baroxdone methyl capsules, Baroxdone 5 mg capsules Baroxdone methyl capsules, Baroxdone 5 mg capsules</td>
<td>31 participants</td>
</tr>
<tr>
<td>Arm/Group Title</td>
<td>Participants with IgA nephropathy (IgAN) who received baroxdone methyl capsules at a starting dose of 5 mg and titrate up to a maximal dose of 20 mg (participants with UACR less than or equal to 300 mg/dl) or 30 mg (participants with UACR greater than 300 mg/dl) daily. Baroxdone methyl capsules, Baroxdone 5 mg capsules</td>
<td>26 participants</td>
</tr>
<tr>
<td>Arm/Group Title</td>
<td>Participants with Type 1 diabetes (T1D) who received baroxdone methyl capsules at a starting dose of 5 mg and titrate up to a maximal dose of 20 mg (participants with UACR less than or equal to 300 mg/dl) or 30 mg (participants with UACR greater than 300 mg/dl) daily. Baroxdone methyl capsules, Baroxdone 5 mg capsules</td>
<td>28 participants</td>
</tr>
</tbody>
</table>

**Figure 2. Example of Baseline Characteristics from ClinicalTrials.gov**

Figure 2 is an example of what the Baseline Characteristics section on ClinicalTrials.gov looks like. A picture of the full content of the site is hard to read, so we have selected a subset of the cohorts to provide an example of what the registry looks like, and have also transformed the results into a more readable format in Figure 3. Displayed in each of the figures is an example study, PHOENIX, containing 4 different treatment cohorts.
We have identified the demographic tables from the CSR that contain these results. For the sake of a complete explanation, and due to the way analysis was done, the results required for this table will span 5 datasets: one for each cohort, and one for the overall treatment group. We have included each below.

Figure 4 is the table dataset supporting the production of demographics for patients in the ADPKD group. Multiple variables are included in this output, so we will take one as an example, and review AGE. Based on the output dataset, there were 31 subjects in the ADPKD cohort, with a mean age of 47.4 and standard deviation of (9.49).
Figure 4. Demographics table dataset for ADPKD patients

Figure 5 is the table dataset supporting the production of demographics for patients in the IgAN group. IgAN contained 26 subjects in the cohort, where the mean and standard deviation for age were 48.5 (9.53).

Figure 5. Demographics table dataset for IgAN patients

Figure 6 is the table dataset supporting the production of demographics for patients in the T1D group. Below, T1D contained 28 subjects, with mean and standard deviation of 49.0 (9.91) in the cohort.

Figure 6. Demographics table dataset for T1D patients

Figure 7 is the table dataset supporting the production of demographics for patients in the FSGS group. The FSGS-specific dataset contains 18 subjects in the cohort, with a mean of 48.6 and standard deviation of 12.79.

Figure 7. Demographics table dataset for FSGS patients

Figure 8 is the table dataset supporting the production of demographics for all patients. Finally, the overall table contains 31 + 26 + 28 + 18 (or 103) subjects. When considering the groups as a whole, the mean and standard deviation are 48.3 (10.12). In addition to checking the counts, we can also verify the
minimum and maximum values. The smallest minimum value in any of the contributing datasets is from the cohort T1D, which is 21. The largest maximum value in any of the contributing datasets is from the cohort ADPKD, which is 69. The values displayed in our overall table for minimum and maximum age are 21, 69, so these counts are also as expected.

<table>
<thead>
<tr>
<th>column_c</th>
<th>parameter</th>
<th>class</th>
<th>class_ord</th>
<th>result_c</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bardoxolone Methyl-ADPKD</td>
<td>AGE</td>
<td>Median</td>
<td>600</td>
</tr>
<tr>
<td>2</td>
<td>Bardoxolone Methyl-IgAN</td>
<td>AGE</td>
<td>N</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>Bardoxolone Methyl-T1D</td>
<td>AGE</td>
<td>Min, Max</td>
<td>700</td>
</tr>
<tr>
<td>4</td>
<td>Bardoxolone Methyl-ADPKD</td>
<td>AGE</td>
<td>Q1, Q3</td>
<td>400</td>
</tr>
<tr>
<td>5</td>
<td>Bardoxolone Methyl-ADPKD</td>
<td>AGE</td>
<td>Mean (SD)</td>
<td>200</td>
</tr>
</tbody>
</table>

Figure 8. Demographics table dataset for all patients

The values from each of these datasets in Figure 4, Figure 5, Figure 6, Figure 7, and Figure 8 (including additional parameters that are not displayed in the example subset) are what has been provided for upload to ClinicalTrials.gov, (the data from Figure 3), and therefore match what is posted there. This exercise has confirmed that the posted results do match the counts we are claiming in the CSR.

