

LEM'S IMMUNOGENICITY ANALYSIS NOW – USER GUIDE

Updated 8/19/19

1. Introduction

1.1 Purpose

This document is meant to serve as a reference for all users in order to enlighten and gain an understanding of how to explore all avenues of functionality within the tool. It has been developed and deployed with the help and interests of the following groups in mind:

- *Scientific Implementation Group (SIG)*
- *Clinical Advisor Group (CAG)*
- *Clinical Laboratory Operations (CLO)*

This tool is meant to automate several data analytics processes for various vendor cumulative files, study reports, and other files that fit the standardized format for processing (point to section for data preprocessing). Logical checks are also built into the tool to flag discrepancies in data entry or identify inconsistent testing between tiered testing results.

1.2 Scope

The application includes generalized calculations for samples and subjects across all visits in each dataset. Standard summary statistics built within this tool include: number of samples tested and detected in each tier, putative positive rate, confirmed positive rate, number of evaluable subjects, baseline positive rate, treatment emergent rate, treatment-induced and treatment-boosted rates, and number of subjects who are unevaluable. Currently, the tool handles cumulative files from the following vendors: BAL, PBI, PPD, and Wuxi.

1.3 System Organization

The R programming language and Shiny package are the primary software tools used to run this application.

R version 3.6.0 (2019-04-26), nicknamed “Planting of a Tree”

Other installed packages and their purpose throughout the script:

dplyr_0.8.1 (filtering and transforming data)

DT_0.6 (provides R interface for data tables on web pages)

ggplot2_3.1.1 (creates aesthetic plots)

readxl_1.3.1 (loads tabular data from Excel spreadsheets)

reshape2_1.4.3 (implemented when creating pivot tables)

shiny_1.3.2 (builds interactive web apps with R)

shinyjs_1.0 (JavaScript-like operations to enhance user-experience)

shinythemes_1.1.2 (includes several Bootstrap themes for styling)
 shinyWidgets_0.4.8 (custom input controls and user interface components)
 xlsx_0.6.1 (provides R functions to read/write/format Excel 2007)

2. Preprocessing Data Files

2.1 Trimming files

The R Shiny app will load any dataset with columns, whether it be .csv, .txt, or .xlsx. However, the application itself is only searching for a few specific columns to conduct analyses and build calculations. Thus, it is recommended to delete unnecessary columns. This will not only reduce processing power and time to load data, but also boost user experience and allow for a much simpler interface on the page.

2.2 Modifying columns to the standardized format

R is case-sensitive when processing columns by name. In a nutshell, correct capitalization, spacing, and spelling are essential to making this Shiny app execute properly. The order of the columns is not critical to how the application performs. At a minimum, the following five columns (and their exact syntax) are required for the tool to run properly:

Subject

Visit

Tier1

Tier2

Tier3

Larger datasets with multi-tier testing can also be processed with the correct column names:

Tier2b

Tier2c

Tier2d

Tier4

Tier4b

Tier4c

Tier4d

1	Subject	Visit	Tier1	Tier2	Tier3	Tier4
2	100-00102	BL/V2	NOTDETEC			
3	100-00102	V3	NOTDETEC			
4	100-00102	V4	NOTDETEC			
5	100-00102	V6	NOTDETEC			
6	100-00102	V7	NOTDETEC			
7	100-00102	EV1	NOTDETEC			
8	100-00102	EV2	DNR	DETECTED	1:10	NOTDETEC
9	100-00102	EV3	DNR	DETECTED	1:10	NOTDETEC
10	100-00102	EV6	NOTDETEC			
11	100-00103	BL/V2	NOTDETEC			
12	100-00103	V3	NOTDETEC			

3. Running the Application

3.1 Understanding the user interface

**Users must first have access to the Shiny Server – requires Lilly username and password.*

***This application lacks some functionality in Internet Explorer – Google Chrome is highly recommended.*

Once the web page has loaded, this is the landing page (“Table” tab) that will appear.

