**Frequently asked questions (FAQ) on the R Shiny Web Application “Safety Monitoring”**

**http://rshiny.gilead.com/dev/safety\_monitoring/**

Version 1.0

Date 12/07/2017

1. **What are the required columns that must be present in the data for the tool to function properly? Are there restrictions on the format property of the columns?**

A: Please refer to User Manual (Step 1. Prepare datasets)

1. **Are there restrictions on the entries (missing or special character) in the data?**

A: Entries for missing values could either be empty or NA. All other entries, such as special characters (e.g. ‘.’ or ‘-‘), are considered as non-missing. Two columns do not allow missing values: TRTSDT (date of first exposure) and ASTDT (AE onset date), and the missing values must be imputed before loading the data to the tool.

1. **Do I still need to upload naming files if I’m just going to use the same ones as in the template?**

A: Yes. Please download both naming files by clicking the ‘Need template?’ hyperlink next to ADSL and ADAE naming files import widget and then upload them to the tool by clicking ‘Browse’ corresponding to each file import widget.

1. **How is TEAE filter applied to the data?**

A: The TEAE checkbox only filters the ADAE data based on ‘TRTEMFL’ column. After ADAE data are imported, user could click the TEAE checkbox to only keep entries with ‘TRTEMFL’ equals to ‘Y’. Note that if the checkbox is checked/unchecked after ADSL and ADAE are already merged, the ‘Merge’ button has to be pressed again to refresh the merged data in order to be used for subsequent safety analyses.

1. **How is exposure time computed?**

A: The exposure time is first computed on subject level, and then aggregated on AE level based on the merged data, possibly TEAE checked or filtered.

***At subject level:***

For a specific subject, if there are multiple occurrences of the same type of AE, only the first onset after first dose will be used for computing exposure time using:

(AE onset date - First dose date + 1)/365.25 (Years).

If all occurrences for a type of AE happened prior to first dose, then exposure for this AE will be indicated by ‘NA’.

For subjects who did not experience a specific type of AE, the duration of entire drug exposure will be used for computing exposure time using the shorter one of:

(Last dose date + 30 - First dose date + 1)/365.25 (Years)

**OR**

(Snapshot date – First dose date + 1)/365.25 (Years).

***At AE level:***

For a specific type of AE, in each arm, all patients’ exposure time will be summed, where each patient’s exposure time is computed as described above.

If any patients returned ‘NA’ for subject-level exposure, the AE-level exposure for this type of AE will be left as ‘NA’ (shown as blank in the output table), and any statistics involving exposure will not be computed (also blank in the output table).

*Note the ‘30’ days following last dose date in the above formulas could be replaced by user entered value.*

1. **How are ratio statistics calculated when there are no events in one of the groups?**

A: For odds ratio, it is common practice to add 0.5 to each of the four cells when there is no event in at least one group.

The HR is commonly estimated by the maximum partial likelihood estimator of the COX PH model. When there is no event in one group, the HR goes to zero (if 0 in TRT) or infinity (if 0 in PLC), and the corresponding confidence interval is always . Under such case, a statistical software can produce a number close to 0 or sufficiently large depending on their numerical computing algorithm. To minimize confusion, we will suppress the results on such HR and its confidence interval estimates and mask them with "-".

1. **Is there a way to order/sort the output table?**

A: The table can be ordered according to the value of a variable by clicking on the small "arrow" on the right hand side of that variable name.

1. **What if the legend labels are cut off in the volcano plot?**

A: Adjusting the download height and width should help fit the legend labels within the pdf. Additionally, please use the slider bar for adjusting the legend label font size.

1. **When I tried using my own data, the safety analysis always returned an error message saying ‘disconnected from server’ and the program crashed.**

A: Please first refer to the above questions 1 and 2, to see if the data meet the format requirement and restrictions on missing values. Another possible cause could be that your ADAE data contain more subjects than your ADSL data, so in the merged data, some of the subjects from ADAE do not have a first dose date (as these subjects were not present in the ADSL data). This could cause errors when computing exposure time. If all these causes are ruled out, please contact the developers with your specific dataset to further look into the issue.

*Thank people who helped on beta-testing and providing valuable feedbacks: Wei Deng, Xiaomin Lu, Gerald Crans, Yongwu, Shao, Hai Liu, Peiwen Wu, Liang Fang. For any other question, please contact the author: Xiaomin Lu (*[*Xiaomin.lu@gilead.com*](mailto:Xiaomin.lu@gilead.com)*) or developers: Qinghua Song (*[*Qinghua.Song@gilead.com*](mailto:Qinghua.Song@gilead.com)*), Shuo Wang (*[*Shuo.Wang@gilead.com*](mailto:Shuo.Wang@gilead.com)*) and Feiyang Niu (*[*Feiyang.Niu@gilead.com*](mailto:Feiyang.Niu@gilead.com)*) for further discussion.*