This exercise can be performed with each of the contributing variables for the Baseline Characteristics section, though slight modification may be required to include the primary efficacy variable. As discussed above, we do recommend including this in the output. Additional modifications to the programs may be needed, such as including a specific age group that may not be considered in the CSR program. These slight modifications should be reviewed on a study-by-study basis, to ensure all pertinent data has been submitted to the clinical registry. The modifications needed for these programs contribute to why we elect to validate this table output again, when we produce the excel file containing the results.

The file we ultimately produce outputs Summary Statistics on one sheet and Frequency Counts on another. Figure 9 is an example of the demographic output.

Figure 9. Sample of Demographics ClinicalTrials.gov file for upload to registry

Please note that ClinicalTrials.gov supports calculation of the overall values, based on the groups, in the case that Frequency Counts are being provided. For this reason, the overall column is not strictly required, but we do choose to include it for consistency with our summary statistics output. Summary Statistics, by group, provided to ClinicalTrials.gov, on the other hand, cannot be used to automatically calculate the overall column, and thus these values should be provided in the demographic output.

ADVERSE EVENTS

As done with Demographics, we can produce and validate tables to provide the information required for the Adverse Events section. What is additionally helpful in this case, is that these files, if produced in the correct format, can be directly uploaded to the registry without a need for manual entry. While all of the Adverse Events sections contain similar information and can be produced in the same way, we have selected a single example for clarity in the explanation. Figure 10 is an example of what the Adverse
Events section looks like on ClinicalTrials.gov. Displayed in each of the figures is an example study, MOTOR, containing 6 different treatment groups, and a placebo group.

![Table of Adverse Events](image)

**Figure 10. Example of Adverse Events from ClinicalTrials.gov**

As was the case for Baseline Characteristics, a picture of the full content of the site is hard to read, so we have also transformed these results into a more readable format in Figure 11. Please note that while an Overall column is required for the Demographics section of the site, the Adverse Events section does not contain one. If the CSR tables you currently produce are only run on the overall population, further modifications are needed before running them through the conversion macro.

![Table of ClinicalTrials.gov Adverse Events](image)

**Figure 11. ClinicalTrials.gov Adverse Event information converted to readable format**

To illustrate the starting point, before creating any additional registry documents, below is the table for Serious, Treatment-Emergent Adverse Events that we included in the CSR, and the associated, supporting table dataset.
Table 14.4.1.5 Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term

<table>
<thead>
<tr>
<th>Body System or Organ Class</th>
<th>Preferred Term</th>
<th>5 MG (N=6)</th>
<th>10 MG (N=6)</th>
<th>20 MG (N=6)</th>
<th>40 MG (N=6)</th>
<th>80 MG (N=6)</th>
<th>160 MG (N=10)</th>
<th>Pooled 408 (N=40)</th>
<th>Placebo (N=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects with Serious TEAE</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td>0 (16.7)</td>
<td>0 (16.7)</td>
<td>0 (16.7)</td>
<td>1 (16.7)</td>
<td>1 (16.7)</td>
<td>1 (16.0)</td>
<td>4 (16.0)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Atioventricular dissociation</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (10.0)</td>
<td>1 (10.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td></td>
<td>0 (16.7)</td>
<td>0 (16.7)</td>
<td>0 (16.7)</td>
<td>0 (16.7)</td>
<td>0 (16.7)</td>
<td>1 (2.5)</td>
<td>1 (2.5)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (10.0)</td>
<td>1 (10.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>1 (2.5)</td>
<td>0 (2.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Optic neuritis</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (2.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Tonic convulsion</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>1 (2.5)</td>
<td>0 (2.5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>1 (2.5)</td>
<td>0 (2.5)</td>
</tr>
</tbody>
</table>

Figure 12. CSR Output for MOTOR: Serious, Treatment-Emergent Adverse Events

Figure 13. Supporting table dataset for MOTOR CSR Output
Figure 12 contains all the adverse events that occurred, and the number and percentage of subjects affected. Figure 13, the table dataset, shows that only 5 treatment groups are represented, in addition to the pooled, overall analysis. This is because the subjects in the 5 MG capsule group and the 20 MG capsule group did not experience any adverse events over the course of the study. Reviewing these outputs, we can anticipate what counts we would expect to see uploaded to the clinical registry. For example, both the 10 MG capsule group and the 160 MG capsule group contained a single subject who experienced a cardiac disorder. This is in alignment with our pooled group which indicates that 2 subjects experienced cardiac disorders.

Therefore, based on these CSR documents, we would anticipate our ClinicalTrials.gov results to match what we have populated in Table 2.