The screenshot displays the 'Table' tab of the Immuno Analysis Now 4 application. The interface is divided into a left sidebar and a main content area. The sidebar contains several sections for dataset loading and configuration, while the main area shows tabs for 'Table', 'Flags', 'Plot', 'Summary', and 'Help'. The 'Table' tab is active, showing a 'Reorganize Visit Codes' input field. Numbered annotations (1-7) point to specific UI elements:

- 1) Points to the 'Browse...' button in the 'Load a dataset:' section.
- 2) Points to the 'Complete the fields below:' section, which includes input fields for 'Baseline Visit', 'Tier 1 'Detected'', 'Tier 1 'NOT Detected'', 'Tier 2(a) 'Detected'', and 'Tier 2(a) 'NOT Detected''.
- 3) Points to the 'If applicable, include additional columns:' section, which includes checkboxes for 'Tier 2b' and 'Tier 4(a)'.
- 4) Points to the 'Enter Minimum Required Dilution:' input field, which contains the value '10'.
- 5) Points to the 'Select a view' dropdown menu, which is set to 'Original'.
- 6) Points to the 'Download All Tables' button.
- 7) Points to the 'Reorganize Visit Codes:' input field in the main content area.

Parts of the primary interface include the following:

- 1) File input field. When clicked, the Browse button will open File Explorer.
- 2) Text input field. The user is required to complete all entry boxes with the corresponding, case-sensitive values for a loaded dataset.
- 3) Checkboxes. When selected, these will show or hide text input fields for additional tier columns.
- 4) Numeric input field. Sets the MRD for this particular dataset and is used for building many tables and summary statistics. Can be altered by the user to reactively update the tables and statistics. Default is set to 10.
- 5) Dropdown list. Shows more tables, many of which are reactively built once the “Baseline Visit” value has been entered. Others will require more user input.
- 6) Download button. Creates an export file that includes the original dataset along with all additional tables created in the app.
- 7) Selection input field for visit codes. This field loads all visit codes from the dataset, plus columns for Subject and highest titer per subject. It allows the user to rearrange the pivot tables in the best chronological order that they see fit.

3.2 First tab: “Table”

As data is being loaded into the page, the main panel will reactively display the table.

Load a dataset:

Browse...

AMAC_PBI

Upload complete

Complete the fields below:

BL/V2

DNR

NOTDETEC

DETECTED

NOTDETEC

DETECTED

NOTDETEC

If applicable, include additional columns:

☐ Tier 2b
 ☒ Tier 4(a)
 ☐ Tier 4b

Enter Minimum Required Dilution:

10

MRD set at 1:10

Select a view

Original

Download All Tables

Table

Flags

Plot

Summary

Help

Reorganize Visit Codes:

Show

10

 entries Search:

Subject	Visit	Tier1	Tier2	Tier3	Tier4
100-00102	Baseline	NOTDETEC		0	
100-00102	V3	NOTDETEC		0	
100-00102	V4	NOTDETEC		0	
100-00102	V6	NOTDETEC		0	
100-00102	V7	NOTDETEC		0	
100-00102	EV1	NOTDETEC		0	
100-00102	EV2	DNR	DETECTED	10	NOTDETEC
100-00102	EV3	DNR	DETECTED	10	NOTDETEC
100-00102	EV6	NOTDETEC		0	
100-00103	Baseline	NOTDETEC		0	

Showing 1 to 10 of 3,404 entries

Previous

1

2

3

4

5

...

341

Next

When the table is loaded on the page, the user should begin completing the text fields on the side panel. These include values for baseline visit, and detected and not detected values for Tier 1 and Tier 2. In the example above, the dataset contains an additional column for Tier 4. The corresponding checkbox for that tier is selected, revealing additional text fields for detected and not detected values in Tier 4.

Text fields are case-sensitive – capitalization, spacing, and spelling must match the values in the table. Copy and pasting values from the table to the text fields works fine, but double check for unnecessary white spaces in the text input field.