Table 2. Compilation of serious adverse events, per treatment group, in MOTOR

<table>
<thead>
<tr>
<th>Placebo group</th>
<th>1 serious adverse event, tonic convulsion, occurring in 1 subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 MG group</td>
<td>0 serious adverse events</td>
</tr>
<tr>
<td>10 MG group</td>
<td>1 serious adverse event, tachycardia, occurring in 1 subject</td>
</tr>
<tr>
<td>20 MG group</td>
<td>0 serious adverse events</td>
</tr>
<tr>
<td>40 MG group</td>
<td>2 serious adverse events, hemiparesis and optic neuritis, occurring in 1 subject</td>
</tr>
<tr>
<td>80 MG group</td>
<td>1 serious adverse event, fatigue, occurring in 1 subject</td>
</tr>
<tr>
<td>160 MG group</td>
<td>2 serious adverse events, atrioventricular dissociation and ventricular tachycardia, occurring in 1 subject</td>
</tr>
</tbody>
</table>

At this point we have defined the information that needs to be uploaded to ClinicalTrials.gov. We have identified where that information can be found in our final table programs, and in this case, we already have a single program including all of the treatment groups, so there is no need to refer to multiple datasets as was the case with PHOENIX and the demographics table. We need only to convert the output to a validated XLSX file for upload. We have displayed only the placebo group in the resulting excel file in Figure 14 to improve readability, but for the sake of completion, we have also included Figure 15, which converts the treatment values into a more readable format.
INTRODUCING THE MACRO

A key piece to this automation is the utilization of a macro, `%ctgovxls`. SAS macros are very powerful tools and are typically used when you are doing a repetitive task and want to ensure consistency. In our
case, we use this SAS macro for the main purpose of ensuring accurate and consistent outputs. Based on our process at Reata, every TLF that is created for the CSR has an associated SAS dataset with a specific, pre-defined structure that contains the relevant information. The macro relies on this pre-defined structure of these TFL datasets to produce the desired XLSX output for ClinicalTrials.gov. In addition, it will produce a dataset that contains the information from the XLSX file, only for the purpose of validating the data in the final document. We have illustrated the process in Figure 16.

**Figure 16. Process flow for creation of files for a clinical registry**

Please note that we anticipate (and hope for) the ability to utilize this macro for demographic tables as well, if it becomes possible to automate the results. At this present time, we only run it on our Adverse Events outputs, to prepare them for direct upload to the registry. Therefore, moving forward, the discussion of the macro will be Adverse Event-specific.

The macro we have discussed above is used to produce each of the necessary adverse events tables in file formats that can be directly uploaded to the site. The required adverse events information can be broken up into 4 tables:

1. All-Cause Mortality,
2. Treatment-Emergent, Serious Adverse Events
3. Treatment-Emergent, Other (Non-Serious) Adverse Events, and
4. Treatment-Emergent, Serious, Related Adverse Events.

We have sourced the information required for the list above from our CSR outputs. Each of the four Adverse Events tables that need to be created will be very similar, so the `%ctgovxls` macro is an ideal tool for producing consistent outputs. As mentioned above, part of our standard process for table creation includes producing a dataset, so that any values can be validated by dual programming. We use these datasets to create the files for upload to the clinical registries, but it would also be possible to read in the values from an RTF file in an analogous process.

**UTILIZING THE MACRO AND FORMATTING THE OUTPUT FILE**

The PHOENIX Treatment-Emergent, Serious Adverse Events that we just explained contains a small number of records and seems as though it could be manually entered easily enough. However, each of these tables has potential to contain many more records than would be reasonable to enter in that manner, hence we elect to automate.

There are some notes to consider when creating the files for automation. They must be in XLSX format, as shown above. Additionally, the headers for the counts must not begin until line 15 of the excel file.
have included text from the template on lines 1-14, which describes that changes to the column headers (names or placement) will cause an upload to fail.

Adverse Event Type (column A) should designate the record as 'Serious' or 'Other' and should always be populated. Assessment Type (Column B) can contain ‘Systematic Assessment’, ‘Non-systematic Assessment’, or can be left blank. Additional Description (Column C) can also be left blank, and there is no suggested text for this field. Organ System Name (Column D) must be comprised of the high-level categories provided on ClinicalTrials.gov, which are listed on the ClinicalTrials website. Source Vocabulary (Column E) may be blank, but we have elected to populate it with the MedDRA dictionary version used. Term (Column F) should never be blank and contain each of the individual AE terms that occurred over the study.

Besides the restrictions on how the text should be entered for columns A through F, the counts are expected to be displayed in a certain format as well. This is where it is advantageous that we have a standard format for CSR-table outputs, because we can write a macro that will reformat the dataset into this three-column format, and output an XLSX file. Therefore we gain the functionality of automation as a post-processing step.

The data displayed on our CSR table is already split into columns by treatment group. While records of no adverse events have been simplified to just '0' for a cleaner looking output, any adverse events that did occur are presented in the form of x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of subjects experiencing treatment-emergent adverse events, and p is the percent of subjects for the given treatment.

Based on the information that has been laid out above, we create a conversion macro:

```%macro ctgovxls(AEType= , DictVer= , Fname= , AType= "Systematic Assessment", Desc= "", intab=other2, outxls=other2);
```

Taking a study we have completed these registry files for, PRIMROSE, as an example, we will illustrate how to populate the macro call based on the structurally pre-defined dataset in Figure 17. (For readability purposes we have only included two treatment groups from this example.)

![Figure 17. Treatment-Emergent, Serious Adverse Event table data for PRIMROSE study](image)

The macro will need to read in the Adverse Event dataset output with the associated table, in Figure 17, and output an appropriately formatted excel file in the format of Figure 18.

**AEType** is the first parameter and the user is intended to enter free text into this field to be displayed in column A of the excel file, AdverseEventType. Since the example we are using is 'Treatment-Emergent, Serious Adverse Events', this input parameter should be set to 'Serious'.

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**DictVer** is the next parameter and the user is intended to enter the corresponding MedDRA dictionary version that was used for coding. By checking study documentation we can confirm that version 17 of MedDRA is used, and thus this parameter should be set to ‘MedDRA (17.0)’. It is displayed in column E, SourceVocabulary, of the excel file.

**Fname** refers to the input dataset being called on. We must differentiate this from the analysis study data, since our goal is to use the values that we displayed on our outputs for the CSR, rather than completely rederive these values. In our case, we must direct the macro to the name of our output dataset – ‘serious_adverse_events’. This will not be displayed anywhere in the output excel file.

**ATYPE** is a free-text parameter that will be used to populate column B, AssessmentType, in the excel file. The recommended text for this field is “Systematic Assessment” so we have set this as a default value.

**Desc** is a free-text parameter that can be used to provide additional description regarding the subset of study data. It is populated in column C of the excel file, AdditionalDescription. While we generally elect to leave this blank, and example of how you may populate this is to set it to “Related” when AdverseEventType is “Serious” and you intend to produce the Treatment-Emergent, Serious, Related Adverse Events. In our case we are not creating an output for related events, so we will leave this blank.

**Intab** and **Outxls** are not displayed in the resulting excel file but are used to provide libraries for the incoming and outgoing data and files. In the example macro call above, both values are set to ‘Other2’, which is indicating that we are pulling the adverse event dataset from the same location that we are outputting the excel file for the registry to.

Once the parameters described above are input to the macro, all information needed for creating this output has been provided. The macro will pick the appropriate information from the corresponding fields of the dataset and output them into an excel file that we can upload. It will additionally include the standard, required text on the first 14 lines of the excel file, and begin the headings on line 15. Once the validator has dual programmed and verified the values in the resulting, associated dataset, the document is ready for upload to the clinical registry.
ClinicalTrials.gov relies on a data entry system called the Protocol Registration and Results System, or PRS. You must have a PRS account in order to register a trial or enter/upload study results to the registry. Before applying for a PRS account, you should consider if that is necessary. To avoid duplication of any registry information, only the Responsible Party should register and submit information. Therefore, be sure that you should, in fact, be registering for this account before you do.

Once you have an account, you will need to log into PRS, and follow the instructions to enter (or upload) information. The system is accompanied by both a Quick Start Guide, and a more detailed PRS User’s Guide that should be able to answer any of your questions. After entering or uploading information, you will need to review it to make sure it’s accurate, and (then and only then) submit. The general process is very similar whether you are registering a study or posting the results. There are also instructions included in the accompanying guides that explain how to edit a record, so if ever you upload errant information that needs to be changed for any reason it can be updated.

CONCLUSION

While setting up the macro and getting the process implemented for the first study did require some effort, it was easy to repeat this process for additional studies. There is admittedly more of an advantage to creating a macro for this process when multiple studies need to be uploaded in a repeatable process, as was our case. However, even if only one study needs to be logged in the registry, it is still a reasonable
way to ensure that no mistakes are made in data-entry. We have found that utilizing this process leads to a more efficient upload of accurate results.

REFERENCES


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RECOMMENDED READING

- ClinicalTrials.gov (http://clinicaltrials.gov/ct2/info/about)
- HL7 Clinical Trial Registration and Results (http://www.hl7.org/special/Committees/projman/searchableProjectIndex.cfm?action=edit&ProjectNumber=372)
- Final Rule for FDAAA 801 and NIH Policy on Clinical Trial Reporting (https://clinicaltrials.gov/ct2/manage-recs/fdaaa#)
- Clinical Trials Regulation EU No 536/2014 (https://ec.europa.eu/health/medicinal-products/clinical-trials_en)

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